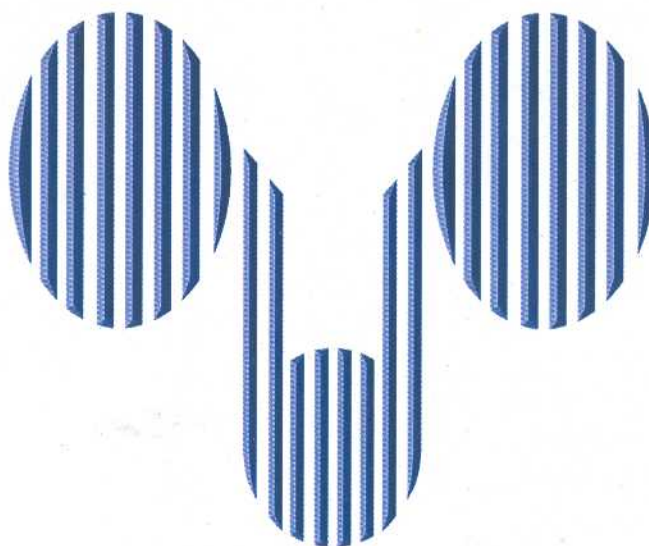


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BRAZILIAN JOURNAL OF UROLOGY

EDITORIAL

This is the first issue of the Brazilian Journal of Urology in the new millenium. The Braz. J. Urol. has been improving tremendously during the last 2 years. The circulation increased from 1,800 to 6,000 copies per issue. Also, the number of articles per issue has grown from 11 to 28. Starting with this issue, 26 (1) 2000, the Braz. J. Urol. will be a bimonthly journal, i.e., the journal will increase from 4 to 6 issues per year. The journal has been definitely internationalized and is by now the most important urological journal in Latin America. Also, we have many readers in Portugal, Spain and United States. We are receiving contributions from many countries and from many prestigious urological services. The Braz. J. Urol. is a peer-reviewed journal and each paper is blind reviewed by at least 2 consultants; nevertheless, 3 consultants review the majority of papers. Also, the Braz. J. Urol. publishes Review, State of the Art, Surgical Technique and Special Articles written by internationally recognized experts.

In this issue, among many excellent regular peer reviewed articles, we have a great pleasure of presenting to our readers 5 articles on **Endourological Techniques**, written by world experts. The first paper is a State of the Art Article on treatment of complex renal stones by "sandwich therapy" authored by Dr. Stevan Strem from Cleveland Clinic, who is a pioneer and have more than 15 years of experience with this technique. The other 4 articles comprise a thorough discussion on indications and techniques for managing the Ureteropelvic Junction Obstruction (UPJO) with contributions from the most important world recognized experts in the field. Dr. Van Cangh, from Catholic University of Louvain Medical School, a pioneer on drawing attention for the importance of selection criteria and prognostic factors of endopyelotomy, presents for us the current indications of the procedure. Dr. Segura, from Mayo Clinic, one of the most prestigious world leaders and a pioneer in endourology, presents important technical details of Percutaneous Endopyelotomy, in addition to discussing the clinical presentation and evaluation of patients with UPJO. Dr. Preminger, from Duke University, who was together with Dr. Clayman from Washington University, a world pioneer and promoter of the minimally invasive technique of Acucise cutting balloon, presents in this issue the main points of this procedure, bringing to our readers important details of his vast personal experience. Dr. Thomas Jarret, from Johns Hopkins University, one of the pioneers and most experienced authorities in the advanced technique of Laparoscopic Pyeloplasty, describes the indications, results and techniques of Anderson-Hynes, Foley Y-V plasty and Heineke-Mikulicz laparoscopic repair of UPJO.

Also, ours readers have the great privilege to find 3 superb Editorial Comments on these articles, which give balance and important critical analysis on the techniques described here. The Editorial Comments were made by our Consulting Editors, who also are world recognized experts on UPJO treatment: Dr. Arthur Smith, from Albert Einstein College of Medicine - Long Island, well known expert and world promoter of endourology, introduced the technique and coined the term "endopyelotomy" in the USA; Dr. Stevan Strem, head of endourology at Cleveland Clinic, is a very recognized expert on various endopyelotomy techniques, was the editor of a recent book on UPJO and gives us an important balance on the techniques; Dr. William Bush, from University of Washington, is one of the most important interventional radiologists of the urinary tract, was one of the recognized pioneers on endopyelotomy in the USA and gives us an important understanding from the radiologist standpoint.

Francisco J.B. Sampaio
Editor-in-Chief

BRAZILIAN JOURNAL OF UROLOGY

EDITORIAL

Este é o primeiro número do Brazilian Journal of Urology publicado no novo milênio. O Braz. J. Urol. tem crescido muito nos últimos 2 anos. A tiragem aumentou de 1.800 para 6.000 cópias por número e a quantidade de artigos também cresceu de 11 para 28 por número. Começando com este número: 26 (1): 2000, o Braz. J. Urol. passa a ser bimensal, publicando agora 6 números por ano. A revista foi definitivamente internacionalizada, e no momento é a revista de urologia mais importante da América Latina. Além disso, a revista é lida por muitos urologistas de Portugal, Espanha e Estados Unidos da América. A revista tem recebido artigos de muitos países e de muitos serviços de urologia de prestígio. O Braz. J. Urol. é uma revista que publica trabalhos que passam por revisão editorial, sendo que cada artigo é revisado de forma anônima por pelo menos 2 consultores, entretanto, a maioria dos artigos passa por revisão de 3 consultores. Além disso, o Braz. J. Urol. publica Artigos de Revisão, de Atualização, de Técnica Cirúrgica e Artigos Especiais, escritos por experts reconhecidos internacionalmente.

Neste número, entre vários excelentes artigos regulares, nós temos o grande prazer de apresentar aos nossos leitores 5 artigos sobre **Técnicas em Endourologia**, escritos por experts mundialmente reconhecidos na área. O primeiro artigo é um "State of the Art Article" sobre o tratamento de cálculos renais complexos por "terapia sandwich" escrito pelo Dr. Stevan Strem da Cleveland Clinic, que é pioneiro e possui mais de 15 anos de experiência com esta técnica. Os outros 4 artigos compõem uma discussão completa sobre as indicações e as técnicas de tratamento para a obstrução da Junção Uretero-Piélica (JUP), com contribuições dos mais importantes experts internacionais no assunto. O Dr. Paul Van Cangh, da Catholic University of Louvain Medical School, Bélgica, foi o pioneiro em chamar a atenção para a importância dos critérios de seleção e dos fatores prognósticos para o tratamento da obstrução da JUP, e apresenta neste número as indicações atuais da endopielotomia. O Dr. Joseph Segura, da Mayo Clinic, um dos mais prestigiados e dos mais importantes endourologistas do mundo, apresenta detalhes importantes da Endopielotomia Percutânea, além de discutir a apresentação clínica e a avaliação dos pacientes com obstrução da JUP. O Dr. Glenn Preminger, da Duke University, que foi junto com o Dr. Ralph Clayman da Washington University, o pioneiro mundial e o divulgador da técnica minimamente invasiva do balão Acucise, apresenta neste número as principais etapas do procedimento, trazendo para os nossos leitores detalhes importantes de sua vasta experiência pessoal. O Dr. Thomas Jarret, da Johns Hopkins University, que é um dos pioneiros e um dos mais experientes urologistas na técnica avançada de Pieloplastia Laparoscópica, descreve as indicações, os resultados e as técnicas de Anderson-Hynes, plástica em Y-V de Foley e de Heineke-Mikulicz para o tratamento da obstrução da JUP por via laparoscópica.

Além disso, os nossos leitores têm o grande privilégio de encontrar 3 excelentes Comentários Editoriais sobre estes artigos, que fornecem equilíbrio e importante análise crítica sobre as técnicas descritas neste número. Os Comentários Editoriais foram apresentados por nossos Consultores Internacionais, que também são especialistas de renome mundial no tratamento da obstrução da JUP: o Dr. Arthur Smith, do Albert Einstein College of Medicine - Long Island, é muito conhecido em endourologia, introduziu nos EUA a técnica e o foi o idealizador do termo endopielotomia; o Dr. Stevan Strem, chefe do setor de endourologia da Cleveland Clinic, é um especialista muito conhecido nas várias técnicas de endopielotomia, foi editor de um livro recente sobre obstrução da JUP e nos fornece um equilíbrio importante sobre as várias técnicas; o Dr. William Bush, da University of Washington - Seattle, é um dos mais importantes radiologistas intervencionistas do tracto urinário, foi um dos pioneiros em endopielotomia nos EUA e nos brinda com comentários muito importantes sob a óptica do radiologista.

Francisco J.B. Sampaio
Editor-Chefe

BRAZILIAN JOURNAL OF UROLOGY

EDITORIAL

In response to the concerns of the editors of scientific medical journals with ethics, quality and seriousness of published articles, a Committee on Publication Ethics (COPE) was established in 1997 and now a guideline document was published. This document was approved and is followed by important urological journals, including The Journal of Urology, BJU International, Urological Research, European Urology and World Journal of Urology.

The Brazilian Journal of Urology also approves and follows these guidelines and ask our readers to inform the editors if they know of any issue of conduct that are not in conformity with these guidelines.

Francisco J.B. Sampaio
Editor-in-Chief

BRAZILIAN JOURNAL OF UROLOGY

EDITORIAL

Os editores de revistas científicas médicas têm grande preocupação com a ética, qualidade e seriedade dos artigos que são disseminados em suas revistas. Como resposta a estas preocupações, o Comitê de Ética em Publicações (COPE) iniciou suas atividades em 1997, e no momento um documento com as diretrizes do Comitê foi produzido e está sendo divulgado por diversas revistas médicas. Este documento foi aprovado e divulgado por importantes revistas da área urológica, como o Journal of Urology, BJU International, Urological Research, European Urology and World Journal of Urology.

O Brazilian Journal of Urology também aprova e segue este documento. Se algum leitor tiver conhecimento de conduta que não está de acordo com a boa prática científico-médica estabelecida neste documento, deve informar aos editores do Brazilian Journal of Urology, que após cuidadosa investigação, poderão impor sanções editoriais aos transgressores.

Francisco J.B. Sampaio
Editor-Chefe

COMMITTEE ON PUBLICATION ETHICS (COPE): GUIDELINES ON GOOD PUBLICATION PRACTICE

Why the guidelines were developed

Cope was founded in 1997 to address breaches of research and publication ethics. A voluntary body providing a discussion forum and advice for scientific editors, it aims to find practical ways of dealing with the issues, and to develop good practice.

We thought it essential to attempt to define best practice in the ethics of scientific publishing. These guidelines should be useful for authors, editors, editorial board members, readers, owners of journals, and publishers.

Intellectual honesty should be actively encouraged in all medical and scientific courses of study, and used to inform publication ethics and prevent misconduct. It is with that in mind that these guidelines have been produced.

Details of other guidelines on the ethics of research and published codes of conduct are listed in the Appendix.

How the guidelines were developed

The guidelines were developed from a preliminary version drafted by individual members of the committee, which was then submitted to extensive consultation. They address: study design and ethical approval, data analysis, authorship, conflict of interests, the peer review process, redundant publication, plagiarism, duties of editors, media relations, advertising, and how to deal with misconduct.

What they aim to do

These guidelines are intended to be advisory rather than prescriptive, and to evolve over time. We hope that they will be disseminated widely, endorsed by editors, and refined by those who use them.

I - STUDY DESIGN AND ETHICAL APPROVAL

Definition

Good research should be well justified, well planned, appropriately designed, and ethically approved. To conduct research to a lower standard may constitute misconduct.

Action

1. Laboratory and clinical research should be driven by protocol; pilot studies should have a written rationale.
2. Research protocols should seek to answer specific questions, rather than just collect data.
3. Protocols must be carefully agreed by all contributors and collaborators, including, if appropriate, the participants.
4. The final protocol should form part of the research record.
5. Early agreement on the precise roles of the contributors and collaborators, and on matters of authorship and publication, is advised.
6. Statistical issues should be considered early in study design, including power calculations, to ensure there are neither too few nor too many participants.
7. Formal and documented ethical approval from an appropriately constituted research ethics committee is required for all studies involving people, medical records, and anonymised human tissues.
8. Use of human tissues in research should conform to the highest ethical standards, such as those recommended by the Nuffield Council on Bioethics.
9. Fully informed consent should always be sought. It may not always be possible, however, and in such circumstances, an appropriately constituted research ethics committee should decide if this is ethically acceptable.

-
10. When participants are unable to give fully informed consent, research should follow international guidelines, such as those of the Council for International Organizations of Medical Sciences (CIOMS).
 11. Animal experiments require full compliance with local, national, ethical, and regulatory principles, and local licensing arrangements. International standards vary.
 12. Formal supervision, usually the responsibility of the principal investigator, should be provided for all research projects: this must include quality control, and the frequent review and long term retention (may be up to 15 years) of all records and primary outputs.

II - DATA ANALYSIS

Definition

Data should be appropriately analyzed, but inappropriate analysis does not necessarily amount to misconduct. Fabrication and falsification of data do constitute misconduct.

Action

1. All sources and methods used to obtain and analyze data, including any electronic pre-processing, should be fully disclosed; detailed explanations should be provided for any exclusions.
2. Methods of analysis must be explained in detail, and referenced, if they are not in common use.
3. The post hoc analysis of subgroups is acceptable, as long as this is disclosed. Failure to disclose that the analysis was post hoc is unacceptable.
4. The discussion section of a paper should mention any issues of bias, which have been considered, and explain how they have been dealt with in the design and interpretation of the study.

III - AUTHORSHIP

Definition

There is no universally agreed definition of authorship, although attempts have been made (see Appendix). As a minimum, authors should take responsibility for a particular section of the study.

Action

1. The award of authorship should balance intellectual contributions to the conception, design, analysis and writing of the study against the collection of data and other routine work. If there is no task that can reasonably be attributed to a particular individual, then that individual should not be credited with authorship.
2. To avoid disputes over attribution of academic credit, it is helpful to decide early on in the planning of a research project who will be credited as authors, as contributors, and who will be acknowledged.
3. All authors must take public responsibility for the content of their paper. The multidisciplinary nature of much research can make this difficult, but this can be resolved by the disclosure of individual contributions.
4. Careful reading of the target journal's "Advice to Authors" is advised, in the light of current uncertainties.

IV - CONFLICTS OF INTEREST

Definition

Conflicts of interest comprise those which may not be fully apparent and which may influence the judgement of author, reviewers, and editors.

They have been described as those which, when revealed later, would make a reasonable reader feel misled or deceived.

They may be personal, commercial, political, academic or financial.

'Financial' interests may include employment, research funding, stock or share ownership, payment for lectures or travel, consultancies and company support for staff.

Action

1. Such interests, where relevant, must be declared to editors by researchers, authors, and reviewers.
2. Editors should also disclose relevant conflicts of interest to their readers. If in doubt, disclose. Sometimes editors may need to withdraw from the review and selection process for the relevant submission.

V - PEER REVIEW

Definition

Peer reviewers are external experts chosen by editors to provide written opinions, with the aim of improving the study.

Working methods vary from journal to journal, but some use open procedures in which the name of the reviewer is disclosed, together with the full or 'edited' report.

Action

1. Suggestions from authors as to who might act as reviewers are often useful, but there should be no obligations on editors to use those suggested.
2. The duty of confidentiality in the assessment of a manuscript must be maintained by expert reviewers, and this extends to reviewers' colleagues who may be asked (with the editor's permission) to give opinions on specific sections.
3. The submitted manuscript should not be retained or copied.
4. Reviewers and editors should not make any use of the data, arguments, or interpretations, unless they have the authors' permission.
5. Reviewers should provide speedy, accurate, courteous, unbiased and justifiable reports.
6. If reviewers suspect misconduct, they should write in confidence to the editor.
7. Journals should publish accurate descriptions of their peer review, selection, and appeals processes.
8. Journals should also provide regular audits of their acceptance rates and publication times.

VI - REDUNDANT PUBLICATION

Definition

Redundant publication occurs when two or more papers, without full cross reference, share the same hypothesis, data, discussion points, or conclusions.

Action

1. Published studies do not need to be repeated unless further confirmation is required.

2. Previous publications of an abstract during the proceedings of meetings does not preclude subsequent submission for publication, but full disclosure should be made at the time of submission.
3. Re-publication of a paper in another language is acceptable, provided that there is full and prominent disclosure of its original source at the time of submission.
4. At the time of submission, authors should disclose details of related papers, even if in a different language, and similar papers in press.

VII - PLAGIARISM

Definition

Plagiarism ranges from the unreferenced use of others' published and unpublished ideas, including research grant applications to submission under "new" authorship of a complete paper, sometimes in a different language.

It may occur at any stage of planning, research, writing, or publication; it applies to print and electronic versions.

Action

1. All sources should be disclosed, and if large amounts of other people's written or illustrative material is to be used, permission must be sought.

VIII - DUTIES OF EDITORS

Definition

Editors are the stewards of journals. They usually take over their journal from the previous editor(s) and always want to hand over the journal in good shape.

Most editors provide direction for the journal and build a strong management team.

They must consider and balance the interests of many constituents, including readers, authors, staff, owners, editorial board members, advertisers and the media.

Action

1. Editors' decisions to accept or reject a paper for publication should be based only on the paper's

-
- importance, originality, and clarity, and the study's relevance to the remit of the journal.
2. Studies that challenge previous work published in the journal should be given an especially sympathetic hearing.
 3. Studies reporting negative results should not be excluded.
 4. All original studies should be peer reviewed before publication, taking into full account possible bias due to related or conflicting interests.
 5. Editors must treat all submitted papers as confidential.
 6. When a published paper is subsequently found to contain major flaws, editors must accept responsibility for correcting the record prominently and promptly.

IX - MEDIA RELATIONS

Definition

Medical research findings are of increasing interest to the print and broadcast media.

Journalists may attend scientific meetings, at which preliminary research findings are presented, leading to their premature publication in the mass media.

Action

1. Authors approached by the media should give as balanced an account of their work as possible, ensuring that they point out where evidence ends and speculations begins.
2. Simultaneous publication in the mass media and a peer reviewed journal is advised, as this usually means that enough evidence and data have been provided to satisfy informed and critical readers.
3. Where this is not possible, authors should help journalists to produce accurate reports, but refrain from supplying additional data.
4. All efforts should be made to ensure that patients who have helped with the research should be informed of the results by the authors before the mass media, especially if there are clinical implications.
5. Authors should be advised by the organizers if journalists are to attend scientific meetings.

6. It may be helpful to authors to be advised of any media policies operated by the journal in which their work is to be published.

X - ADVERTISING

Definition

Many scientific journals and meetings derive significant income from advertising.

Reprints may also be lucrative.

Action

1. Editorial decisions must not be influenced by advertising revenue or reprint potential: editorial and advertising administration must be clearly separated.
2. Advertisements that mislead must be refused, and editors must be willing to publish criticisms, according to the same criteria used for material in the rest of the journal.
3. Reprints should be published as they appear in the journal unless a correction is to be added.

Dealing with misconduct

1 Principles

1. The general principle confirming misconduct is intention to cause others to regard as true that which is not true.
2. The examination of misconduct must therefore focus, not only on the particular act or omission, but also on the intention of the researcher, author, editor, reviewer or publisher involved.
3. Deception may be by intention, by reckless disregard of possible consequences, or by negligence. It is implicit, therefore, that 'best practice' requires complete honesty, with full disclosure.
4. Codes of practice may raise awareness, but can never be exhaustive.

2 Investigating misconduct

1. Editors should not simply reject papers that raise questions of misconduct. They are ethically obliged to pursue the case. However, knowing how to investigate and respond to possible cases of misconduct is difficult.

-
2. COPE is always willing to advise, but for legal reasons, can only advise on anonymised cases.
 3. It is for the editor to decide what action to take.

3 *Serious misconduct*

1. Editors must take all allegations and suspicions of misconduct seriously, but they must recognize that they do not usually have either the legal legitimacy or the means to conduct investigations to serious cases.
2. The editor must decide when to alert the employers of the accused author(s).
3. Some evidence is required, but if employers have a process for investigating accusations - as they are increasingly required to do - then editors do not need to assemble a complete case. Indeed, it may be ethically unsound for editors to do so, because such action usually means consulting experts, so spreading abroad serious questions about the author(s).
4. If editors are presented with convincing evidence perhaps by reviewers - of serious misconduct, they should immediately pass this on to the employers, notifying the author(s) that they are doing so.
5. If accusations of serious misconduct are not accompanied by convincing evidence, then editors should confidentially seek expert advice.
6. If the experts raise serious questions about the research, then editors should notify the employers.
7. If the experts find no evidence of misconduct, the editorial processes should proceed in the normal way.
8. If presented with convincing evidence of serious misconduct, where there is no employer to whom this can be referred, and the author(s) are registered doctors, cases can be referred to the General Medical Council.
9. If, however, there is no organization with the legitimacy and the means to conduct an investigation, then the editor may decide that the case is sufficiently important to warrant publishing something in the journal. Legal advice will then be essential.
10. If editors are convinced that an employer has not conducted an adequate investigation of a serious accusation, they may feel that publica-

tion of a notice in the journal is warranted. Legal advice will be essential.

11. Authors should be given the opportunity to respond to accusations of serious misconduct.

4 *Less serious misconduct*

1. Editors may judge that it is not necessary to involve employers in less serious cases of misconduct, such as redundant publication, deception over authorship, or failure to declare conflict of interest. Sometimes the evidence may speak for itself, although it may be wise to appoint an independent expert.
2. Editors should remember that accusations of even minor misconduct may have serious implications for the author(s), and it may then be necessary to ask the employers to investigate.
3. Authors should be given the opportunity to respond to any charge of minor misconduct.
4. If convinced of wrongdoing, editors may wish to adopt some of the sanctions outlined below.

5 *Sanctions*

1. Sanctions may be applied separately or combined. The following are ranked in approximate order of severity:
 2. A letter of explanation (and education) to the authors, where there appears to be a genuine misunderstanding of principles.
 3. A letter of reprimand and warning as to future conduct.
 4. A formal letter to the relevant head of institution or funding body.
 5. Publication of a notice of redundant publication or plagiarism.
 6. An editorial giving full details of the misconduct.
 7. Refusal to accept future submissions from the individual, unit, or institution responsible for the misconduct, for a stated period.
 8. Formal withdrawal or retraction of the paper from the scientific literature, informing other editors and the indexing authorities.
 9. Reporting the case to the General Medical Council, or other such authority or organization which can investigate and act with due process.
-

Appendix

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“SANDWICH” THERAPY FOR THE TREATMENT OF COMPLEX RENAL STONES

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ABSTRACT

Purpose: Shock wave lithotripsy (SWL) and percutaneous nephrolithotomy (PCNL) are well accepted, minimally invasive modalities available for the treatment of calculi. In this paper we review and discuss the technique of combination “sandwich therapy” for the treatment of select patients with large, extensively branched, or otherwise complex stones.

Materials and Methods: A review of the literature on combined percutaneous nephrolithotomy and shock wave lithotripsy for the management of “staghorn” calculi was performed and evaluated.

Results: Stone free rates after one month of follow up approach 70%, while the remaining patients are left with residual dust or gravel. Complications occur in less than 30% of patients, and no nephrectomies or mortality have been reported with this approach. The probability of new stone formation has been estimated to be 37% at five years, and renal function has been shown to remain stable or improve in 96% of patients.

Conclusion: The use of combination therapy for the treatment staghorn calculi is safe and effective and can limit much of the associated morbidity of SWL or PCNL monotherapy. We recommend this combined “sandwich” approach as the treatment of choice for select patients with large, extensively branched, or otherwise complex staghorn calculi.

Key words: kidney, calculi, shock wave lithotripsy, percutaneous nephrostolithotomy
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INTRODUCTION

“Sandwich therapy” provides a minimally invasive alternative endourologic approach for the management of large, extensively branched or otherwise complex calculi for patients with stones that might otherwise require operative intervention, or who would not likely benefit from percutaneous nephrolithotomy (PCNL) or shock wave lithotripsy (SWL) alone (1). In these patients, sandwich therapy minimizes the risk of bleeding and sepsis associated with PCNL monotherapy, and decreases the number of shock waves otherwise required for SWL alone. Furthermore, prolonged nephrostomy drainage, which had been a part of earlier approaches, can be avoided when utilizing this combined management.

Sandwich therapy involves the use of primary percutaneous debulking followed by SWL of residual

“inaccessible” infundibulocalyceal stone extensions or fragments. Following SWL, a secondary percutaneous procedure is done through the mature tract to hasten clearance of fragments from SWL. Additional percutaneous or SWL treatments can be utilized as necessary to achieve a stone free state within a reasonable time period.

Use of this approach limits the number of punctures needed to manage large stones to one or two tracts. Limiting the number of access tracts can help avoid the bleeding complications that can be associated with the multiple percutaneous tracts that would be required for percutaneous monotherapy. Furthermore, the use of upper pole access is often not required, therefore avoiding the increased risk of pleural complications.

Utilizing percutaneous debulking prior to SWL also allows for a significantly reduced number

of shock waves required compared to SWL monotherapy, and this reduces the potential toxicity of a large number of shock waves. Finally, having a large caliber nephrostomy tube indwelling at the time of SWL decreases the risk of sepsis by providing proximal diversion, especially in patients with infection-related (struvite) calculi.

This combination therapeutic approach has been proven to be safe and effective. It has also been demonstrated that immediate and long term results are at least comparable to other forms of management in this setting, specifically with respect to rates of recurrent stones, infection, and maintenance of renal function (2-4).

PATIENT SELECTION

Even patients with very large, extensively branched calculi can be managed with this protocol. Currently, open operative intervention is reserved only for patients in whom percutaneous techniques and SWL have failed or are contraindicated or for patients with associated anatomic abnormalities requiring open operative reconstruction. Occasionally, anatomic nephrolithotomy is utilized for a stone burden so large and complex that open operative intervention more likely will render the patient stone free in a safer manner than would the multiple percutaneous procedures and SWL that would be otherwise be required.

In 1994 the AUA Nephrolithiasis Guidelines Panel on staghorn stones recommended percutaneous stone removal as the primary treatment modality, followed by shock wave lithotripsy and/or repeat percutaneous procedures as warranted. SWL monotherapy and percutaneous monotherapy were recommended as effective treatment choices only for small volume struvite staghorn calculi in collecting systems that were anatomically normal or nearly so (5).

POTENTIAL RISKS

The potential risks are explained to the patient including the unlikely but potential need for emergent open operative intervention, and the need

for secondary or even tertiary endourologic procedures that may be required to achieve a stone free result. Bleeding requiring transfusion has been reported in up to 14 % of patients, which compares favorably to percutaneous monotherapy for staghorn calculi with a reported transfusion rate of up to 53% (4,6), but this risk is also explained.

Fever and/or sepsis has been reported in 20% of patients undergoing sandwich therapy, and up to 27% being treated with percutaneous monotherapy (4,6). Many patients undergoing sandwich therapy have magnesium-ammonium-calcium phosphate stones associated with chronic bacterial infection. For these patients, sensitivity-specific oral antibiotic therapy is administered for at least 1 to 2 weeks prior to intervention, and broad-spectrum antibiotic therapy is given intravenously just prior to instrumentation.

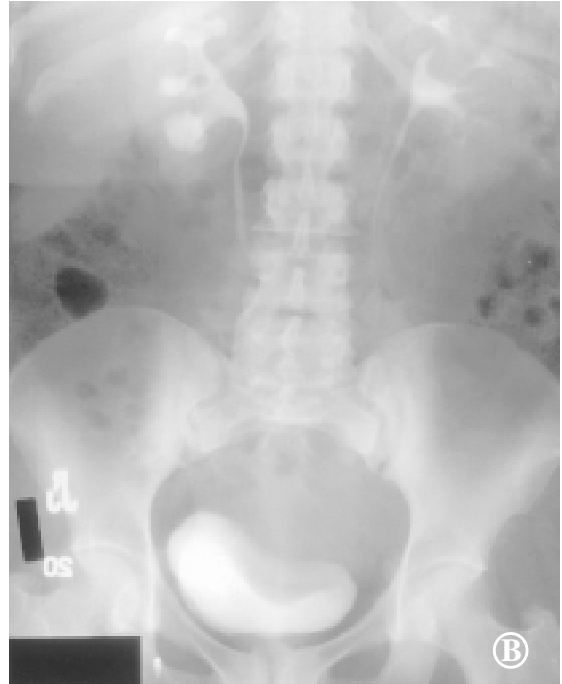
TECHNIQUE

The technique is illustrated in the Figures. The site for the initial percutaneous puncture is chosen with the intention of providing access to the greatest stone burden. This usually allows for removal of the lower infundibulocalyceal and renal pelvic portions of the stone (Figures-1 and 2). Rarely, two or more tracts may be required to access particularly heavily involved collecting systems, especially those that are somewhat bifid. General anesthesia is used routinely. A Foley catheter is placed at the beginning of the procedure, and the patient is then positioned prone. Care is taken to ensure proper padding of the face, legs and arms, and two chest rolls are placed longitudinally under the chest.

Stone debulking then proceeds as a standard percutaneous nephrolithotomy. This initial percutaneous debulking is performed using a rigid 24.5 or 26F nephroscope and an ultrasonic lithotrite. For some especially hard non-struvite stones, electrohydraulic or Holmium laser lithotripsy is utilized as an adjunct. At this point, no attempt is made to reach calyceal extensions of the calculus that are located at acute angle to the existing tract and are therefore inaccessible to the rigid nephroscope. After extracting the entire accessible stone burden with this initial percutaneous debulking, a 24F nephrostomy tube



Figure 1 – A) Plain film reveals completely branched “staghorn” calculus involving the right kidney. B) Intravenous pyelogram. Note relatively high location of the right kidney. Percutaneous monotherapy would require two or more tracts, including access via an upper pole infundibulocalix. However, upper pole access would require supra 11th rib puncture, placing the patient at significant risk for hydro, pneumo, or hemothorax.



is left indwelling to gravity. The Foley catheter is removed within the next 12-24 hours, and ambulation is begun.

A nephrostogram, which includes oblique views before and after contrast is administered, is obtained 48 hours after the initial procedure. The nephrostogram is used to evaluate the extent and location of residual stones, and also to assess for urinary extravasation, as this would result in postponement of the subsequent SWL.

If the urine is relatively clear and there is no evidence of extravasation on the nephrostogram, SWL is performed for the “inaccessible” stones the following day. One to 2 days following the SWL, the previously “inaccessible” stones have migrated to an accessible location in the renal pelvis or lower calyces (Figure-3), and secondary rigid and/or flexible nephroscopy is then performed via the mature tract or tracts. If the entire stone burden has been cleared, the nephrostomy tube can be removed with the next 12-24 hours. However, for those patients with persistent calculi, additional treatment including secondary SWL or tertiary percutaneous extraction may be required.

One month following the final interventional procedure, a plain radiograph and renal ultrasound



Figure 2 – Access via an involved lower lateral infundibulum allows “debulking” of the pelvic and lower infundibulocalyceal portions of the stone (inverted image).

THERAPY FOR COMPLEX RENAL STONES

or alternatively an intravenous pyelogram is obtained (Figure-4). For those patients with infection related stones, chronic antibiotic prophylaxis is prescribed

for the first 6-12 months of follow up. A metabolic evaluation can be completed at this time, and any associated problems also addressed.

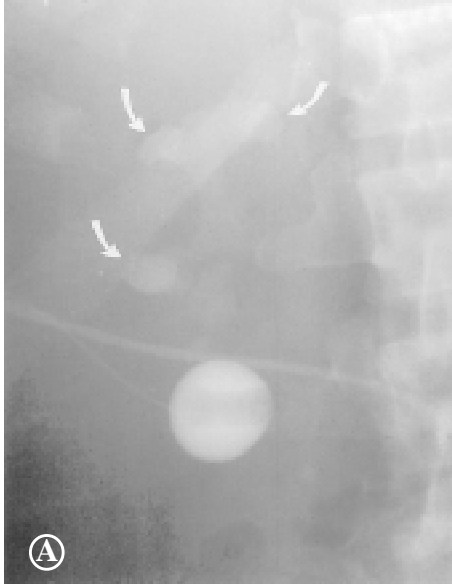


Figure 3 – A) “Inaccessible” mid and upper pole stone extensions remain and will be treated with shock wave lithotripsy 48-72 hours later.

B) Within 24 hours of shock wave lithotripsy, the post SWL fragments from the previously “inaccessible” stone extensions have migrated toward the renal pelvis. These residual fragments are now easily accessible with secondary rigid and/or flexible nephroscopy performed via the original access tract, which has now matured.

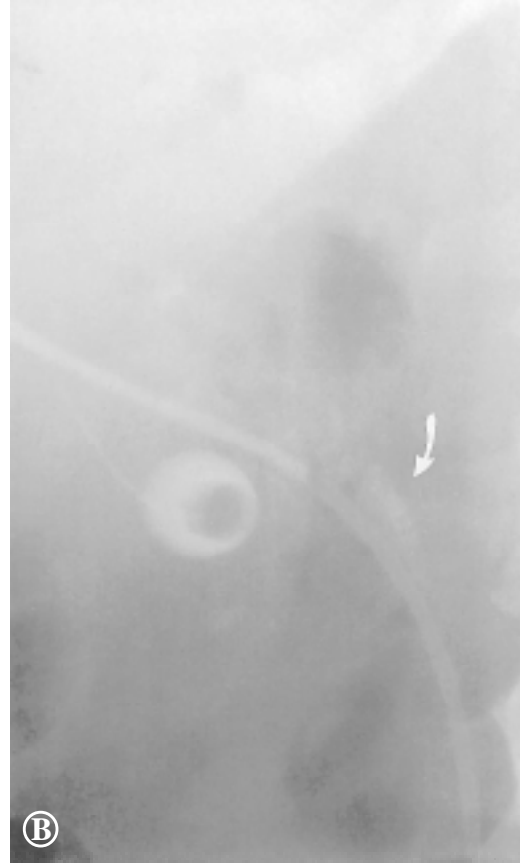


Figure 4 – A) Follow-up scout film reveals a stone free system.
B) Post “sandwich” therapy intravenous pyelogram confirms an excellent anatomic and physiology result.

RESULTS

We recently reviewed our results with 100 patients who underwent sandwich therapy for renal calculi. Magnesium-ammonium-calcium phosphate was the major component of the stone in 40.2% of patients. Calcium oxalate/phosphate was the major component in 37.1%, and uric acid combined with calcium oxalate/phosphate was the major component in 10.3%. Approximately 12% were primarily uric acid, cystine, or ammonium acid urate. The mean number of percutaneous procedures was just over 1.06 per patient, and fewer than 10% of patients required multiple access tracts, despite a mean stone burden of 20.8 cm². The mean number of shock waves to the involved renal unit was 3,100, divided over a mean 1.4 SWL treatments/patient (4).

Significant complications, which included bleeding requiring transfusion or fever delaying any planned treatment or hospital discharge, affected less than 30% of patients. No patients required a nephrectomy and there was no mortality. Early in our experience the average hospital stay approached 15 days. Over the past 10 years, the total length of hospitalization has decreased significantly and now averages less than 6 days. The stone free rate has also improved with experience. Of the first 25 patients in our series, 52% were stone free at one month follow up, while in comparison, 70% of the last 25 patients were rendered completely stone free, while the remainder had only residual calyceal dust or gravel.

There was a significantly higher rate of transfusion (20.5%) and fever or sepsis (33.3%) in patients with struvite stones. Of those patients with non-infection related stones, the rates of transfusion or fever/sepsis were significantly less at 10.3% and 12.1% respectively (4).

The long-term results of this sandwich approach have been evaluated, specifically for patients with infection related stones (3). With a mean follow up of 31 months, and as long as 5 years, the rate of new stone formation or stone growth has been 22%, while recurrent infection has developed in 30% of patients. In a more recent study using Kaplan-Meier estimates, the risk of new stone formation was estimated to be 36.8% over 5 years following combina-

tion therapy (7). Risk factors for recurrence have been evaluated and demonstrate that rates of recurrent stones are equivalent between patients undergoing percutaneous nephrolithotomy alone or percutaneous nephrolithotomy and SWL combined in a sandwich protocol. Finally, renal function has been shown to remain stable or improve in 96% of patients undergoing combination therapy (3), and this approach has also been shown to maintain or improve renal function even in patients with a solitary kidney (2).

CONCLUSIONS

The need for early and aggressive intervention for the treatment of staghorn calculi has been accepted practice for over 25 years (8). The goals of treatment of patients with complex stone disease include achieving a stone free renal unit, prevention of recurrent stones and infection, and preservation of renal function. Traditionally, the best therapeutic option for the treatment of staghorn calculi had been open operative intervention, as "medical" management of these complex stones has been shown to have a much higher renal related morbidity and mortality than operative stone extirpation (9,10).

Though some smaller staghorn calculi may be treated successfully with SWL or PCNL alone, there is a relatively high incidence of complications associated with either one of these treatment modalities as monotherapy for extensively branched or otherwise complex stones, and there are now several studies that have demonstrated that patients with this problem will benefit from a combined approach (4,11-13). For the most difficult patients, the immediate and long term results have been shown to be at least comparable to any other form of management currently available, and for almost 15 years, we have found this approach applicable to virtually any patient with large, extensively branched or otherwise complex renal calculi.

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EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY FOR CALCULI IN HORSESHOE KIDNEY

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ABSTRACT

Objectives: The goal of this study was to determine the efficacy of lithotripsy in the treatment of lithiasis in horseshoe kidneys.

Material and Methods: From 1984 to 1996, 10 renal units (8 patients) with stones in horseshoe kidney were admitted in our hospital and submitted to monotherapy with extracorporeal shock wave lithotripsy (SWL) in a Dornier Philips MFL 5000. The group consisted of 7 men and 1 woman, 20 to 84 years old (mean age = 51 years). Two patients had bilateral lithiasis and 2 renal units had staghorn calculi. The treatment results were evaluated by comparing the stone burden pre and post SWL according to a previous described formula: stone burden = (diameter of the greatest stone + diameter of the smallest stone) X number of stones / 2. The mean stone burden was 21mm³ and the mean sessions per patient were 5.

Results: Reduction of stone burden was observed in 4 of 10 renal units and complications (ureteral fragments) were observed in four patients. Of the 6 patients that did not improve with the treatment, all presented impaired collecting system peristalsis diagnosed by intravenous urography. Of the 4 patients that presented treatment complications, 2 had positive urine culture.

Conclusion: Treatment of calculi in horseshoe kidney with extracorporeal shock wave lithotripsy monotherapy had poor results, especially when associated with impaired collecting system peristalsis.

Key words: kidney, lithiasis, horseshoe kidney, extracorporeal shock wave lithotripsy, treatment, monotherapy
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INTRODUÇÃO

Rim em ferradura é a anomalia de fusão renal mais comum (1) com uma incidência de 0,25% na população (2). Dados epidemiológicos sugerem uma maior incidência no sexo masculino com proporção de 2:1 e um alto índice de associação com outras malformações (3-6).

A dilatação do trato urinário é mais frequente em pacientes com rim em ferradura, estando presente em 15 a 35% dos casos (7,8). A causa provável é a implantação alta dos ureteres e seu curso anômalo, anteriorizado e passando por sobre o istmo renal. Existe ainda nestes pacientes uma possibilidade maior de cruzamentos vasculares anômalos, uma vez que a irrigação destes rins é frequentemente feita por múltiplas artérias com grande variedade de percurso

(4). Infecções do trato urinário também são mais frequentes em pacientes com rim em ferradura. Estima-se que 25 a 41% destes pacientes irão apresentar episódios de infecção de trato urinário em alguma fase de sua vida (4,7,9).

A litíase também parece ser mais comum em pacientes portadores desta variação anatômica, sendo descrita uma frequência que varia de 21 a 60% dos casos (4,9,10). Alguns autores, como Evans & Resnick (4), encontraram até 75% de alterações metabólicas em pacientes portadores de rim em ferradura, enquanto outros autores como Koff et al. (11) encontraram taxas semelhantes àquelas dos pacientes portadores de rins sem anomalias de fusão.

Apresentamos nossa experiência e resultados no tratamento da litíase através de litotripsia ex-

tra-corpórea por ondas de choque (LEOC) em 8 pacientes portadores de rim em ferradura.

MATERIAL E MÉTODOS

Foram analisados retrospectivamente os dados de 8 pacientes portadores de rim em ferradura tratados com LEOC. Destes, 7 eram do sexo masculino e 1 do sexo feminino. A idade variou de 25 a 84 anos com média de 51 anos. Dos 8 pacientes, 2 apresentavam cálculos bilaterais, (10 unidades renais). Todos os pacientes foram investigados previamente ao procedimento quanto à presença de infecção e dilatação do trato urinário por meio de urocultura e urografia excretora. A LEOC foi realizada com aparelho Dornier Phillips MFL5000, focalizando-se o cálculo com fluoroscopia. Analisou-se o número de sessões, o número total de ondas de choque empregados e eventuais complicações do tratamento (Tabela-1).

A avaliação dos resultados foi feita por meio de comparação da massa de cálculos inicial e após o tratamento segundo a fórmula descrita por Locke et al. (8): Massa de cálculos = (diâmetro do maior cálculo somado ao diâmetro do menor cálculo) multiplicados pelo número de cálculos e dividido por 2. Dois rins apresentavam cálculos coraliformes, sendo a massa de cálculos média nos demais de 21 milíme-

tros cúbicos. Realizou-se em média 5 sessões por rim acometido tendo cada um recebido em média 11.154 ondas de choque. Os procedimentos foram realizados em regime ambulatorial sendo utilizado meperidina endovenosa para analgesia, a dose aplicada variou conforme solicitação de cada paciente sendo em média de 3 mg. Não houve dificuldade de focalização do cálculo em nenhuma das aplicações sendo todos os procedimentos realizados em decúbito dorsal.

RESULTADOS

Das 10 unidades renais consideradas, em 3 casos houve crescimento bacteriano à urocultura (bacteriúria assintomática) e em 7 existia dilatação pielocalicinal aos exames de imagem.

Em 8 dos 10 rins tratados houve fragmentação dos cálculos, porém em apenas 4 unidades renais houve eliminação de fragmentos com redução da massa de cálculos. Nos 2 rins restantes não se obteve fragmentação ou eliminação. Em nenhuma das 10 unidades renais observou-se eliminação completa dos cálculos (Figuras-1 e 2).

Os piores resultados foram obtidos no grupo em que se observou dilatação pielocalicinal. Nestas 7 unidades renais, em apenas uma houve redução da massa de cálculos. No grupo sem dilatação, formado

Tabela 1 – Litotripsia extra-corpórea por ondas de choque em rim em ferradura

Unidade Renal	Idade	Sexo	Dilatação	Infecção	Massa Inicial	No. de Impulsos	Massa Final	Complicações
1	59	M	N	S	31	26.689	8	S
2	84	M	S	N	17	13.507	30	N
3	54	M	N	N	41	21.086	30	N
4	25	M	S	N	15	7.076	15	N
5	25	M	S	N	12	14.180	17	S
6	48	F	S	N	coral	4.900	25	N
7	48	F	S	N	coral	4.904	coral	N
8	33	M	S	S	20	9.291	20	N
9	43	M	S	S	30	4.600	30	S
10	65	M	N	N	8	4.910	4	S

Massa Inicial = massa de cálculos em mm³ antes do tratamento

Massa Final = massa de cálculos em mm³ após o tratamento

Coral = coraliforme

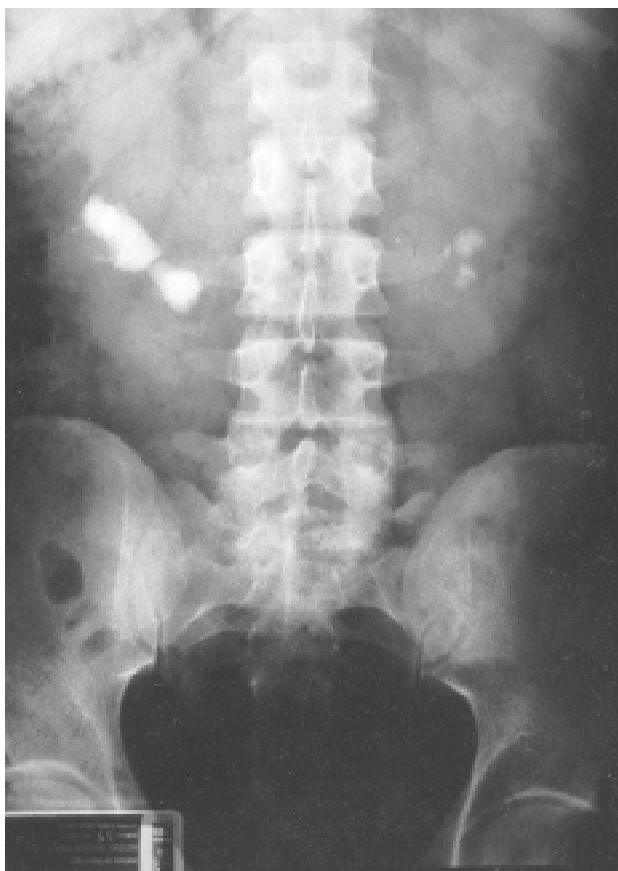


Figura 1 – Rx simples de abdomen pré LEOC mostrando cálculos bilaterais em rim em ferradura.

por 3 unidades renais, observou-se redução em todas as unidades.

Das 10 unidades renais tratadas, obteve-se complicações em 4, sendo em todos os casos a não eliminação de fragmentos pelo ureter com formação de rua de cálculos. Destes pacientes 2 foram tratados com ureteroscopia e 2 com nova LEOC sobre o cálculo ureteral. Considerando-se que cada unidade renal foi submetida em média a 5 sessões de LEOC, o índice de complicações por procedimento foi de 8%.

DISCUSSÃO

A litíase é um achado mais freqüente em pacientes portadores de rim em ferradura. A LEOC tem sido amplamente utilizada no tratamento destes pacientes por ser um método pouco invasivo e de baixo custo em nosso meio.

Os primeiros casos descritos de LEOC em rins em ferradura datam do início da década de 80 (12). Dados de várias publicações sobre o uso de LEOC neste grupo especial de pacientes estão apresentados na Tabela-2.

Em nossos pacientes, obtivemos redução da massa de cálculos em 40% dos casos, porém não se observou em nenhum deles eliminação completa dos fragmentos. Comparando-se nossos resultados aos obtidos por outros autores, observa-se que o número de respostas no nosso grupo foi inferior ao obtido em outros serviços, onde o índice de respostas completas foi entre 50 e 60% (Tabela-2). O grande tamanho dos cálculos tratados em nosso serviço (2 cálculos coraliformes e o restante com massa de cálculos média de 21 mm³) provavelmente contribuiu para que não se obtivesse eliminação completa dos fragmentos.



Figura 2 – Rx de abdomen pós LEOC apontando fragmentação parcial e eliminação incompleta dos cálculos.

Tabela 2 – Diferentes casuísticas e resultados de litotripsia extra-corpórea em rim em ferradura: dados publicados

Autor (ref.)	Número de Pacientes	Número e Impulsos	Aparelho Utilizado	Livre de Cálculos (%)	Complicações (%)
Smith (14)	14	1700	HM3	57	28
Locke (8)	10	2207	HM3	55	?
Esuvaranathan (13)	6	6	Edap Sonolit	50	?
Serrate (15)	15	?	HM3	60	0
Vandeursen (16)	11	3852	Lithostar	54	0
Wei Chuan Chen (17)	4	1850	?	100	0
Lampel (18)	38	2500	HM3	78	21
Kirkali (19)	18	11437	Lithostar	78	22
Martinez(20)	27 (31UR)	?	?	80.6	19

A presença de dilatação do trato urinário foi o fator mais importante nos resultados de nossa série de pacientes. Dos 7 casos com dilatação pielocalicinal, apenas um apresentou diminuição da massa de cálculos. No grupo formado por 3 pacientes em que não se observou este achado, todos responderam ao tratamento. O número de complicações em nosso estudo (8%) foi semelhante ao descrito por outros autores (Tabela-2).

CONCLUSÃO

O tratamento da litíase em rim em ferradura através de monoterapia por LEOC apresenta baixos índices de sucesso, principalmente quando as unidades renais submetidas a tratamento apresentam dilatação do sistema coletor.

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RESUMO

TRATAMENTO DE LITÍASE EM RIM EM FERRADURA POR MEIO DE LITOTRIPSIA EXTRACORPÓREA POR ONDAS DE CHOQUE

Entre 1984 e 1996 8 pacientes (10 unidades renais) portadores de litíase em rim em ferradura, foram tratados em nosso serviço por meio de litotripsia extra-corpórea por ondas de choque. Obteve-se diminuição da massa de cálculos em 4 dos 10 rins submetidos a tratamento, e complicações (não eliminação de fragmentos ureterais) em 4 unidades renais. Dos 6 pacientes que não responderam ao tratamento, todos apresentavam dilatação pielocalicinal à urografia excretora. Dos 4 pacientes que apresentaram complicações, 2 tinham uroculturas com crescimento bacteriano. O tratamento de pacientes com litíase em rim em ferradura por meio de litotripsia extra-corpórea por ondas de choque apresentou resultados pouco satisfatórios especialmente quando havia dilatação de vias excretoras ou infecção associada.

Unitermos: rim, litíase, rim em ferradura, litotripsia extra-corpórea por ondas de choque, tratamento, monoterapia
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ANALYSIS OF DNA PLOIDY HETEROGENEITY IN PROSTATE CANCER

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ABSTRACT

The objectives of this study were to assess DNA ploidy heterogeneity and thus the specificity of digital cytometry for prostate adenocarcinoma, as intratumoral variation of DNA content is believed to exist among these cells, as occurs with histological differentiation.

Fifteen prostate adenocarcinoma patients were selected. They underwent radical prostatectomy and the tissue obtained had 3 distinct areas analyzed to determine cellular ploidy and tumor grade (Gleason score). Statistical analysis has described the values in the Gleason score in the different areas, both in the diploid and aneuploid groups, in relation to average, standard deviation, median, and maximal and minimum values.

The prostatic tissue studied showed only diploid tumors in some patients and only aneuploid tumors or an association between diploid and aneuploid tumors in others. There were 11 tumors where the areas were diploid (73.3%), 3 aneuploid tumors (20%) and a tumor with 2 diploid areas and an aneuploid one (6.7%). There was thus homogeneity among the areas studied in 93.3% of the prostatic tumors. The values in the Gleason score were compared with the ploidy of each area in the several tumors. The average of values in the Gleason score in the tumor areas of the diploid group was significantly smaller ($p < 0.05$) than the observed average in the areas of aneuploid group of tumors. This relationship occurred globally in the areas of tumors.

In conclusion, ploidy analysis of the cellular DNA in prostate adenocarcinoma through digital cytometry shows high specificity (93,3%) and cellular differentiation rate was significantly lower in diploid tumors.

Key words: prostate, prostatic neoplasms, DNA ploidy, heterogeneity

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INTRODUCTION

Neoplasias are widely recognized by inter and intratumoral heterogeneity characterized by several aspects: morphological, phenotypic and genetic. This diversity does not, however, imply necessarily in chaotic behavior. If there is any structure in a system, and if anybody understands the rules and interactions of this system, they may understand the ways of its evolution and its potential behavior (1). The natural history of the prostatic adenocarcinoma is still poor known. The factors that trigger prostate cancer, that make it develop, penetrate the prostatic capsule, send metastases or become refractory to hormone therapy are still hardly known. Some of these tumors evolve rapidly, while others

stay quiescent (2). It is early to assert that all prostate cancers begin with the same rate of cellular multiplication and become more aggressive with the passage of time or whether they begin already at different growth rates (3). The forecast of the potential malignity of the tumors is thus one of the greatest problems in handling prostate cancer. The clinical and pathological stage, the tumor grade, volume and PSA levels are the principal methods used. However, they cannot be considered to be consistently objective and trustworthy. This is the context in which DNA ploidy analysis has emerged as a promising technique for the classification of the malignity potential of the tumor. Tumor cells with a nucleic acid content similar to normal cells are believed to have a less aggressive behavior.

The objectives of this study were to assess DNA ploidy heterogeneity and thus, the specificity of digital cytometry for prostate adenocarcinoma, besides verifying the existence of a corresponding of this with the variation of cellular differentiation.

MATERIAL AND METHODS

The group studied consisted of 15 patients with prostate adenocarcinoma, verified by transrectal biopsies, who underwent radical prostatectomy. The tissue obtained in these surgeries was submitted to histopathological routine preparation and kept in paraffin.

In order to evaluate the heterogeneity of prostate tumors, the cellular ploidy and the tumor grade (Gleason score) were determined in 3 distinct areas of each tumor, area A being the most expressive and area C the least frequent.

The quantitative DNA analysis was made in 5- μ m sections of prostatic material by Feulgen stoichiometric method. The new slides were observed in an optic videomicroscopy system joined to an IBM-PC compatible microcomputer. The tumor images generated by the camera were frozen and fed into software specifically designed for nucleic tracing, named W.ING.

The total optical density of the nucleus represents its DNA content. In this manner, when measuring the amount of DNA of a certain cellular population, a chart is obtained, called a DNA histogram, representing the ploidy pattern of this cellular population. The determining of the control histograms was made by the analysis of DNA content of the cells of either normal prostatic tissue or tissue with benign hiperplasia in the sample of each patient. Comparing the histograms of the DNA of neoplastic cells to those of normal cells we obtained its DNA index, meaning the proportion between the DNA of cells at rest (G0/G1) in neoplasia and in the normal population. So, a DNA index equal to one marks a diploid pattern, while a DNA index markedly different from one determines an aneuploid pattern.

Statistical analysis has described the values in the Gleason score in the different areas, both in the diploid and aneuploid groups, in relation to average,

standard deviation, median, and maximal and minimum values. The non-parametric test of Mann-Whitney was used for determining the significance, with the adoption of "p" values smaller than 0.05 as statistically significant.

RESULTS

The prostatic tissue studied showed only diploid tumors in some patients and only aneuploid tumors or an association between diploid and aneuploid tumors in others. There were 11 tumors where the areas were diploid (73.3%), 3 aneuploid tumors (20%) and a tumor with 2 diploid areas and an aneuploid one (6.7%). There was thus homogeneity among the areas studied in 93.3% of the prostatic tumors.

The values in the Gleason score were compared with the ploidy of each area in the several tumors. The average of values in the Gleason score in the tumor areas of the diploid group was significantly smaller ($p < 0.05$) than the observed average in the areas of aneuploid group of tumors. This relationship occurred globally in the areas of tumors (Table-1).

Table 1 – Average of values in the Gleason score in each area of the groups of diploid and aneuploid prostate tumors

	Aneuploid Average	Diploid Average	(Significance)
Area A	7.67	6.08	p = 0.0176
Area B	8.33	6.00	p = 0.0176
Area C	8.00	6.36	p = 0.0059

DISCUSSION

The real value of ploidy in estimating the potential malignity of prostate tumors and the survival of patients remains controversial. Some studies show a strong forecast value while others failed in attempt of proving the significance of this relationship.

As a group, diploid tumors present a disease-free period after treatment greater than shown by the

group of patients with aneuploid tumors. Determination of the ploidy of a given tumor cannot, however, be useful to determine the survival chance of a particular patient (4).

Some 30% of the tumors restricted to the gland are "pure" non-diploid (4). In this study, there were 73.3%, which were homogeneously diploid tumors. This predominance is probably due to our having studied the tumors localized in the prostate, for which surgery was indicated.

In a recent consensus meeting on ploidy of prostate tumors, the conclusion was reached that there is a significant relationship between DNA content and the evolution, survival and response to hormone therapy. It was also established at the meeting that there were tumors heterogeneous as to ploidy, with diploid and aneuploid areas, and that this variation could compromise the results of ploidy determination in prostatic tumors (5). Studies of ploidy heterogeneity of prostate tumors through digital cytometry have shown that patients with a localized disease, restricted to the prostate, aneuploid tumors are rare (13%) and that ploidy heterogeneity occurs in less than 10% of these tumors (2,6).

We demonstrated that, as far as the correspondence of ploidy with the Gleason score is concerned, the values of Gleason score of diploid tumors are in average significantly smaller than the values for aneuploid tumors. As the degree of cellular differentiation is a well-established parameter in determining the aggressiveness of tumor cells, despite its subjective component, the association of ploidy gives probably greater objectivity to the forecast of the potential malignity of the tumor.

CONCLUSIONS

We conclude that ploidy analysis of cellular DNA in prostate adenocarcinoma through digital cytometry shows high specificity (93.3%). This permits cellular ploidy to be determined by simple transrectal biopsy, while yet in the pre-operative phase. Biopsy cannot determine the degree of histological differentiation as reliably (6). We have also concluded that the cellular differentiation rate

was significantly higher in diploid tumors, which probably represent diseases that are really less aggressive than aneuploid tumors.

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OPEN-ENDED, NON-COMPARATIVE STUDY TO EVALUATE THE EFFICACY AND TOLERABILITY OF *Serenoa repens* EXTRACT IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA

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ABSTRACT

Purpose: The objective of this study was to evaluate the efficacy and tolerability of a lipido-sterolic extract of *Serenoa repens* (LSESr, Permixon®) in benign prostatic hyperplasia (BPH).

Materials and Methods: An open-label, non-comparative study was performed for at least 6 months in 50 patients (mean age = 64.5 years) with symptomatic BPH. The initial evaluation was performed through the international prostate symptom score (I-PSS), quality of life index, uroflowmetry, transabdominal ultrasound of the prostate (prostate weight, residual urine volume), PSA, heart rate and blood pressure. The inclusion criteria were I-PSS ≥ 8 and a maximum urinary flow rate ≤ 12 ml/s for a urinary volume ≥ 150 ml. The patients received a daily dose of 160-mg bid of LSESr and evaluations were performed after 30 and 90 days of treatment.

Results: The I-PSS analysis showed a significant decrease of this index and the quality of life index was significantly improved. The maximum urinary flow rate was improved and the residual urinary volume was decreased. There was no reduction in prostatic weight and no change in PSA levels. Neither serious adverse events nor changes in hemodynamic parameters were observed.

Conclusion: The LSESr was efficacious in improving the symptoms of BPH without adverse effects.

Key words: prostate, benign prostatic hyperplasia, pharmacotherapy, extract of *Serenoa repens*, efficacy, tolerability
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INTRODUÇÃO

A obstrução do fluxo urinário decorrente da hiperplasia prostática benigna (HPB) pode acarretar manifestações clínicas relacionadas ao aumento progressivo da próstata. Estas manifestações incluem tanto os sintomas obstrutivos associados ao estreitamento da uretra prostática, como sintomas irritativos decorrentes da instabilidade do detrusor vesical. Sua história natural transcorre com fases de melhora e de exacerbação, não havendo constância das manifestações clínicas (1,2).

O principal objetivo do tratamento do paciente com HPB é obter a melhora dos sintomas e do incômodo decorrente destes. Assim, a abordagem terapêutica medicamentosa da HPB pode incluir fármacos que reduzem o tônus da musculatura lisa prostática ou as dimensões da próstata (3).

O extrato lipido-esterólico da palmeira anã *Serenoa repens* (LSESr) age sobre o metabolismo das prostaglandinas nas células prostáticas de cultura (4), modula a 5 alfa-redutase humana (5), exerce atividade anti-edematosa nos animais (6) e demonstra atividade estrogênica em humanos (7).

O objetivo do presente trabalho foi avaliar a eficácia e tolerabilidade da LSESr em pacientes com HPB.

MATERIAL E MÉTODOS

Este foi um estudo aberto, não-comparativo, aprovado pelo Comitê de Ética em Pesquisa do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo e todos os pacientes forneceram consentimento escrito e informado.

Um total de 50 pacientes com HPB foi admitido no estudo para análise da eficácia e tolerabilidade da LSESr.

Os critérios de inclusão foram os seguintes: pacientes ambulatoriais de sexo masculino, acima de 50 anos de idade, com diagnóstico de HPB sintomática, confirmado através do toque retal e determinação do nível plasmático do PSA, I-PSS 8 na escala, taxa máxima de fluxo urinário igual a 12 ml/s para um volume urinário igual a 150 ml, além de estarem em boas condições mentais.

Os critérios de exclusão compreendiam pacientes com câncer prostático, HPB com indicação cirúrgica, história prévia de cirurgia vesical ou prostática, disfunção neurológica da bexiga, estenose do colo da bexiga ou uretral, bem como litíase, carcinoma e polipose da bexiga, ITU recorrente, uso concomitante (ou no mês anterior à inclusão) de qualquer droga com ação sobre a função urinária.

Os pacientes receberam uma cápsula de 160 mg de LSESr, administrada por via oral duas vezes ao dia, por um período de 3 meses. O ensaio foi conduzido de acordo com os princípios éticos da Declaração de Helsinque e a Boa Prática Clínica para Estudos de Produtos Medicinais.

Os pacientes foram avaliados clinicamente em 3 ocasiões: no pré-tratamento, após 30 e após 90 dias de tratamento. A avaliação clínica compreendia as medidas de pressão sistólica, pressão diastólica, pulso radial, fluxometria e PSA. A eficácia do tratamento foi avaliada por meio da evolução de dados obtidos pela fluxometria, PSA, I-PSS e ultrasonografia prostática transabdominal, sendo avaliados seu peso e resíduo urinário. Os valores de fluxometria e pressão arterial são a média de três diferentes medidas. O índice de qualidade de vida foi avaliado na visita inicial, após 30 e 90 dias de tratamento, através das questões e do escore. A média dos escores do D30 e D90 foram comparados à média dos escores basais.

A análise dos dados foi realizada através do teste de Hartley, onde se observou a homogeneidade da amostra, seguida da análise ANOVA e o teste de McNemar. O limiar de significância para todos os testes foi selecionado como sendo $p < 0,05$.

RESULTADOS

A pressão arterial sistólica e diastólica e a frequência cardíaca não sofreram alterações significativas durante o tratamento (Tabelas-1, 2 e 3).

Tabela 1 – Pressão arterial sistólica (mm-Hg)

	DIA 0	DIA 30	DIA 90
$\mu \pm dp$	134,8 \pm 11,8	134,6 \pm 11,1	133,7 \pm 10,9
Mediana	130,0	130,0	132,5
Variacão	110 - 165	110 - 160	110 - 160

Anova: $F = 0,534$ (ns)

$F_{max} = 1,164$ (amostra homogênea)

Tabela 2 – Pressão arterial diastólica (mm-Hg)

	DIA 0	DIA 30	DIA 90
$\mu \pm dp$	84,6 \pm 7,3	84,5 \pm 6,3	84,5 \pm 5,6
Mediana	85,0	85,0	85,0
Variacão	70 - 100	70 - 95	70 - 95

Anova: $F = 0,010$ (ns)

$F_{max} = 1,659$ (amostra homogênea)

Tabela 3 – Pulso radial (bat./min.)

	DIA 0	DIA 30	DIA 90
$\mu \pm dp$	69,6 \pm 8,3	69,4 \pm 6,2	69,1 \pm 7,4
Mediana	68,0	68,0	68,0
Variacão	58 - 90	60 - 84	58 - 90

Anova: $F = 0,082$ (ns)

$F_{max} = 1,769$ (amostra homogênea)

Pudemos verificar uma discreta melhora na fluxometria a partir do primeiro mês de tratamento (Tabela-4). A diferença é estatisticamente significativa.

Os valores de PSA não sofreram alteração durante o tratamento (Tabela-5).

Os exames ultra-sonográficos da próstata, realizados nos dias 0 e 90, demonstraram uma redução significativa do resíduo urinário sem alteração no peso prostático (Tabela-6).

A análise da escore internacional de sintomas prostáticos (I-PSS) revelou uma redução deste

índice ($p < 0,001$). Considerando como melhora do I-PSS os pacientes cuja redução foi igual ou superior a 3 pontos, temos que 84% deles (42 pacientes) melhoraram e apenas 1 paciente (2%) apresentou piora do quadro inicial (Tabela-7).

Tabela 4 – Fluxometria (ml/s)

	DIA 0	DIA 30	DIA 90
$\mu \pm dp$	5,5 1,7	7,5 2,0	7,9 2,1
Mediana	5,5	7,5	7,7
Variacão	2,5 - 10,1	3,7 - 12	4,2 - 12,8

Anova: $F = 117,114 - p < 0,001$ (diferença significativa a partir de 30 dias de tratamento)

$F_{max} = 1,471$ (amostra homogênea)

Tabela 5 – Evolução dos níveis de PSA (ng/ml)

	DIA 0	DIA 90	TESTE
$\mu \pm dp$	2,1 \pm 1,1	2,0 \pm 0,9	
Mediana	1,85	1,9	$t = 0,37$ (ns)
Variacão	0,1 - 3,9	0,8 - 3,7	

Tabela 6 – Evolução do resíduo urinário avaliado através de ultra-sonografia da próstata (ml)

	DIA 0	DIA 90	TESTE
PESO (g)	N = 50	N = 50	
$\mu \pm dp$	45,8 \pm 14,3	45,1 \pm 13,5	$t = 1,88$ (ns)
Mediana	44,5	42,5	
Variacão	22 - 89	22 - 80	
RESÍDUO (ml)	N = 50	N = 50	
$\mu \pm dp$	61,4 \pm 24,4	41,0 \pm 20,6	$t = 7,23$ ($p < 0,001$)
Mediana	60,0	43,5	
Variacão	15 - 120	0 - 90	

Tabela 7 – Evolução do I-PSS (dia 0 - dia 90)

I-PSS (dia 0 - dia 90)	No. de pacientes
≥ 3	42 (84,0)
2	5 (10,0)
Inalterado	2 (4,0)
Piora	1 (2,0)

A qualidade de vida apresentou pequena melhora, que mostrou ser estatisticamente significativa. (Tabela-8).

Tabela 8 – Qualidade de vida relacionada a sintomas urinários

	DIA 0	DIA 60	DIA 90
$\mu \pm dp$	3,4 \pm 0,6	2,2 \pm 0,6	2,0 \pm 0,5
Mediana	3,0	2,0	2,0
Variacão	2 - 5	1 - 3	1 - 3
Muito bem	–	5 (10,0)	5 (10,0)
Satisfeito	2 (4,0)	32 (64,0)	38 (76,0)
Satisfeito na maior parte do tempo	29 (58,0)	13 (26,0)	7 (14,0)
Insatisfeito na maior parte do tempo	17 (34,0)	–	–
Insatisfeito Muito insatisfeito	2 (4,0)	–	–
	–	–	–
	–	–	–

Anova: $F = 171,646 - p < 0,001$ (diferença significativa a partir de 30 dias de tratamento)

$F_{max} = 1,659$ (amostra homogênea)

Nenhum paciente reportou qualquer evento adverso nem descontinuou prematuramente o tratamento.

DISCUSSÃO

Atualmente existem diversas opções terapêuticas disponíveis para o tratamento de pacientes portadores de HPB, variando desde a terapia medicamentosa, até o tratamento cirúrgico, como a ressecção transuretral da próstata (RTUP) e os procedimentos minimamente invasivos (1).

Os resultados deste estudo demonstraram que o tratamento com 160 mg de LSESr 2 vezes ao dia é eficaz na melhora da sintomatologia da HPB sem causar efeitos colaterais importantes. Houve uma redução no valor absoluto do I-PSS,

sendo considerada melhora uma diminuição igual ou superior a 3 pontos, em 84% dos pacientes (42 pacientes). Houve piora de sintomas em 1 paciente (2%). Se considerarmos a história natural da HPB e a melhora da sintomatologia, observamos que a medicação possui ação efetiva e não apenas o efeito placebo (8,9).

Cerca de 92% dos pacientes expressaram aumento de satisfação de sua qualidade de vida, que é o objetivo de qualquer conduta que venha a ser instituída no tratamento da HPB.

Houve um aumento estatisticamente significativo dos resultados da urofluxometria a partir do primeiro mês de tratamento, porém, com significado clínico discreto, possivelmente devido à variabilidade deste parâmetro no paciente prostático. Uma recente análise de fator dos dados derivados de um estudo de larga escala salientou a baixa concordância entre os sintomas e a urodinâmica (10). Foi sugerido que a falta de correlação pode ser devida à imprecisão das mensurações, e que determinações basais repetidas são necessárias. Em nosso estudo, a melhor apreciação do fluxo foi obtida pela média obtida de 3 diferentes medidas de fluxo (8).

O valor do PSA não sofreu alteração significativa durante o tratamento, confirmando que o diagnóstico de câncer prostático não é mascarado pela droga do estudo (2,11).

A avaliação do resíduo urinário através da ultra-sonografia demonstrou uma diminuição média de 20 ml que, apesar de ser estatisticamente significativa, têm significado clínico discreto (12). O peso prostático, também avaliado pela ultra-sonografia, não apresentou variação no período de tratamento.

O LSESr não apresentou efeitos sobre a pressão arterial e a frequência cardíaca dos pacientes tratados, fatos estes que associados à ausência de eventos adversos nesta amostra, confirmam seu excelente perfil de tolerabilidade (11).

A *Serenoa repens* demonstrou ser clinicamente efetiva em alguns estudos controlados com placebo (2,13). Seriam oportunos, para uma melhor avaliação do efeito terapêutico da LSESr, estudos comparativos, randomizados e duplo cego mais prolongados, de pelo menos seis meses, com outros medicamentos e com placebo.

CONCLUSÃO

Os resultados demonstrados em relação ao fluxo e resíduo urinários foram clinicamente discretos, entretanto, a melhora na sintomatologia (I-PSS) e na qualidade de vida, além do perfil muito bom de tolerabilidade, fazem da LSESr uma opção no tratamento medicamentoso da HPB.

O laboratório ASTA Medica forneceu o produto Permixon

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COMENTÁRIO EDITORIAL

Este estudo, como tantos outros abertos e não comparativos, permite em realidade poucas conclusões, e necessita muita cautela em sua interpretação, principalmente por se tratar de farmacoterapia da hiperplasia prostática benigna (HPB).

Já está razoavelmente estabelecido que a simples análise do International Prostate Symptom Score (I-PSS) não é parâmetro que defina a qualidade de um determinado tratamento para esta doença, pois em alguns estudos o placebo foi capaz de melhorar este índice em até 76% dos pacientes.

Os critérios urodinâmicos, principalmente as curvas de fluxo-pressão, são muito mais fidedignos neste tipo de análise. Além disso, é indiscutível a influência do pesquisador ao lidar com o paciente, na análise da melhora dos sintomas, dado este tão subjetivo e influenciável.

Estudos deste tipo devem ser no mínimo comparativos e duplo-cegos. Sem isto, qualquer conclusão carece de sustentação científica.

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RESUMO

ESTUDO ABERTO, NÃO COMPARATIVO, PARA AVALIAR A EFICÁCIA E TOLERABILIDADE DO EXTRATO LÍPIDO-ESTERÓLICO DA *Serenoa repens* EM PACIENTES COM HIPERPLASIA PROSTÁTICA BENIGNA

Objetivo: Estudar a eficácia e tolerabilidade do extrato n-hexano lípido-esteróico da *Serenoa repens* (LSESr) na hiperplasia prostática benigna (HPB).

Material e Métodos: Este foi um estudo aberto, não-comparativo, com 3 meses de duração, onde foram avaliados 50 pacientes com HPB, com média de idade de 64,5 anos, sintomáticos há pelo

menos 6 meses. A avaliação inicial foi realizada através de Pontuação Internacional de Sintomas Prostáticos (I-PSS), Qualidade de Vida, Toque retal, PSA, Fluxometria, Ultra-sonografia prostática transabdominal (peso da próstata, resíduo urinário) e medidas de frequência cardíaca e pressão arterial. Após a utilização de duas doses diárias de 160 mg de LSESr, novas avaliações foram realizadas após 30 e 90 dias de tratamento.

Resultados: Houve redução significativa do I-PSS e da melhora na qualidade de vida, bem como do fluxo e do resíduo urinário. Não houve redução no peso da próstata e alteração dos níveis séricos do PSA. Não houve reações adversas graves e nem alteração dos parâmetros hemodinâmicos.

Conclusão: O extrato lipido-esterólico da *Serenoa repens* foi eficaz na melhoria da sintomatologia da HPB sem causar efeitos colaterais.

Unitermos: próstata, hiperplasia prostática benigna, terapia, extrato de *Serenoa repens*, eficácia, tolerabilidade.
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CARCINOMA OF THE PENIS: THE VALUE OF PROLIFERATING CELLULAR NUCLEAR ANTIGEN (PCNA)

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ABSTRACT

Objectives: To compare the proliferating cellular nuclear antigen (PCNA) immunoeexpression with biological aggressiveness (stage and grade) of squamous cell carcinoma of the penis.

Material and Methods: Between 1976-95, 50 patients with squamous cell carcinoma of the penis underwent surgical penile amputation (total or partial). Fifteen of them required associated inguinal lymphadenectomy due to suspicion of lymph node metastasis. The material kept into formalin or paraffin was recovered to study the immunoeexpression of PCNA by the avidin-biotin-peroxidase method. Metastases occurred in 4 of 34 well-differentiated tumors, in 4 of 12 moderately differentiated and in 2 of 4 undifferentiated tumors.

Results: A diffuse and strong pattern of staining (D+++) was found in 18/34 well-differentiated, in 10/12 moderately differentiated and in 4/4 undifferentiated tumors. All tumors with metastasis were D+++ , including 4/18 well-differentiated and 4/10 moderately differentiated tumors exhibiting such pattern of staining.

Conclusion: There is a strong positive relation between pattern D+++ of PCNA staining and tumor staging ($p = 0.003$), but not with grading ($p = 0.06$). The authors conclude that PCNA seems an independent marker and suggest that hosts with tumors bearing PCNA pattern of staining other than D+++ may be sparing from lymphadenectomy, while those with D+++ tumor should be submitted to lymphadenectomy and/or kept under strict observation.

Key words: penis, carcinoma, squamous cell carcinoma of penis, PCNA, prognosis

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INTRODUÇÃO

É comum a heterogeneidade celular e, mesmo um tumor considerado homogêneo e de baixo grau pode conter um ou mais clones celulares indiferenciados. Há subjetividade na graduação histológica e a identificação desses clones nem sempre é percebida na análise patológica convencional. Daí o interesse de se investigar as neoplasias através de técnicas modernas de biologia molecular.

O antígeno nuclear de proliferação celular (PCNA) é uma molécula de 36 kDa que funciona como co-fator da DNA-polimerase (1). Ela está presente em todas as fases do ciclo celular, mas sua síntese é maior na fase S além de também estar associa-

da ao reparo do DNA (2). Sua identificação por imunohistoquímica indica que a célula está em processo ativo de divisão celular ou em processo de reparo do DNA (3,4). Pelo fato da imunohistoquímica ser uma técnica de baixo custo e de fácil execução, com potencial de uso prático rotineiro, há trabalhos procurando relacionar a imunoeexpressão do PCNA com o grau, bem como com o comportamento biológico de diversos tumores: carcinoma epidermóide de esôfago (5), câncer pulmonar (6), carcinoma de células transicionais da bexiga (7), hipernefroma (8), câncer de mama (9).

O carcinoma do pênis é mais comum em países pobres e nas regiões mais desenvolvidas de nosso país a incidência vem declinando (10). O método

de manejo desses tumores é controvertido porque a agressividade biológica é variável não podendo ser caracterizada com precisão pelas técnicas clássicas de gradação histológica (11-13).

O objetivo deste trabalho é estudar a imunexpressão do PCNA em carcinoma epidermóide de pênis procurando verificar se existe correlação com o grau e o estágio, bem como observar se é possível definir um novo parâmetro que reflita a agressividade biológica.

MATERIAL E MÉTODOS

Entre 1976 e 1995, foram tratados no Hospital das Clínicas de Ribeirão Preto, SP, com penectomia parcial ou total, 50 pacientes com carcinoma epidermóide de pênis. No momento do diagnóstico a idade deles variou de 32 a 80 anos, com média de 58,2 anos. Todos receberam alta em boas condições, mas 9 não retornaram para seguimento. Nos 41 restantes o tempo de acompanhamento variou de 6 meses a 7 anos. Em 15 pacientes com suspeita de metástases linfonodais fez-se linfadenectomia inguinal bilateral (linfonodos superficiais e profundos). O exame histológico confirmou metástases linfonodais em 10 deles, dos quais 4 eram do grupo dos 9 pacientes que não retornaram para seguimento.

Como complementação diagnóstica do estadiamento, além da palpação inguinal e da linfadenectomia dos casos suspeitos, empregou-se no atendimento inicial e durante o seguimento, o RX de tórax e a ultra-sonografia abdominal. A tomografia computadorizada de região inguinal e abdome foi empregada nos 15 pacientes com suspeita de metástases inguinais. O mapeamento ósseo com tecnécio radioativo foi indicado em 1 paciente com dores ósseas e suspeito de portar metástase em coluna lombar. Dos 10 casos com metástases ganglionares inguinais, 3 desenvolveram também metástases à distância (pulmão – 2, coluna – 1).

As peças cirúrgicas conservadas em formol tamponado a 10%, os blocos de parafina e respectivas lâminas foram identificados e recuperados do arquivo do Departamento de Patologia da FMRP-USP. Após revisão das lâminas, cortes adicionais para co-

loração em hematoxilina-eosina foram efetuados para exame histológico, de modo que em cada caso selecionou-se cuidadosamente a porção tumoral que seria estudada. Para o estudo do PCNA empregou-se o método convencional de desparafinação com xilol seguido de hidratação com álcool etílico, assim como recuperação antigênica (14). Cortes de 4 micra foram então processados para detecção imunohistoquímica do PCNA pelo método da avidina-biotina-peroxidase conforme proposição de HSU et al. (15). Empregou-se o anticorpo primário monoclonal anti-PCNA, PC-10, DAKO®, na diluição 1:60, e o anticorpo secundário produzido em coelho contra camundongo (Kit ABC Vector®, pK 4002). A revelação da reação foi realizada com substrato cromogênico DAB- Sigma®, código N.º D 5637. Adotou-se análise semiquantitativa para a leitura das lâminas tanto no padrão de marcação difusa (D) quanto focal (F), conforme o critério seguinte: material não corado (-), levemente positivo - área com até 25% de marcação (+), moderadamente positivo - 25 a 50% da área corada (++) e fortemente positivo - >50% da área corada (+++).

Para a análise estatística empregou-se o teste exato de Fischer.

RESULTADOS

Na Tabela-1 estão os resultados da imunexpressão do PCNA conforme a gradação histológica dos tumores; o coeficiente Phi das 3 proporções D+++ versus diferenciação celular dos tumores é 0,34 e o valor $p = 0,06$.

Pela Tabela-2 observa-se que a associação entre as proporções do padrão D+++ em 10 pacientes com metástases é diferente daquela encontrada nos 40 pacientes sem metástases ($p = 0,006$ e coeficiente Phi = 0,37). A correlação entre o padrão de marcação D+++ e o estágio local (T) revelou coeficiente Phi de 0,36 e $p = 0,07$. Dos 50 pacientes, 32 eram D+++ e 18 não revelaram esse tipo de marcação, proporção essa que cotejada com os diversos estádios mostrou coeficiente Phi = 0,44 e $p = 0,003$.

A análise do conjunto de 32 tumores com padrão D+++ mostra que em 10 (31,2%) surgem metástases, o que indica que o valor preditivo positi-

Tabela 1 – Grau de diferenciação celular e expressão do PCNA

Grau	-	F+	P F++	C F+++	N D+	A D++	D+++	Total
Diferenciado	0	5	2	0	4	5	18	34
Moderadamente diferenciado	0	0	0	0	0	2	10	12
Indiferenciado	0	0	0	0	0	0	4	4
Total	0	5	2	0	4	7	32	50

Tabela 2 – Padrões de imunexpressão do PCNA versus estágio tumoral.

Estádio	-	F+	P F++	C F+++	N D+	A D++	D+++	Total
T ₁ N ₀ M ₀	0	5	1	0	2	3	11	22
T ₂ N ₀ M ₀	0	0	0	0	1	2	10	13
T _{3/4} N ₀ M ₀	0	0	1	0	1	2	1	5
N ₊ M _{0/+}	0	0	0	0	0	0	10	10

vo para metástases desse padrão de marcação do PCNA é de 31,2%, a sensibilidade é de 100% e a especificidade é de 45%.

DISCUSSÃO

A análise dos resultados revela relação positiva da atividade proliferativa celular medida pelo PCNA com o estágio, mas não com o grau tumoral. É possível que a falta de correlação entre padrão de coloração e o grau tumoral se deva ao tamanho da amostra, com um pequeno número de tumores indiferenciados, pois o valor encontrado para o p (0,06) está muito próximo do nível de significância.

Chama a atenção que todos os pacientes com metástases eram D+++ . Dos 18 tumores bem diferenciados com padrão de marcação D+++ , 4 (22,2%) evoluíram com metástases, o que indica que aproximadamente em 1/4 desses casos a agressividade biológica é maior. Já no grupo de 10 pacientes com tumores moderadamente diferenciados e marcação D+++ , 4 (40%) apresentaram metástases (o estágio local de 1 deles era pT1). Esse percentual foi de 50% para os tumores indiferenciados.

Os resultados deste trabalho permitem sugerir, que independentemente do estágio local (T),

os tumores bem diferenciados com padrão focal de coloração para o PCNA não necessitariam de esvaziamento ganglionar inguinal. Já aqueles corados com padrão difuso fortemente positivo, deveriam ser submetidos à linfadenectomia inguinal ou então ficar sob estrita observação para intervenção posterior caso necessário. Essa proposta, que embora pareça lógica pela análise retrospectiva, deve ser testada em estudos prospectivos no futuro para verificar se realmente traz algum benefício para os pacientes.

Não encontramos na literatura artigos sobre o PCNA em carcinoma epidermóide de pênis, o que impede qualquer comparação. Mas, o cotejamento futuro será importante, pois frequentemente são observados resultados contraditórios sobre o valor prognóstico deste e de outros marcadores tumorais, tanto em neoplasias de um mesmo tipo histológico quanto de tipos diversos (3,6,7,10,16-18), o que provavelmente se deve às variações da amostragem ou detalhes técnicos na execução dos exames. Em tumores epidermóides de outros locais, como a cavidade oral encontramos tanto artigos que revelam relação entre a imunexpressão do PCNA com o prognóstico (19), quanto que não demonstram essa relação (20).

CONCLUSÕES

A imunexpressão do PCNA mostrou correlação positiva com o estágio de carcinomas epidermóides de pênis, mas não com o grau. O PCNA parece um marcador independente e quando revela coloração forte e difusa, mesmo em tumores bem diferenciados, indica agressividade biológica maior.

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RESUMO

CARCINOMA DE PÊNIS: IMPORTÂNCIA DO ANTÍGENO NUCLEAR DE PROLIFERAÇÃO CELULAR

Objetivo: Comparar a imunoexpressão do PCNA com a agressividade biológica (estádio e grau) do carcinoma epidermóide do pênis.

Material e Métodos: No período 1976/1995, 50 pacientes com carcinoma epidermóide de pênis, idades entre 32 e 80 anos, média de 58,2 anos, foram submetidos à penectomia total ou parcial e em 15 deles associou-se linfadenectomia inguinal por suspeita de metástases. As peças mantidas em arquivo foram reexaminadas pela histologia convencional com coloração hematoxilina-eosina e recuperadas para estudo imunohistoquímico do PCNA, método da avidina-biotina-peroxidase. As metástases ocorreram em 4 de 34 tumores diferenciados, em 4 de 12 tumores moderadamente diferenciados e em 2 dos 4 tumores indiferenciados.

Resultados: Padrão forte de marcação difusa (D+++) foi observado em 18/34 tumores diferenciados, em 10/12 moderadamente diferenciados em 4/4 indiferenciados. O cotejamento grau versus marcação D+++ mostrou $p = 0,06$. A análise das proporções entre esse padrão de marcação e estágio mostrou diferença mais expressiva ($p = 0,003$). Todos os tumores com metástases eram D+++ , incluindo-se 4/18 diferenciados e 4/10 moderadamente diferenciados.

Conclusão: O estudo mostra uma forte correlação entre a imunoexpressão do PCNA e o estágio, mas não com o grau do tumor. O marcador parece independente e com potencial para nortear a conduta inicial em portadores da neoplasia.

Unitermos: pênis, câncer, carcinoma epidermóide de pênis, PCNA, prognóstico
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SPERM STIMULATION WITH PEPTIDES

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ABSTRACT

Objective: Sperm motility has an important role in the normal fertilization process. The motility of post-thaw sperm is so poor and represents a problem, even in some assisted reproduction techniques. Until now, we get few improvements in this field using pentoxifilin and platelet-activating factor. Pituitary adeny-late cyclase-activating polypeptide (PACAP27) is a peptide, which has the capacity to stimulate guanilatocyclase. It is present in sperm tails and could have a relationship with sperm motility. The aim of this study is to establish if the PACAP27 and vasoactive intestinal polypeptide (VIP) have any action in the motility of the post-thaw sperm.

Material and Methods: We mixed 12 post-thaw sperm samples with peptides (PACAP27 and VIP) to improve the sperm motility. The percent motility, viability and motion parameters were evaluated by using a computerized analyzer system.

Results: Viability in the initial moment was 33.5% in the 3 groups. After 60 minutes was 27.9%, 29.2% and 30% in the control, VIP and PACAP27 groups, respectively. After 180 minutes was 26.8%, 29.6% and 27,6% in the same groups. The motility after 60 minutes in the PACAP27 and VIP groups was similar to the controls (22.5%, 22.4% and 21.1%, respectively; $p > 0.05$), and after 180 minutes was 22.5%, 21.4% and 21.5% in control, VIP and PACAP27 groups, respectively. Also, there were no differences in the motion parameters among the groups, when evaluated by the computerized analyzer system.

Conclusion: We concluded that PACAP27 and VIP had no effects upon motility and viability of post-thaw semen.

Key words: sperm, motility, PACAP27, polypeptide, VIP, spermatozoa

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INTRODUÇÃO

Os peptídeos são agentes de comunicação intercelular que participam do programa de sobrevivência celular, modulam o sinal neuronal e a diferenciação celular. Podem agir no meio intercelular e determinar o desenvolvimento e a sobrevivência da célula. O sinal destes peptídeos geralmente é mediado por alterações intracelulares que envolvem a enzima adenilatociclase (1). Myiata et al. (2,3) descobriram 2 peptídeos amidados com 38 e 27 resíduos de aminoácidos provindos do hipotálamo de ovinos. Os autores perceberam que estes peptídeos tinham uma potente capacidade de estimular a atividade da

adenilatociclase, sendo então denominados polipeptídeos pituitários ativadores da adenilatociclase (PACAP38 e PACAP27), baseados no número de resíduos de aminoácidos que cada um possuía. O PACAP27 corresponde aos 27 resíduos N-terminais do PACAP38. A análise estrutural demonstrou que a formação destes peptídeos é a mesma em humanos, ovinos e ratos, e apresentam uma seqüência 68% homóloga ao polipeptídeo intestinal vasoativo (VIP) (1). Então, pode-se dizer que tanto PACAP27 como o 38 pertencem à mesma família de peptídeos do VIP, secretina, glucagon e hormônio liberador de gonadotrofinas (1,4). Os sítios de ligação (receptores) do PACAP foram localizados, por meio de auto-

radiografia, nos testículos, epidídimos, adrenais, pulmões, fígado, próstata e vesículas seminais. Também foram identificados no hipotálamo, pituitária anterior, cultura de esplenócitos e de astrócitos (1). O PACAP está presente nos testículos e poderia regular a função das células germinativas, através de um mecanismo parácrino, e, devido a isto, possuir um importante papel na espermatogênese (5,6). Leung et al. (7) demonstraram a presença de PACAP, através de imunofluorescência indireta, no epidídimo, principalmente ao nível da cabeça e corpo. É bem conhecido o fato de que também existem receptores do PACAP na cauda dos espermatozóides, envolvendo a adenilatociclase e a motilidade (1). El-Gehani et al. (8) perceberam que alguns fatores parácrinos (PACAP27 e VIP) provavelmente iniciam e mantêm a esteroidogênese testicular precoce fetal em ratos, antes do início da secreção do hormônio luteinizante.

A motilidade espermática é importante no processo normal de fertilização. Devido à preocupação com a SIDA e outras doenças sexualmente transmissíveis, tem sido utilizado somente sêmen criopreservado para a fertilização artificial. Porém, ocorre uma importante perda de motilidade espermática após o descongelamento, o que representa um grande problema a ser resolvido nos processos de fertilização assistida. O processo congelamento/descongelamento causa dano à membrana do espermatozóide, reduzindo a motilidade e, automaticamente, a fertilidade. O dano é determinado pela peroxidação lipídica de ácidos graxos insaturados e pela geração e liberação de radicais livres. Também ocorre alteração no balanço de íons, diminuição da produção de ATP pela mitocôndria e diminuição da produção de energia levando a uma menor motilidade. É claro que a motilidade diminuída torna-se irrelevante quando falamos em injeção intra-citoplasmática de espermatozóides. Até agora, em poucos casos foram obtidos bons resultados na melhora da motilidade após o processo congelamento/descongelamento de sêmen, através do emprego de pentoxifilina e fator de ativação de plaquetas (9-11).

Com o intuito de recuperar a motilidade dos espermatozóides após o descongelamento do sêmen, realizamos este estudo *in vitro*, na tentativa de me-

lhorar a motilidade através da associação com os peptídeos PACAP27 e VIP.

MATERIAL E MÉTODOS

Os peptídeos (PACAP27 e VIP) foram desenvolvidos pelo Departamento de Fisiologia e Farmacologia da Universidade de Tulane e o sêmen foi oriundo do Banco de Sêmen do Departamento de Urologia da mesma universidade.

Foram utilizadas 12 amostras de sêmen humano, congelado de forma habitual em meios de cultura Ham F10 (GIBCO, Long Island, New York) e YOLK (GIBCO, Long Island, New York). As amostras que apresentavam motilidade normal no período pré-congelamento foram selecionadas ao acaso e descongeladas através da incubação à 37°C, durante 5 minutos. O sêmen foi lavado e colocado em meio de cultura Ham F10, com uma concentração média de 80×10^6 espermatozóides/ml. Cada amostra foi dividida em 3 grupos contendo 500 μ L, sendo adicionado 7 μ L de PACAP27, VIP ou Ham F10 (controle). Então foram avaliados a porcentagem de motilidade, a viabilidade espermática e os parâmetros de motilidade, com o sistema de análise computadorizado. A motilidade foi avaliada através de uma câmara de Makler (Sefi Medical Instruments, Inc., Haifa, Israel) onde foi contado o número de espermatozóides móveis em uma população de 100 espermatozóides. A viabilidade espermática foi medida através da mistura de 10 μ L da amostra com igual volume de eosina-Y a 0,5% (Sigma Chemical Co., St. Louis, MO) durante 2 minutos. Então, 100 espermatozóides foram contados com auxílio de uma objetiva de contraste de fase com aumento de 400X. Os espermatozóides não corados foram considerados vivos. Para análise dos parâmetros de motilidade foi empregado um sistema computadorizado de análise de esperma (Cell Track/Sperm analysis system, Motion Analysis Corporation, Santa Rosa, CA) que avalia a motilidade, velocidade curvilínea, linearidade média, velocidade progressiva e deslocamento lateral da cabeça. Sete μ L de cada amostra foram colocados sobre uma câmara de Makler para a videomicrografia, com uma objetiva de fase com aumento de 20X. O sistema foi calibrado para detectar 30

imagens/segundo com 15 segundos de duração para captura de imagem, e uma média de 4 a 8 pixels por espermatozóide móvel, sendo então contados aproximadamente 100 espermatozóides. Todas as análises foram realizadas de modo cego por um único observador. Estes parâmetros foram analisados aos 0, 60 e 180 minutos.

Para a análise estatística foi utilizado a análise de variância para comparar os grupos tratados contra o controle, através do programa Staquik statistical package (Lundon Software Inc., Chagrin Falls, OH). Um valor de $p < 0,05$ foi considerado estatisticamente significativo.

RESULTADOS

A motilidade espermática média do grupo controle foi de 22,54%, no grupo do VIP foi 22,19% e no PACAP27 foi 22,24% ($p > 0,05$). Quanto à motilidade, aos 60 minutos após a administração dos peptídeos ao sêmen, identificamos: 21,1% de espermatozóides móveis no grupo controle, 22,4% no grupo do VIP e 22,5% no grupo de PACAP. E estes valores continuaram semelhantes aos 180 minutos também, isto é, 22,5%, 21,4% e 21,5% nos grupos controle, VIP e PACAP ($p > 0,05$) (Tabela-1). A

Tabela 1 – Análise da motilidade dos espermatozóides por grupo estudado

Tempo (minutos)	Controle (%)	VIP (%)	PACAP27 (%)
0	23,5*	23,5*	23,5*
60	21,1*	22,4*	22,5*
180	22,5*	21,4*	21,5*

* $p > 0,05$

viabilidade dos espermatozóides foi, aos 0 minutos, 33,5% para todos os grupos, enquanto que aos 180 minutos foi 26,8%, 29,6% e 27,6%, respectivamente para controle, VIP e PACAP27 ($p > 0,05$) (Tabela-2). Os demais parâmetros de motilidade, isto é, velocidade curvilínea, linearidade média, velocidade progressiva e deslocamento lateral da cabeça dos espermatozóides, analisados pelo computador, tam-

Tabela 2 – Análise da viabilidade dos espermatozóides por grupo estudado

Tempo (minutos)	Controle (%)	VIP (%)	PACAP27 (%)
0	33,5*	33,5*	33,5*
60	27,8*	29,2*	30*
180	26,8*	29,6*	27,6*

* $p > 0,05$

bém não demonstraram qualquer diferença entre os grupos ($p > 0,05$).

DISCUSSÃO

Existem muitas investigações sobre estimulação da motilidade espermática com o objetivo de aumentar as taxas de fertilização. A pentoxifilina produz uma estimulação in vitro dose-dependente da porcentagem de motilidade e da velocidade curvilínea (9). Este efeito pode ser causado pela inibição da AMPc-fosfodiesterase e também por aumento do AMP cíclico intracelular (9). Outras metilxantinas e fatores de ativação plaquetária podem também estimular os movimentos dos espermatozóides (9-11).

Existem 3 receptores de grande afinidade para o PACAP, espalhados no organismo: tipo I - específico para o PACAP27 e 38, e que fracamente apreende o VIP; tipo II (VIP 1) - não apresenta nenhuma diferença de afinidade entre PACAP e VIP (5); e tipo III (VIP 2) - está presente nos testículos (4). O hipotálamo contém as maiores concentrações destes peptídeos e seus respectivos receptores. Foram ainda identificados receptores em muitos outros tecidos, incluindo os testículos (1,12). Nos testículos, o PACAP foi localizado no interior dos túbulos seminíferos, nas espermátides próximas do lúmen, espermatogônias e espermatócitos primários (1,10,13), e também nas caudas de espermatozóides maduros (1). Através de radio-imunoensaio (imunoreatividade com um anti-soro específico), Li et al. (6) e Yanaihara et al. (14) localizaram PACAP nos acrossomas em desenvolvimento das espermátides, mas não em espermátides maduras. As células germi-

nativas mais maduras apresentam um grande número de receptores tipo I do PACAP27, principalmente nas suas caudas (1). A distribuição do receptor VIP II dentro dos túbulos seminíferos sugere um envolvimento com a maturação dos espermátócitos (10). O PACAP pode ainda modular a função das células de Sertoli (9,15).

Usando antagonistas do PACAP, Gozes et al. (16) demonstraram uma inibição da motilidade espermática, evidenciando o papel destes peptídeos na motilidade dos espermatozóides. Foi demonstrado que 200 nM de PACAP38, de PACAP27 e de VIP inibem a síntese de proteínas secretadas pela espermátide (5). O PACAP27 e VIP não apresentaram efeito sobre a viabilidade ou motilidade em geral dos espermatozóides, nesta série. Provavelmente o problema apresentado neste estudo está relacionado com a dose dos peptídeos, uma vez que os dados da literatura sugerem um efeito benéfico sobre a motilidade. Estes estudos com peptídeos devem ser desenvolvidos usando outras doses para tentar obter melhora da qualidade do sêmen descongelado.

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RESUMO

ESTIMULAÇÃO DA MOTILIDADE ESPERMÁTICA COM PEPTÍDIOS

A motilidade espermática é muito importante no processo normal de fertilização. Esta motilidade, após o descongelamento do sêmen, fica muito prejudicada e representa um problema, mesmo para alguns dos processos de fertilização assistida. Até agora poucos avanços ocorreram neste campo, através do emprego de pentoxifilina e fator de ativação de plaquetas. O polipeptídeo pituitário ativador da adenilatociclase 27 (PACAP 27) é um peptídeo com capacidade de estimular a guanilatociclase, e pertence à mesma família do polipeptídeo intestinal vasoativo (VIP). Está presente na cauda dos espermatozóides e pode estar relacionado com a motilidade espermática. O objetivo deste estudo é estabelecer se o PACAP 27 e o VIP apresentam alguma ação sobre a motilidade espermática após o descongelamento do sêmen.

Foram misturadas 12 amostras de sêmen descongelado com peptídeos (PACAP 27 e VIP) com o intuito de melhorar a motilidade espermática. Avaliamos a viabilidade e a percentagem de motilidade espermática, bem como parâmetros de motilidade analisados por computador.

O índice de viabilidade no momento inicial foi de 33,5%, nos 3 grupos. Aos 60 minutos foi de 27,9%, 29,2% e 30% nos grupos controle, VIP e PACAP, respectivamente, e aos 180 minutos, foi de 26,8% no grupo controle, 29,6% no grupo de VIP e 27,6% no grupo do PACAP ($p > 0,05$). Quanto à motilidade, aos 60 minutos após a administração dos peptídeos ao sêmen, identificamos: 21,1% no grupo controle, 22,4% no grupo do VIP e 22,5% no grupo de PACAP ($p > 0,05$). E estes valores continuaram semelhantes aos 180 minutos também, isto é, 22,5%, 21,4% e 21,5% nos grupos controle, VIP e PACAP. Não houve diferença estatisticamente significativa em relação aos demais parâmetros de motilidade, avaliados por computador, entre os 3 grupos.

Concluímos que tanto o PACAP27 como o VIP não apresentam nenhum efeito sobre a viabilidade ou motilidade dos espermatozóides descongelados.

Unitermos: fertilidade, motilidade espermática, PACAP, polipeptídeo, VIP, espermatozóides
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RETROPERITONEAL SCHWANNOMA OBSTRUCTING THE URETEROPELVIC JUNCTION

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ABSTRACT

Schwannoma (neurilemoma) of the retroperitoneum is a rare lesion. This is the second case reported of retroperitoneal schwannoma causing obstruction of ureteropelvic junction. The patient is a 46 year-old man, presenting weakness backache without urinary symptoms. He was submitted to echography, intravenous pyelography and abdominal computed tomography scan. The imaging analysis showed a large retroperitoneal mass with benign characteristics and producing external compression of the left ureteropelvic junction. Nephrectomy was performed together with tumorectomy because there was close adhesion between the kidney and the tumor. The anatomopathological examination revealed benign schwannoma with degenerative characteristics (ancient schwannoma).

The presence of a large well-delineated complex cystic mass in deep soft tissues should rise the possibility of an ancient schwannoma. With multiple presentation and difficult preoperative diagnosis, it is important to recognize these tumors as benign with excellent prognosis so as to avoid unnecessary radical surgery.

Key words: retroperitoneal tumors, schwannoma, neurilemoma, ureteropelvic junction obstruction
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INTRODUÇÃO

Schwannoma (neurilemoma) é uma neoplasia capsulada originada da bainha do nervo, surgindo em qualquer idade, porém mais comum entre os 20 e 50 anos de idade e sem predileção por sexo. Os locais mais freqüentemente acometidos são a cabeça, o pescoço e as superfícies flexoras das extremidades, sendo pouco freqüente em sítios profundos, onde há predominância pelo mediastino posterior e retroperitônio. Geralmente ocorre de forma solitária, porém lesões múltiplas podem fazer parte da neurofibromatose (doença de von Recklinghausen) (1).

O schwannoma situado profundamente geralmente cresce de modo silencioso, com grandes massas tumorais, que podem apresentar alterações degenerativas intensas, fenômenos estes que incluem a formação de cistos, hemorragia, calcificações e hialinização. Tal lesão é denominada de schwannoma ancião ou neurilemoma degenerado (2).

O presente trabalho descreve as particularidades diagnósticas e terapêuticas deste caso, e em nosso conhecimento é o segundo descrito na literatura (3).

RELATO DE CASO

Paciente de 46 anos, masculino, procurou o serviço de urologia para avaliação prostática, porém relatou dores lombares ocasionais à esquerda de leve intensidade. Negava antecedente de urolitíase ou sintomas urinários. Ao exame não se detectou massa abdominal palpável e o toque prostático foi normal. A ultra-sonografia de vias urinárias mostrava cálculos em cálices renais médio e inferior à esquerda, ectasia moderada do sistema coletor e massa de aproximadamente 8 cm anexa ao pólo inferior do rim. A urografia excretora confirmou cálculos calcínicos, com dilatação pielocalicinal moderada associada a deslocamento lateral da junção uretero-piéllica à esquerda por efeito de massa. A tomografia computadorizada demonstrou



Figura 1 – Aspecto tomográfico de massa encapsulada comprimindo a junção uretero-piélica.



Figura 2 – Superfície de corte da neoplasia aderida à junção uretero-piélica. Notar as áreas de degeneração cística e de hemorragia na lesão.

formação expansiva de 8 x 6 cm, capsulada, com espaços císticos e calcificações, e rechaçando lateralmente o rim esquerdo e comprimindo a junção uretero-piélica na face ínfero-medial do rim. Não foi observada linfadenomegalia (Figura-1).

Com suspeita de tumor retroperitoneal benigno, foi indicado ressecção cirúrgica por via lombar. Devido a aderência da massa na junção uretero-piélica, optou-se pela retirada em bloco (rim e tumor).

O exame anatomopatológico mostrou massa encapsulada medindo 7 x 5 cm, de consistência

elástica com espaços císticos. Achava-se aderida à junção uretero-piélica causando dilatação difusa do sistema pielocalicinal onde foram detectados 3 cálculos (Figura-2). Na microscopia o tumor exibia cápsula fibrosa formada por epineuro e áreas periféricas com neoplasia benigna constituída por células fusiformes, constituindo corpúsculos de Verocay (schwannoma tipo A de Antoni) (Figura-3A). Outras áreas eram formadas por matriz mixóide frouxa, com áreas císticas e proliferação vascular (schwannoma tipo B de Antoni) (Figura-3B). O rim

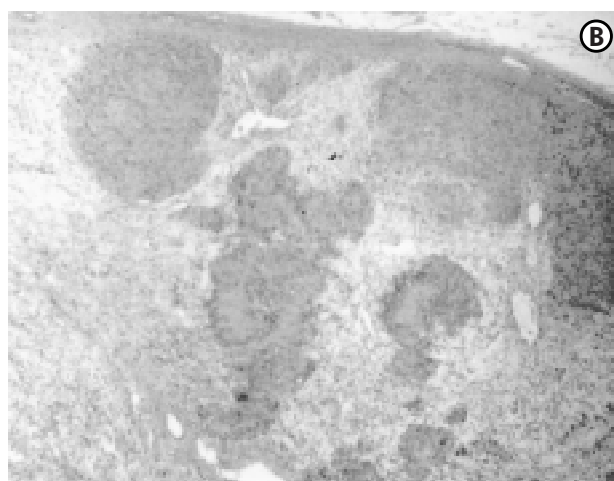
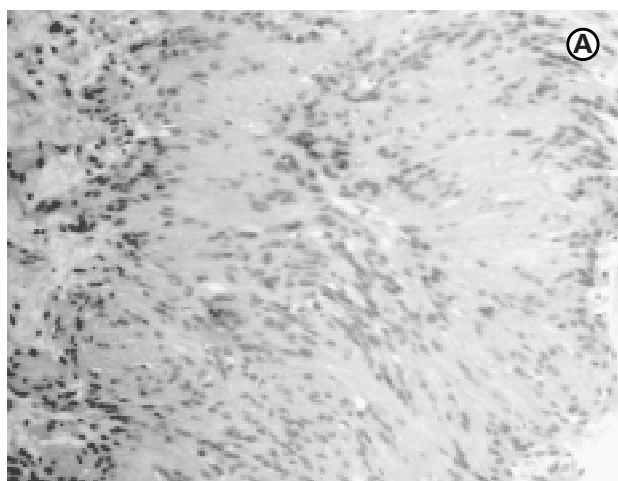


Figura 3 – A) Detalhe microscópico de área típica do schwannoma tipo A de Antoni, com células em “paliçada” circundando fibrilas neurais (HE, X40).

B) Concomitância dos padrões tipo A e B de Antoni; as áreas de aspecto mixóide e degenerado são vistas nas regiões mais profundas (HE, X40).

mostrava alterações atróficas e inflamatórias decorrentes da hidronefrose e nefrolitíase. O paciente evoluiu bem no pós-operatório.

COMENTÁRIOS

O schwannoma é um tumor de crescimento lento, sendo dor ou comprometimento neurológico manifestações tardias somente quando a lesão atinge grandes dimensões e causa compressão de estruturas vizinhas. É uma neoplasia benigna de prognóstico favorável cujo tratamento implica na ressecção cirúrgica total do tumor. Formas malignas são raras e normalmente associadas com

neurofibromatose, onde as lesões podem ser múltiplas, sendo importante avaliar no paciente outros sítios possíveis de aparecimento de lesões, como mediastino e mesentério.

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BLADDER UROTHELIAL CARCINOMA WITH TROPHOBLASTIC DIFFERENTIATION

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ABSTRACT

Although β -human chorionic gonadotropin (β -HCG) immunoreactivity can be found in neoplastic urothelial cells, morphological trophoblastic differentiation of human urinary bladder carcinomas is extremely uncommon. In some cases, the evolution to choriocarcinoma is well documented.

We report a case of a 65 year-old man who died of extensive metastatic spreading 6 months after the diagnosis of a high-grade papillary urothelial carcinoma. After necropsy, it was verified that the primary tumor contained areas of trophoblastic and squamous differentiation. The immunohistochemical study indicated that the trophoblastic giant cells were positive for β -HCG. The other neoplastic cells showed frequent positivity for the carcinoembryonic antigen (CEA) and placental alkaline phosphatase (PLAP) and for high molecular weight cytokeratin (AE1/AE3) in the squamous component.

The trophoblastic differentiation has been referred to be associated with aggressive behavior of the urothelial neoplasm. This report indicates the potential of neoplastic urothelium to develop divergent differentiation and suggests that primary urinary bladder choriocarcinoma may develop through metaplasia.

Key words: bladder, urothelial carcinoma, trophoblastic differentiation, choriocarcinoma

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INTRODUÇÃO

Os carcinomas uroteliais de bexiga podem mostrar diferentes tipos de diferenciação terminal e, portanto, aspectos histológicos variados. Raros carcinomas apresentam diferenciação trofoblástica, sendo que em alguns deles a evolução para coriocarcinoma está documentada. A diferenciação trofoblástica está associada à maior agressividade da neoplasia e, conseqüentemente, pior prognóstico. A produção de β -gonadotrofina coriônica humana (β -HCG) pelos carcinomas uroteliais é freqüente e não necessariamente associada à diferenciação trofoblástica (1-3).

Neste artigo é relatado o caso de um paciente do sexo masculino com carcinoma urotelial papilífero de alto grau com áreas de diferenciação trofoblástica e epidermóide, além de extensa disseminação metastática. Este relato documenta a capacidade do urotélio neoplásico originar diferentes li-

nhagens celulares, sugerindo gênese metaplásica para os raros coriocarcinomas primários da bexiga.

RELATO DO CASO

Paciente masculino com 65 anos apresentou-se com carcinoma urotelial papilífero de alto grau, infiltrando o meato ureteral esquerdo e o tecido conjuntivo da parede homolateral da bexiga (estádio pT1NxMx). Após o diagnóstico, não retornou para tratamento. Após 6 meses foi readmitido caquético, desidratado, com ascite volumosa e insuficiência renal aguda. Evoluiu para coma, falecendo menos de 24 horas após a internação.

Na autópsia, o carcinoma vesical (estádio pT3aN0M1) tinha aspecto pouco diferenciado, com numerosas figuras de mitose e áreas de necrose e de diferenciação trofoblástica e escamosa. As áreas de diferenciação trofoblástica eram caracterizadas por células gigantes multinucleadas, com núcleos bizar-

ros, associadas a células mononucleares e canais vasculares (Figura-1). O estudo imuno-histoquímico mostrou que as células gigantes eram fortemente po-

alcalina placentária (PLAP), e para citoceratina de alto peso molecular (AE1/AE3) no componente escamoso.

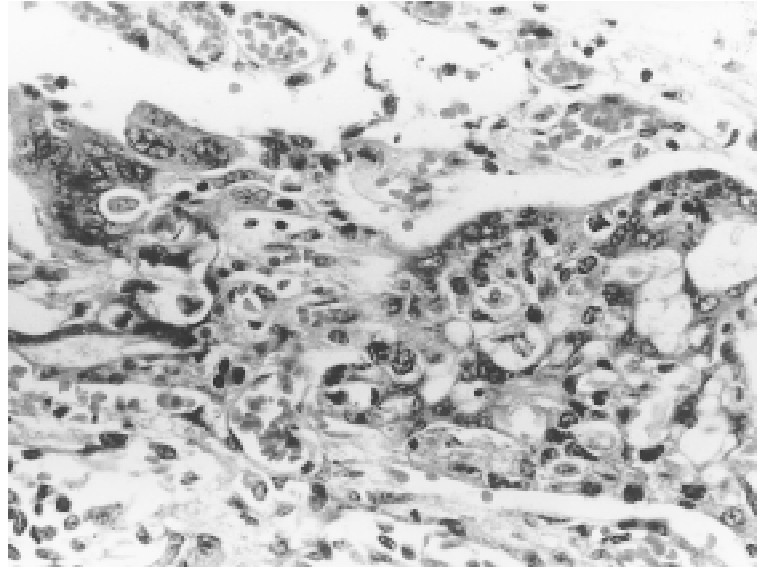


Figura 1 – Componente sinciotrofoblástico do carcinoma urotelial de alto grau (HE, X400).

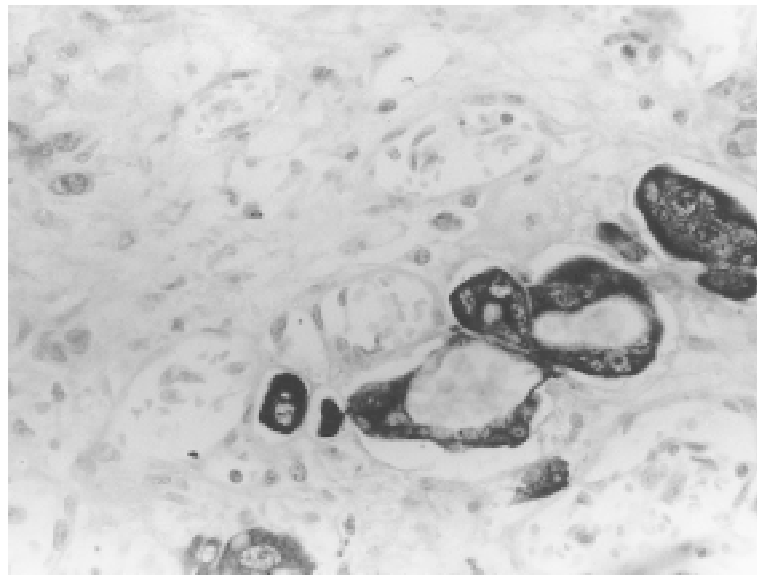


Figura 2 – Expressão de sub-unidade beta de gonadotrofina coriônica (β -hGC) pelo componente sinciotrofoblástico do carcinoma (imunomarcção, X400).

sitivas para β -HCG (Figura-2). As demais células neoplásicas mostravam freqüente positividade difusa para antígeno carcino-embriônico (CEA) e fosfatase

O fígado e a superfície abdominal do diafragma mostravam-se comprometidos por múltiplos nódulos metastáticos, constituídos por carcinoma

urotelial usual, com áreas papilíferas e de diferenciação epidermóide, de permeio a necrose.

DISCUSSÃO

Tumores vesicais com morfologia semelhante a coriocarcinoma e produção de β -HCG têm sido relatados raramente, e em geral associados a carcinomas uroteliais (1,2). No presente caso, o tumor primário era predominantemente indiferenciado, com áreas uroteliais e áreas de diferenciação escamosa e sinciciotrofoblástica, esta última caracterizada através de imuno-histoquímica pela positividade para β -HCG. Esta expressão é também vista em carcinomas uroteliais usuais sem diferenciação trofoblástica, de modo que foi sugerido que o carcinoma urotelial inicialmente produz β -HCG e depois desenvolve células trofoblásticas e coriocarcinoma (3). Em geral, a diferenciação trofoblástica está associada a metástases precoces e óbito, correlacionando-se com maior grau histológico e presença de metaplasia escamosa (1,3). O significado da expressão de β -HCG quanto ao com-

portamento agressivo de carcinomas uroteliais usuais é controverso (1,3). No presente caso, as metástases disseminadas e a rápida evolução para o óbito, corroboram as informações de que focos de diferenciação trofoblástica desenvolvem-se por metaplasia do carcinoma urotelial e quando presentes indicam pior prognóstico.

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CURRENT INDICATIONS FOR ENDOPYELOTOMY

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ABSTRACT

Results of endopyelotomy fall somewhat short of contemporary open pyeloplasty (67-95% versus 95-100%). As most endopyelotomy series using different techniques achieve approximately the same results, it appears likely that selection criteria play a major role. Risk factors have been identified: the presence of vessels crossing directly the ureteropelvic junction stands out as a major prognostic factor of outcome; the degree of hydronephrosis, the type of obstruction and renal function also play a role, although of lesser importance. Long avascular strictures and major alteration of renal function clearly contraindicate the procedure. In our view, the presence of a crossing vessel should be ascertained preoperatively as it significantly influences the outcome. Modern diagnostic techniques such as spiral-computed tomography, color Doppler and endoluminal ultrasonography have replaced the more invasive procedures such as angiography.

With careful attention to operative details, endopyelotomy produces outstanding results with minimal morbidity. The present development of retrograde techniques avoiding the morbidity of a percutaneous access and achieving comparable success are promising. We believe that with better definition of the indications one will further improve the outcome and match open pyeloplasty in well selected patients: in the absence of vessels crossing the UPJ and of massively dilated renal pelvis, a 95% success rate can be expected.

Key words: ureteropelvic junction, obstruction, treatment, endopyelotomy, indications

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INTRODUCTION

For many years open surgery has been recommended as the optimal therapy for ureteropelvic junction (UPJ) obstruction; of the existing operations, dismembered pyeloplasty still stands out today as the gold standard. Percutaneous surgery was developed in the early 1980's for the treatment of nephrolithiasis. Its intrinsic advantages of minimal invasiveness were rapidly perceived and applied to the management of UPJ obstruction. As of 1983 several reports of endoscopic management began to appear under various denominations, such as percutaneous pyeloplasty (1), pyelolysis, endopyelotomy (2) and endoureteropyelotomy (3). This last term "endoureteropyelotomy" was coined to underscore the impor-

tance of a combined ureteropelvic incision, as "endopyelotomy" sounded restrictive to the renal pelvis (pyelon).

The basic principle of these procedures consists of a full thickness incision of the narrow segment followed by prolonged stenting and drainage to allow regeneration of an adequate caliber ureter around the stent. This concept was first described in 1903 by the French urologist Joachin Albarran ("urétérotomie externe"), and was popularized by D. Davis in 1943 as an open procedure ("intubated ureterotomy"). Although confirmed by experimental and clinical data, this pioneer work remained under-exploited in UPJ obstruction because of the excellent results of open pyeloplasty, both procedures necessitating an open surgical approach. The devel-

opment of minimally invasive endourological techniques revived the interest in intubated ureterotomy, which could at that time be performed percutaneously. With continuing progresses in endourology, refined techniques designed to further reduce the operative morbidity were developed, such as the retrograde approaches performed either under direct endoscopic vision by ureterorenoscopy or under simple fluoroscopic control [balloon dilation (4) and rupture (5) as well as the “cutting balloon” or Acucise] (7-12).

Reported success rates for such procedures vary from 50 to 98%, but remain inferior to open pyeloplasty. Nowadays enthusiastic endourologists do not hesitate to recommend endopyelotomy as the primary procedure for every UPJ obstruction management, estimating that inherent advantages far compensate for the inferior results. There is an obvious divergence of opinion between those proponents of unselected indication of endopyelotomy and the persistent reluctance of the general urological community (13). In our view, success appears to depend more on selection factors than on the type of operation or on technical variations, thereby underscoring the importance of prognostic factors determination (14). In this paper we will review the factors influencing the outcome of endopyelotomy and from there make suggestions for the optimal indications of the procedure.

We believe that careful preoperative evaluation of risk factors is the best way to make endopyelotomy accepted as a first therapeutic option in UPJ obstruction (15,16).

SIGNIFICANT RISK FACTORS

Crossing Vessels

In our experience, the presence of vessels crossing the site of the UPJ and the degree of hydronephrosis are the most significant factors influencing the outcome of endopyelotomy. The significance of vessels crossing the ureteropelvic junction (UPJ) remains a matter of debate: their exact role in the pathogenesis of the obstruction, as well as their influence on the outcome of various therapeutic procedures are still contro-

versial. We published an extensive historical review in 1996 (17).

In 1994 we showed that crossing vessels bore a statistically significant negative influence on the outcome of endo(uretero)pyelotomy in a totally unselected prospective study enrolling 87 consecutive patients presenting with symptomatic UPJ obstruction between 1986 and 1989 (18). Sixty-seven adults underwent a systematic preoperative angiographic study and endoureteropyelotomy was performed regardless of its results. In 26/67 patients (39%), vessels were demonstrated in close contact with the site of the obstruction. The presence of crossing vessels reduced the final success rate from 86 to 42%. The degree of hydronephrosis was also a negative factor, but of lesser significance. The influence of the combination of both factors was highly significant on final outcome, with a 95% success rate when there was no crossing vessels and a moderate degree of hydronephrosis, and only 39% when crossing vessels were associated with high grade hydronephrosis (odds ratio = 28.29, 95% confidence interval 24.91; 31.66, $p < 0.001$). We later reported on the preoperative vascular surroundings in 85 patients with a follow up extending more than 12 years (mean 6.5 years) (19). The importance of these prognostic factors was confirmed: the success rate was 33% and 82% with and without crossing vessels respectively. Crossing vessels were present in only 18% of successful cases as opposed to 67% of failures. Moreover significant crossing vessels were demonstrated in 15/18 patients undergoing secondary open pyeloplasty for endopyelotomy failure; concomitant high-grade hydronephrosis was present in 13 instances. Our latest results were presented at the 17th World Congress of Endourology, and our conclusions are unchanged with 111 patients having had a detailed investigation of their vascular anatomy (Table-1) (20). As our proactive search for significant crossing vessels continues, spiral CT and color Doppler ultrasonography - either simple or contrast enhanced - have presently replaced angiography (21-23).

Others have also commented on the negative influence of crossing vessels, although without statistical evidence (24-26). Bogaert et al. (11) report a high success rate of retrograde endopyelotomy in

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Table 1 – Success rate of endopyelotomy according to prognostic factors: vessel crossing UPJ and degree of hydronephrosis (form reference 20). Data presented at the 17th World Congress of Endourology, Rhodes, September 1999

Risk factors	No.	% Success
• Vessel absent and low-grade (1-2) hydronephrosis	41/46	89
• Vessel absent	66/80	82.5
• Low-grade (1-2) hydronephrosis	48/59	81
• Vessel absent and high-grade (3-4) hydronephrosis	25/34	72.5
• High-grade (3-4) hydronephrosis	31/52	60
• Vessel present and low-grade (1-2) hydronephrosis	7/13	54
• Vessel present	13/31	42
• Vessel present and high-grade (3-4) hydronephrosis	6/18	33

children, but state that open surgery remains the standard, particularly when crossing vessels are identified preoperatively; their only failure occurred in a patient with a crossing lower pole vessel. Bagley et al. (27) report a lower success rate when crossing vessels are detected preoperatively by endoluminal ultrasounds (27). In Cohen et al. experience (9), 1/2 unexplained failures after Acucise endopyelotomy occurred in patients with a crossing vessel. Figenshau et al. (28) reported a similar experience with percutaneous endopyelotomy in children. Lim & Walker (29) identified crossing vessels in 2/3 recurrent UPJ obstruction after pyeloplasty in children. At Washington University, Wolf et al. (30) observed that all four patients treated with laparoscopic pyeloplasty after failed endo(uretero)pyelotomy had vessels crossing the ureteropelvic junction. Similar findings were reported by Faerber et al. (10) with Acucise endopyelotomy: 3 of 4 failures re-operated by open pyeloplasty had vessels crossing the UPJ; they therefore recommend to obtain a spiral CT to identify crossing vessels preoperatively and to select another form of therapy when they are present. Although there is no dispute on the influence of crossing vessels on outcome, their relative importance remains a matter of debate. In a series of 401 percutaneous antegrade endopyelotomies, there were 60 failures; 54 were explored and crossing vessels were present in 13 or 24% of cases. The authors concluded that obstructing crossing vessels were potential factors of failure in only 4% of endopyelotomies and that preoperative

identification was not indicated (31). This difference can best be explained by patient selection. Our data are based on the prospective recruitment of every consecutive patient presenting with symptomatic UPJ obstruction during the study period and endoureteropyelotomy was performed regardless of the results of the preoperative work up for crossing vessels. This appears to be the closest one can get to do a randomized study, which is impractical to perform (32). Also in our population more than 80% of patients had a primary type of UPJ obstruction which has a higher likelihood of crossing vessels, whereas in the majority of other series only half of the cases are of congenital origin.

The argument that crossing vessels are present around the UPJ in as many as 71% of kidneys, and that, therefore, they cannot be detrimental to the success of endo(uretero)pyelotomy is not relevant (33,34). Those important and elegant data were obtained from anatomical studies on normal kidneys and clearly demonstrate their vascular anatomy, including their situation in relation to the UPJ, but bear no relation with the actual crossing of the junction in clear cut cases of UPJ obstruction (35). On the contrary, the literature on surgical pyeloplasty is replete with accurate illustrations relevant to UPJ obstruction, and confirms our findings at surgery in case of failed endo(uretero)pyelotomy (36).

The incidence of late failures or recurrences is diversely appreciated. Many authors found that failures occur early, and that late failures or recur-

rences are distinctly uncommon (31,37). A higher incidence of late failures or recurrences was noted in our series (18). Seven of the 18 failures occurred after one year; one even occurred more than 6 years postoperatively. That this might be due to inadequate follow up is unlikely, as all those patients had been followed according to a strict study protocol. As a matter of interest, the 2 patients with the longest time to recurrence (74 and 64 months) have a redundant amount of studies, one being a radiologist's wife (expert in ultrasonography), and the other a urology nurse. In our opinion, corroborated by our operative findings, those cases of late failure are very similar to the well known entity of intermittent hydronephrosis, where a crossing vessel is almost universally present (38); as previously mentioned, in 15 of the 18 failures treated by open pyeloplasty a crossing vessel was found.

These observations do not contradict the fact that long-term success has been achieved in many instances in the presence of crossing vessels. In those instances, we postulate that the operation succeeds in correcting both the intrinsic and the extrinsic factors of obstruction: the functional permeability of the UPJ is reestablished, and also the crossing vessels become somewhat fixed in a silent non-threatening position. In recurrences, we assume that either or both corrections are insufficient, or that the hypotonic renal pelvis is unable to recuperate a minimal function; at the slightest diuretic solicitation the renal pelvis balloons out and protrudes through the vascular window making recurrence inevitable.

The presence of vessels directly crossing the UPJ not only influences the final outcome, but is also a source of potential complications. Vascular complications of endo(uretero)pyelotomy can be significant, and although seldom mentioned and possibly under-reported in the literature, they remain a constant preoccupation to both patient and endourologist (24,39). Because they are rare in some authors' experience, this illustrates their expertise in technique as well as in patient selection (31,37); complications can nevertheless occur and are acknowledged as potentially serious (2). Careful visual inspection of the operative site in order to direct the incision away from pulsating vessels is in-

deed strongly advocated, and is a recognized advantage of endoscopic over blind techniques (37). Reported vascular complications have been summarized in our recent review paper (17); additional reports have been published. Malden et al. (40) described an arteriovenous fistula complicating antegrade endopyelotomy. Brooks et al. (24) needed to transfuse 4/22 (18%) of their endopyelotomy patients. Cohen et al. (9), Stroom et al. (41) and Wagner et al. (42) have each described significant bleeding from direct vascular injury after retrograde endopyelotomy. Cohen et al. (9) acknowledges a 10-15% risk of bleeding from crossing vessels, and suggests that full patient's information is warranted. Gelet et al. (12) reported 2/44 cases of significant bleeding after Acucise endopyelotomy, one originating in an arteriovenous fistula of a crossing vessel. Recent reports confirmed the potential for complex and potentially life-threatening complications after Acucise endopyelotomy: 4% significant bleeding in the report of Kim et al. (43), and 4 vascular lesions in 52 cases (8%) in Schwartz & Stoller's experience (44).

Those data are judged of sufficient importance to justify preoperative documentation of crossing vessels, and the selection of an alternative therapy when they are present (especially when associated with high grade hydronephrosis), at least until one can determine with accuracy which crossing vessels are truly significant, or which renal pelvis will fully recuperate its tone (15,17,23,41,45). Following those guidelines, hemorrhagic complications have all but disappeared and success rate has dramatically increased; Quillin et al. (21) reported the absence of failures in patients without crossing vessels documented by spiral CT. Similarly several authors obtained a success rate of almost 100% in the confirmed absence of crossing vessels (26,46).

The documentation of crossing vessels has the additional benefit to improve postoperative follow up planning, as the risk of long term recurrence increases when crossing vessels are present; moreover, several diagnostic techniques (angiography, spiral CT) reliably detect vessels crossing the contralateral UPJ, which might be advantageous in the follow up of a syndrome that can be bilateral in as many as 10% of cases (20,21).

Degree of Hydronephrosis

By essence endourologic procedures can only address intrinsic factors of obstruction, and extrinsic factors cannot be corrected by a strictly endourologic technique; in addition they cannot reduce the size of a massively distended renal pelvis. From early experience the negative influence of the size of the renal pelvis on the results of endopyelotomy was suspected (3,47). A careful analysis of prognostic factors in our prospective series proved that the degree of hydronephrosis was of statistical significance when combined with the presence or absence of crossing vessels: in the presence of crossing vessels, the risk of failure was more than tripled by high grade versus low grade hydronephrosis; the final success rate was found to drop from 81% to 54% when high grade hydronephrosis was present. In a recent review of 401 percutaneous antegrade endopyelotomies from a single Institution, the overall success rate was 85%; high grade hydronephrosis as well as poor renal function were significant causes of failure: patients with massive hydronephrosis had only a 50% success rate compared to 96% for those with moderate hydronephrosis (31). Unfortunately in this monumental study no correlation with crossing vessels can be drawn as any systematic data have been obtained.

Length of Stricture

Long avascular strictures, total obliteration of the ureteropelvic junction and severe periureteral fibrosis are clear contraindications to endourological procedures; they should be treated by open repair. Although isolated cases may have been successfully managed, global results are in general unsatisfactory (3,25,47-51).

Renal Function

Renal function is a significant prognostic factor. A high risk of failure has been reported when the function of the affected kidney is greatly impaired (30,49,52,53). Unfortunately the isolated impact of this factor is difficult to assess as no prospective data have been collected. In most series preoperative function of the involved kidney has been systematically assessed only recently and in selected cases, and its influence cannot be dissociated from that of the degree of hydronephrosis (30,54).

NON SIGNIFICANT RISK FACTORS

Type of Obstruction:

Primary versus Secondary UPJ Obstruction

Initially, only secondary cases of ureteropelvic junction obstruction were considered ideally suited for endopyelotomy, as the endourological procedure avoided a difficult open reintervention and did not interfere with the delicate periureteral vasculature that could be injured by open dissection. It was later recognized that primary cases of UPJ could also be treated endoscopically, and commendable success rates have been achieved. In most recent series, secondary cases of UPJ obstruction appear to respond slightly better to antegrade endopyelotomy: a cumulated success rate of 84% is achieved, as opposed to 79% for primary type of obstruction (55).

Type of Procedure: Antegrade versus Retrograde Endo(uretero)Pyelotomy

The success rate of endopyelotomy appears to be independent of the type of surgical approach. Results of contemporary series of retrograde endopyelotomy compare favorably with antegrade percutaneous procedures; no difference is noted between procedures performed under direct ureterorenoscopic approach and indirect fluoroscopic control (4,56,57). Although simple dilation of the UPJ does not appear to be sufficient, at least in adults, growing evidence is showing that similar results on secondary UPJ strictures can be obtained with endoballoon rupture as well as with Acucise (1) endopyelotomy (6,8,57-59). Also with antegrade endopyelotomy, the invagination technique and the classical percutaneous technique have similar success rates (12,60,61). Neither does the type of incisional device significantly influence the outcome: similar results are obtained with laser incision, cold and hot knives, semi-lunar or hook knives. The type of stent and the experience of the surgeon (once the operative technique has been mastered) do not influence the outcome (18,31).

Age, Sex and Side of Obstruction

Pediatric experience was slow to accumulate; only limited and selected series are available for review and the procedure is not recommended

in small children (62). Recently however interesting results have been obtained in children older than age 4 with the Acucise balloon, especially in the absence of crossing vessels (11,29). Preliminary experience with smaller children is being reported with encouraging results (11,63,64). In a limited experience, simple balloon dilation appears to be sufficient, and disruption of the UPJ may not be required as it is in adults (65).

The place of endopyelotomy remains controversial in children and open pyeloplasty remains therefore the preferred procedure due to its consistently superior results, especially in primary cases, and to its better tolerance in this age group. In addition most cases are diagnosed very early in life, and surgical correction is recommended at a very early age, where endoscopy remains technically problematic. In secondary cases of UPJ obstruction such as failures of open pyeloplasty, endopyelotomy is however safe and effective and with further refinements and miniaturization of equipment, it may become a preferred option (28,63).

At the other end of the spectrum, in elderly patients, endopyelotomy offers results comparable to the adult group (64,66). Neither the sex of the patient, or the side of the obstruction influences the outcome (1,31).

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Results of endopyelotomy fall somewhat short of contemporary open pyeloplasty (67-95% versus 95-100%). As most endopyelotomy series using different techniques achieve approximately the same results, it appears likely that selection criteria play a major role. Risk factors have been identified: the presence of vessels crossing directly the ureteropelvic junction stands out as a major prognostic factor of outcome; the degree of hydronephrosis, the type of obstruction and renal function also play a role, although of lesser importance (16,55). Long avascular strictures and major alteration of renal function clearly contraindicate the procedure (48).

In our view, the presence of a crossing vessel should be ascertained preoperatively as it signifi-

cantly influences the outcome. Modern diagnostic techniques such as spiral-computed tomography, color Doppler and endoluminal ultrasonography have replaced the more invasive procedures such as angiography (22,23,67). When a significant crossing vessel has been documented, a classical endopyelotomy is likely to provide inadequate results especially in the presence of a large size renal pelvis. When a small artery or a venous channel is encountered, consideration can be given to transection of the crossing vessel (45,55). If a major vessel is present, we would prefer an alternative treatment, such as open or laparoscopic pyeloplasty.

CONCLUSION

With careful attention to operative details, endopyelotomy produces outstanding results with minimal morbidity. The present development of retrograde techniques avoiding the morbidity of a percutaneous access and achieving comparable success are promising.

Prognostic factors such as crossing vessels and high-grade hydronephrosis have been identified. We believe that with better definition of the indications one will further improve the outcome and match open pyeloplasty in well selected patients: in the absence of vessels crossing the UPJ and of massively dilated renal pelvis, a 95% success rate can be expected (20).

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ADDENDUM

ATLAS OF TECHNICAL CONSIDERATIONS ON ENDOPYELOTOMY MODALITIES
(From Reference 55)

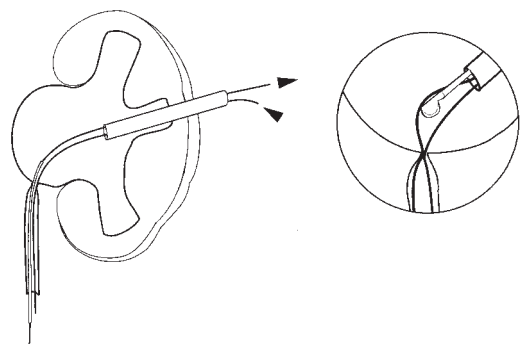


Figure-1: ANTEGRADE PERCUTANEOUS ENDOPYELOTOMY: CLASSICAL TECHNIQUE
In this technique, the UPJ is incised under direct vision until the peripelvic fat is clearly visible. A second guide wire is advantageous to straighten and stiffen the tissues: the cutting knife is literally railroaded on the track (3).

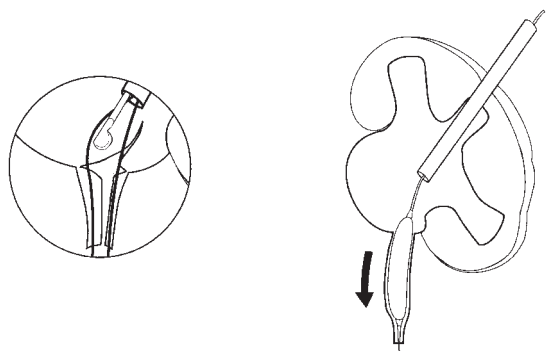


Figure-2: ANTEGRADE PERCUTANEOUS ENDOPYELOTOMY: INVAGINATION TECHNIQUE
A dilation balloon is inflated below the UPJ and attracted inside the renal pelvis by traction on the exteriorized guide wire, thereby invaginating the UPJ and the proximal ureter. The double layer of the renal pelvis and ureter is incised using an electrocautery and a small electrode (60). This technique facilitates the incision as the tissue is stabilized on the dilated balloon; it may also reduce the risk of damaging crossing vessels, although such complications have occurred (61).

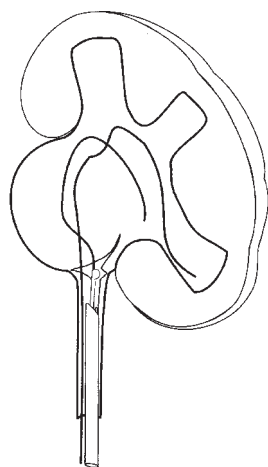


Figure-3: RETROGRADE URETEROSCOPIC ENDOPYELOTOMY
A small caliber ureterorenoscope is advanced up to the level of the UPJ and a postero-lateral incision is performed under direct vision. A preliminary insertion of a double-J stent remaining in-situ for two weeks greatly facilitates this maneuver, but adds to the complexity of the procedure, which remains technically difficult, especially in male patients (56).

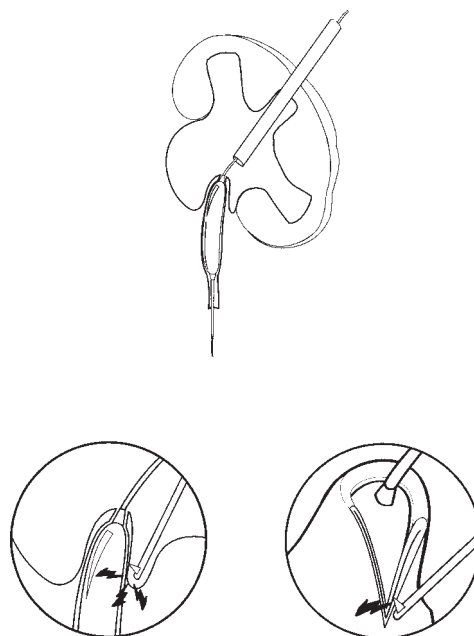


Figure-4: ACUCISE ENDOPYELOTOMY
The device consists of a low-pressure balloon fitted with an electrocautery wire active over the 2-cm expandable portion of the balloon. The UPJ is not forcibly disrupted, but cleanly cut by the wire that is activated during inflation of the balloon positioned across the UPJ (51).

TECHNIQUE OF PERCUTANEOUS ENDOPYELOTOMY

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ABSTRACT

Percutaneous endopyelotomy is an effective treatment for patients with ureteropelvic junction obstruction. This report describes the clinical presentation and preoperative evaluation for a patient with a UPJ obstruction. We describe the technical aspects of antegrade endopyelotomy in detail. The controversies regarding surgical technique and contraindications to treatment are presented. With percutaneous endopyelotomy, patients can expect up to a 90% success rate with little morbidity and minor disability.

Key words: ureteropelvic junction, stenosis, endopyelotomy, percutaneous surgery
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INTRODUCTION

Since the introduction of percutaneous techniques initially for the treatment of stones, the management of ureteropelvic junction (UPJ) obstruction has radically changed. Dismembered pyeloplasty remains the gold standard for treatment of UPJ obstruction, however minimally invasive procedures in the properly selected patient can provide excellent success rates with little patient morbidity. In comparison to other endoscopic treatments for UPJ obstruction, percutaneous endopyelotomy has consistently achieved success rates closest to those observed with open procedures (1-4). Patient selection, however, is paramount to the success of any treatment for UPJ obstruction (5). In this report we address patient selection, surgical technique, possible complications, success rates, and controversies associated with percutaneous pyelotomy.

The clinical presentation for patients with UPJ obstruction is varied. Classically, patients with UPJ obstruction present with flank pain often exacerbated by increased fluid intake and evidence of obstruction on excretory urogram. In this situation, we proceed to definitive treatment without additional

investigation. For less straightforward cases, we recommend additional testing that can include diuretic renograms, diuretic urograms, or Whitaker pressure-perfusion tests. Retrograde pyelography is sometimes obtained as the initial imaging test for patients with contrast allergies. In other instances, retrograde pyelography is completed as a confirmatory test prior to definitive treatment. We do not routinely assess patients with a primary UPJ obstruction for presence of crossing vessels. We do carefully review the imaging studies and laboratory reports for other abnormalities such as marked hydronephrosis and poor renal function as these factors can influence treatment outcome (1).

Other considerations, besides high-grade hydronephrosis and poor renal function, can also influence treatment of UPJ obstruction with percutaneous endopyelotomy. Long avascular strictures, total obliteration of the UPJ, and severe periureteral fibrosis are contraindications not only for percutaneous endopyelotomy but also for other endourologic techniques (6). Other contraindications include an uncorrected bleeding diathesis or untreated urinary tract infection. Patient age is not a contraindication to treatment, although the patient must be

a suitable candidate for either regional or general anesthesia. Patient size also does not preclude use of the procedure, however percutaneous endopyelotomy is less frequently used in the pediatric age group for treatment of a primary UPJ obstruction. Body habitus should be evaluated; the patient's anatomy should be such that percutaneous access is practical and safe. Furthermore, while presence of a horseshoe kidney may not preclude an attempt at antegrade endopyelotomy, (7) presence of a UPJ obstruction in other types of anomalous kidneys is sometimes best treated with open techniques. In fact, little information currently exists regarding use of any endourologic techniques for treatment of a patient with a UPJ obstruction in a duplicated or ectopic kidney (8). Use of antegrade endopyelotomy for patients with a secondary UPJ obstruction is also not a contraindication, but details of the previous procedure should be carefully reviewed prior to repeat surgery. Indeed, treatment of secondary UPJ obstruction has been associated with success rates at least equal to those observed with primary UPJ obstruction in prior reports (9).

Clinical history and results of imaging ultimately guide selection of the ideal patient for percutaneous endopyelotomy. In our experience, we believe percutaneous endopyelotomy is the best treatment when the UPJ is relatively dependent and no gross anatomic abnormalities are present (5).

SURGICAL TECHNIQUE

Percutaneous Access

Percutaneous endopyelotomy is completed with the patient in the prone position. To minimize risk of infection, all patients are given intravenous antibiotics prior to the procedure. Percutaneous access to the renal pelvis is completed optimally through an upper pole or middle pole calyx to aid visualization of the UPJ. After obtaining access, a wire is placed in antegrade fashion under fluoroscopic guidance across the UPJ obstruction, down the ureter, and into the bladder. Alternatively, in situations where antegrade guidewire placement is difficult, a guidewire can initially be placed in retrograde fashion. The guidewire, placed in retrograde

fashion, is then ultimately exchanged for a percutaneous wire after dilation of the percutaneous tract.

Placement of a guidewire across the UPJ obstruction is of critical importance since direct endoscopic vision of the renal pelvis is often unreliable to identify a pinpoint UPJ that not uncommonly is in an aberrant position. The percutaneous tract is dilated to 28-F in preparation for nephroscopic examination of the renal pelvis. During nephroscopic examination, the UPJ obstruction is inspected and all blood clots are removed. If any stones are present, they are removed prior to incision of the UPJ obstruction. If the guidewire was placed initially in retrograde fashion, this wire is grasped with the forceps and pulled through the nephroscope sheath. The wire is pulled out only a sufficient distance to allow placement of an open-ended catheter over the wire, across the UPJ, and down the ureter so that the open-ended catheter extends from above the nephroscope sheath to about the midureteral position. The original wire is then removed, and a new relatively rigid wire is passed down the catheter through the ureter and into the bladder. The wire that we prefer is a Lunderquist-Ring 0.038 torque wire. Since the endopyelotomy is completed over this wire, careful attention should be undertaken to prevent the wire from bending or kinking. In addition, the wire should be positioned well into the bladder so that a double-J stent is easily placed after endopyelotomy.

Endopyelotomy

At our institution, the endopyelotomy is completed with the cold cutting knife. This endopyelotomy knife is commercially available from Richard Wolf, Inc. and is designed for use in conjunction with standard nephroscopy equipment. While the endopyelotomy knives are sharp when they arrive from the supplier, we recommend that the knives be sharpened in the hospital machine shop prior to each use. The endopyelotomy knife is passed over the working wire and is seen under direct vision through the percutaneous nephroscope (Figure-1).

Before proceeding with the incision it is important to determine if the UPJ is wide enough to accommodate the knife. If the UPJ is not wide enough to accept the knife, the UPJ is balloon-dilated so the

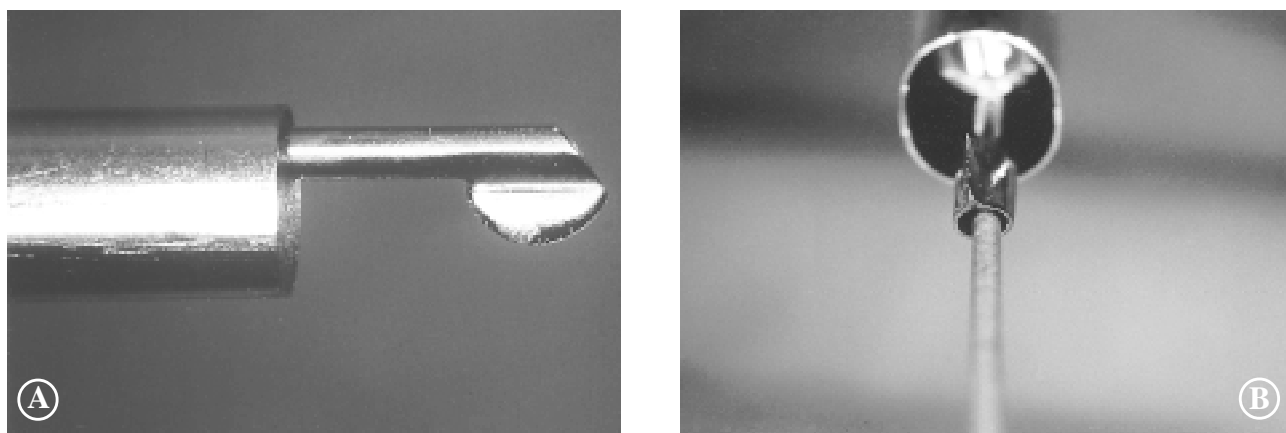


Figure 1 – A) Side view of commercially available endopyelotomy knife.
 B) The endopyelotomy knife is passed over the guidewire and used under direct vision.

knife can easily be passed through the UPJ. Gentle dilation of the UPJ in this situation is critical so that ultimately the knife cuts the UPJ smoothly rather than pushing the UPJ away. To decrease the likelihood of tearing the UPJ during dilation, a 12F ureteral dilation balloon is used rather than the larger 15F to 18F dilation balloons.

Placement of the endopyelotomy knife is then completed to allow incision of the UPJ in the due-lateral position. The lateral position is determined by orienting the knife to the lateral position of the patient's flank while referencing the position of the kidney on the excretory urogram or CT scan. The orientation of the cut is relatively easy to complete; however, in situations where the kidney is malrotated the orientation of the cut can be more challenging. The cut should also be made cautiously in patients that have previously undergone a failed UPJ repair. In this situation the vascular supply of the kidney relative to the UPJ may have changed. For example, if a patient previously underwent a dismembered pyeloplasty, the vessels are usually transposed posterior to the UPJ and the new cut should be made anteriorly.

After proper orientation, the knife is engaged under direct vision along the curve of the guidewire to allow a smooth, clean cut (Figure-2). Not uncommonly the guidewire will straighten as the cut is made. The incision should extend down the ureter at least one centimeter beyond the area of UPJ obstruction and should be continued laterally up into the renal

pelvis an additional one or two centimeters. By performing the incision under direct vision, the operator can identify the exact location and depth of the cut. In addition, extrapelvic structures such as aberrant vessels, often visualized by pulsation, can be identified and avoided. If significant bleeding is encountered at the time of the incision, allowing clot to form in the renal pelvis with subsequent vascular tamponade, typically controls hemorrhage. If arterial bleeding were to persist despite these measures, embolization may be required.

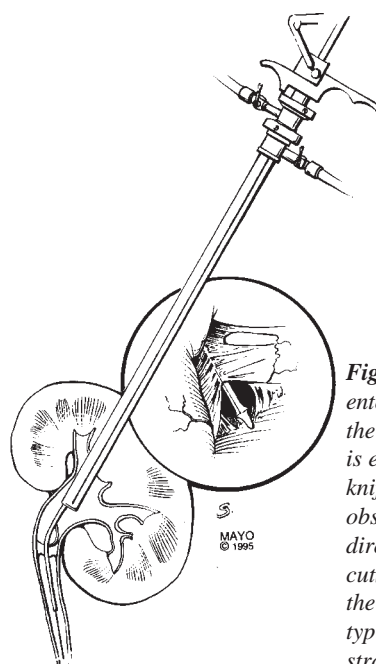


Figure 2 – The nephroscope enters the kidney through the upper pole and the UPJ is easily visualized. The knife will incise the UPJ obstruction laterally under direct vision. As the knife cuts the UPJ, the curve of the wire is followed and typically the wire is straightened in the process.

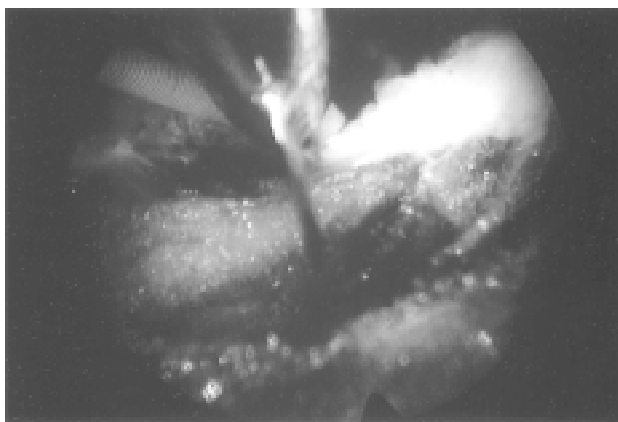


Figure 3 – The endopyelotomy should be completed so that peripelvic fat, seen in the lower half of the photo, is visualized.

The antegrade technique also allows for the endopyelotomy incision to be extended under direct vision with excellent precision. This ability is in contrast to blind techniques where the location of a repeat cut cannot be exactly determined. A full thickness incision of the renal pelvis and ureteral wall must be completed prior to removal of the endopyelotomy knife. Fat or wispy retroperitoneal tissue is visual-

ized after completion of a full thickness cut (Figure-3). In patients undergoing a second procedure, however, previous scarring can make determination of the proper incision depth more challenging. While balloon dilation is sometimes required to gently dilate the UPJ prior to endopyelotomy, balloon dilation is not indicated following endopyelotomy.

Stent Placement

Following completion of endopyelotomy, the knife is carefully removed to prevent inadvertent removal of the guidewire. Over the guidewire a double-J stent is placed. At our institution, we use an 8.0/8.5F standard stent. The stent is placed over the guidewire with a combination of fluoroscopic and visual control until the distal curl is clearly seen within the bladder. We use a 26-cm stent for increased flexibility in positioning the stent so that the distal curl is clearly seen in the bladder.

Postoperative Management

After placement of the double-J stent, a 22F nephrostomy tube is positioned in the renal pelvis.



Figure 4 – A) Preoperative excretory urogram for a middle-aged woman that presented with left flank pain. B) Excretory urogram of the same patient one year after endopyelotomy. The patient's flank pain has completely resolved.

The nephrostogram should reveal excellent drainage of the renal pelvis and some extravasation. While the nephrostomy tube is commonly left indwelling for 48 hours, a trial of tube clamping is completed prior to removal. If significant bleeding is encountered upon removal of the nephrostomy tube, the nephrostomy tube is immediately replaced and arteriography is arranged. The routine hospitalization for most patients is 2-3 days, however some patients have been dismissed much earlier. Most patients are able to return to normal activity one week after surgery. Patients return six weeks from the time of surgery for cystoscopic stent removal and an excretory urogram is completed three months after surgery to further assess the repair. All patients are then followed at periodic intervals for signs or symptoms of late failure. Percutaneous endopyelotomy is considered successful when the patient is asymptomatic and the excretory urogram shows improved drainage (Figure-4).

COMMENTS

Percutaneous endopyelotomy is a minimally invasive treatment with proven effectiveness for patients with UPJ obstruction. Advantages of antegrade endopyelotomy in comparison to open repair include shorter hospitalization, shorter operating time, decreased disability, and quicker return to work (1-4). While percutaneous endopyelotomy was initially offered to only patients with secondary UPJ obstructions, today the procedure is considered increasingly safe and effective for practically any patient with a UPJ obstruction (1-4,6-9). For patients with primary UPJ obstructions, success rates of 76-90% have typically been reported (1-4). Although intuitively one would expect that the treatment of failed previous repairs would be less successful, the results reported in the literature for secondary UPJ obstruction are similar to those reported for primary UPJ obstruction (8). Factors that undoubtedly influence the success of percutaneous endopyelotomy include the anatomic characteristics of the patient population, the surgeon's comfort level with the procedure, and postoperative surveillance protocols. Indeed, whereas some clinicians gauge success of treatment

on the basis of symptom improvement and appearance of postoperative excretory urography, other clinicians rely on more objective criteria to gauge treatment success (5).

Treatment failure generally becomes evident in the early postoperative period. Gupta et al. have reported only 8% of treatment failures occur after the first postoperative year (1). Kletscher et al. similarly reported all observed treatment failures at our institution occurred within the first 2 months after surgery (3). Long-term surveillance is required, nonetheless, as late failures do occur (5,6). The range of late failure rates and predisposing risk factors are poorly understood. Whereas the importance of crossing vessels is controversial, there is general agreement that marked hydronephrosis and poor renal function impact on the failure rate (1,6). Indeed, for patients with marked hydronephrosis, the physiology of the renal pelvis may still be abnormal and contribute to failure for some of these patients following endopyelotomy.

While antegrade endopyelotomy is associated with little patient morbidity, a variety of complications can be associated with the procedure. As with any surgical procedure, all patients are at risk for bleeding, infection, and anesthesia complications. The urologic complications of antegrade endopyelotomy in general fall into two categories: those related to percutaneous access and those directly related to the endopyelotomy. As with percutaneous stone surgery, the complications related to percutaneous access are frequently more varied and often more severe. Vascular injuries resulting in significant bleeding are the most worrisome complications associated with endopyelotomy (10). These injuries can occur during dilation of the percutaneous tract or during incision of the UPJ. The transfusion rates associated with percutaneous endopyelotomy vary from 1-6% (1-4,6,7,9). As the time required to complete endopyelotomy is shorter, complications related to fluid absorption are typically decreased. The incidence of urosepsis associated with endopyelotomy is 2-4% (10). Other previously reported rare complications unique to endopyelotomy include ureteral necrosis, ureteral avulsion, urinoma, inadvertent incision of the renal pelvis, and stent migration (10).

Despite excellent results and low overall morbidity, controversy does exist regarding various technical aspects of percutaneous endopyelotomy. With the introduction of spiral CT and endoluminal ultrasound, some investigators have stressed a preoperative evaluation for crossing vessels, whereas other investigators have not routinely favored this approach (1-3). In a recently reported series of 401 patients undergoing antegrade endopyelotomy, crossing vessels were attributed to only 4% of treatment failures, while extrinsic fibrosis was the most common cause of failure (1). Additional imaging studies may possibly improve the surgical approach to patients with ectopic or malrotated kidneys and to patients with secondary UPJ obstructions.

The method and orientation of the UPJ incision is also debatable. While we prefer use of the cold knife for endopyelotomy, others have reported equivalent success rates with other techniques including laser and electrocautery (5). We believe the surgeon has less control of the depth of the incision when using the Bugbee electrode rather than the cold knife. Previous reports have also suggested the risk of vascular injury may be increased with use of electrocautery (10). Based on the work of Sampaio et al. regarding the location of crossing vessels, we now advocate use of a lateral incision rather than a posterolateral incision (11). Obviously, the orientation of the incision is even more controversial when faced with treating an ectopic kidney, malrotated kidney, or secondary UPJ obstruction.

The issue of stenting has also been controversial. Initially a 14/7-F endopyelotomy stent was favored following the procedure. These stents were very difficult to place in the previously unstented ureter and did not appear to improve the success rate (3,5). Currently, the trend is to use smaller-caliber stents that are less expensive and easier to place. While many have recommended leaving a stent indwelling for 6 weeks after endopyelotomy, (1-3) other groups have removed stents earlier without untoward results at least in short-term follow-up (4).

Percutaneous endopyelotomy has become a procedure of choice for many patients with UPJ obstruction. Overall success rates up to 90% can be ex-

pected in a wide range of carefully selected patients (1-4,6-9). By avoiding patients with uncorrected bleeding diathesis, untreated infection, and anatomic abnormalities precluding safe access, percutaneous endopyelotomy is a safe, effective treatment for patients with UPJ obstruction that is associated with limited disability and minimal morbidity. As similar results have been noted for patients undergoing endopyelotomy with a variety of subtle technical differences, likely no specific technique of percutaneous endopyelotomy is superior and the primary factors determining success of the procedure are appropriate patient selection and effective release of the UPJ obstruction.

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TECHNIQUE OF ENDOPYELOTOMY WITH THE ACUCISE CUTTING BALLOON

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ABSTRACT

Historically, upper urinary tract strictures have been managed by open surgery. It was after the research studies by Davis in the early 1940's that clinical foundations for current endourological management were set. When describing his "intubated ureterotomy" Davis stated that a stented incision of the ureteropelvic junction (UPJ) took one week for complete epithelization and six for muscular regeneration.

Endopyelotomy has withstood the test of time and is currently considered first line therapy for primary and secondary UPJ obstruction in adults and secondary UPJ obstruction in children. Acucise endopyelotomy has the major advantage of being performed under fluoroscopic imaging without the need for ureteroscopy, thereby reducing the need for general anesthesia and prolonged hospitalization.

Herein we discuss the procedural aspects of Acucise endopyelotomy.

Key words: ureteropelvic junction, stenosis, endopyelotomy, Acucise balloon
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INTRODUCTION

Acucise endopyelotomy is based on the principle of the simultaneous dilation and incision of a ureteral stricture under fluoroscopic guidance. The Acucise cutting balloon catheter (Applied Medical Technologies, Laguna Hills, CA) incorporates both a monopolar electrocautery cutting wire and a low-pressure balloon. The balloon is used to define the area of stenosis and to carry the cutting wire into the area to be incised. The electrically active surface on the cutting wire is 2.8 cm in length and 150 mm in diameter. The device has radiopaque markers located on the catheter body, which assist in locating the position of the balloon and the cutting wire during positioning (Figure-1). The position of the cutting wire, in relation to the inside guide wire, facilitates alignment of the device prior to the incision of the stenotic area. The balloon is designed to accept a



Figure 1 – Placement of the Acucise cutting balloon catheter across the UPJ in a lateral orientation.

maximum of 2.5 cc of fluid. It is intended for use with fluoroscopy and designed to interface with presently marketed electrosurgical units.

SURGICAL TECHNIQUE

Need for preoperative stenting

Originally, due to the large size of the original Acucise catheter and the standard post-operative placement of a 7/14F endopyelotomy stent, preoperative stenting for passive ureteral dilation was highly recommended. Yet, the advent of the smaller Acucise RP (reduced profile) catheter and the achievement of equally successful long-term outcomes with the post-operative use of smaller stents, have obviated the need for pre-treatment stent placement. The Table-1 compares the characteristics of the first and second-generation Acucise catheters.

passage of the Acucise catheter and stent, directly through the cystoscope.

Technique

1)- An open-ended ureteral catheter is placed into the distal ureter, and a retrograde pyelogram is performed to define the area of stenosis at the UPJ. A guidewire is then advanced into the renal collecting system. If a regular ureteral guidewire cannot be passed beyond the UPJ, we have found that a “glidewire” is very helpful in negotiating the stenotic segment. Progression of the open ended stent into the renal collecting system allows for the exchange of the original wire for a super stiff guidewire since we have found that this more sturdy

Table 1 – Comparison between the characteristics of the first and second-generation (RP) Acucise catheters.

	ACUCISE	ACUCISE RP
Deflated balloon profile	13F	10F
Inflated balloon profile	24F	24F
Catheter size	7F	5F
Length of active cutting wire	3 cm	3 cm
Width of active cutting wire	150 micron	150 micron
Working length of catheter	40 cm	40 cm
Maximum inflation volume	2 cc	2.2 cc
Guidewire used	.035”	.028”
Generator setting	75 watts	75 watts
Preoperative stenting	Recommended	Not required

Equipment

Only basic cystoscopic equipment and real-time fluoroscopy are needed for this procedure. It is essential to have real-time fluoroscopy to visualize the markers and the cutting wire of the balloon to ensure that they straddle across the area of stenosis. C-arm fluoroscopy is useful in allowing rotational views of the cutting balloon within the ureteropelvic junction (UPJ) ureter, where the wire should be positioned in a lateral plane.

The Acucise balloon catheter will pass through a standard 25F cystoscope sheath. However, one must use a cystoscopic bridge which will accommodate the catheter, and if desired a 7/14F endopyelotomy stent. This bridge should not have any severe angles, allowing for straight, direct

guidewire provides better purchase for the passage of the Acucise catheter. A “safety” wire should never be used during the Acucise procedure, given the possibility of conducting electrical current from the cutting wire of the Acucise device, thereby potentially damaging a large portion of the ureter.

2)- The Acucise catheter is placed over the guidewire and passed through the cystoscope. Prior to insertion at the ureteral orifice, the Acucise catheter should be rotated under direct cystoscopic vision enabling the cutting wire to be positioned in the correct lateral orientation. This maneuver minimizes the need for rotation of the device once it has been placed across the ureteropelvic junction.

3)- The cutting balloon catheter is advanced over the super stiff guidewire until the UPJ stenosis lies between the two radiopaque markers. At the UPJ and in the proximal and mid ureter, the cutting wire is positioned **laterally** (Figure-1). Only in the distal ureter is the cutting wire activated in a medial position. Real time fluoroscopy is essential in the proper positioning of the catheter across the UPJ, in a lateral orientation.

4)- Once the wire is seen in the lateral position, the balloon is gently inflated with dilute contrast media to ensure correct positioning across the UPJ, demonstrated by a characteristic “waist” of the balloon (Figure-2). If the balloon waist is not seen, the Acucise device may have migrated cephalad into the dilated renal pelvis, or may have been positioned



Figure 2 – Gentle inflation of the Acucise balloon demonstrates a waist, which documents correct position of the device across the UPJ obstruction.

too distally. If waisting of the balloon is not seen, the balloon should be deflated, advanced or withdrawn, and re-inflated until a waist is identified. When confirmed, the balloon is deflated prior to activation of the cutting wire.

5)- After insuring proper grounding of the patient, the cutting wire is activated at 75-100 watts (pure cut) and simultaneously, dilute contrast is again instilled into the dilating balloon under continuous, fluoroscopic guidance. As the balloon inflates, the

stricture is incised. The waist of the stricture should disappear as the balloon progressed to full inflation (Figure-3). The cutting wire is typically activated for a total of 5 seconds during the initial cut. If a waist persists after instillation of 2.5 cc of contrast, the



Figure 3 – With activation of the cutting wire, the UPJ is incised, allowing full inflation of the balloon.

cutting wire may be reactivated for an additional 3-5 seconds. After completion of the incision, a retrograde pyelogram is performed through the Acucise catheter to confirm extravasation at the incision site (Figure-4). If extravasation is not confirmed, the Acucise catheter can be withdrawn distal to the UPJ, and a retrograde ureterogram performed. Once the adequacy



Figure 4 – Following deflation of the balloon, a retrograde pyelogram performed through the Acucise catheter demonstrates contrast extravasation, documenting a through-and-through incision of the UPJ.

of the incision is confirmed the balloon is repositioned across the UPJ and maximally inflated for 10 minutes to provide tamponade of the incised area. If extravasation is not confirmed, delivery of the electrical current to the cutting wire should be checked. Alternatively, ureteroscopy can be performed to visually inspect the UPJ and the incised area. Identification of fat through the incised UPJ confirms a through-and-through incision. The cutting balloon catheter is deflated and removed and a 7/14F endopyelotomy stent or a 7-8F internal stent is placed over the guidewire (Figure-5). Once the stent is in proper position, the bladder is evacuated and a Foley catheter is placed for 48 hours to prevent extravasation of urine into the retroperitoneum. We do not routinely perform a cystogram prior to removal of the catheter.



Figure 5 – An internal ureteral stent is placed into the renal collecting system. Extravasation is still documented at the site of the UPJ incision.

6)- The internal stent is removed at 6 weeks postoperatively with a flexible cystoscope in males or a rigid cystoscope in females.

7)- Patients return 12 weeks following stent removal for post-operative intravenous pyelography and/or differential renal scan with Lasix washout to confirm efficacy of the endopyelotomy. These studies allow the detection of early failures, thereby allowing salvage of an obstructed kidney. The majority of failures from the Acucise catheter have been discovered within 3 months of the procedure and late

failures (after 1 year) are generally uncommon. In the largest series of endopyelotomy patients reported thus far, 85% of failures occurred within 6 months, and 92% within the first year (1). However, a 10-13% late failure rate (i.e. > 1 year) has been reported independently by other investigators (2). We recommend, therefore, that the patient, who is asymptomatic, with improvement on postoperative IVP, should be followed yearly with an IVP for a period of 5 years.

Postoperative stenting

Recent reports have suggested that after endopyelotomy management of primary UPJ obstruction, stenting for less than 6 weeks with a 7F or 8F internal stent produce comparable results to those achieved by the placement of a “standard” 7/14F endopyelotomy stent for 6 weeks (3-5). However, it would seem that ischemic strictures (e.g. secondary UPJ obstruction) might benefit from a larger-sized stent (8F or larger) placed for the full 6-week course.

The different response to stent size and duration may be due to the fact that the underlying etiology in primary UPJ strictures is muscle derangement and in secondary strictures, is mostly a result of ischemia. Further randomized prospective studies are warranted to better define the optimal stent size and duration following endopyelotomy.

Complications

Since a “safety wire” should not be used during Acucise endopyelotomy, one must avoid “losing access” to the collecting system with the working guidewire after incising the UPJ. Regaining access may be quite difficult. Therefore, loss of the working wire with subsequent inability to place a stent would necessitate insertion of a percutaneous nephrostomy tube, or possibly conversion to an open surgical repair if a ureteral stent cannot be placed.

Prolonged hematuria of early onset (i.e. after removal of the Acucise catheter) is generally due to a vascular injury that may need to be managed with arterial embolization. Therefore, Acucise endopyelotomy is not recommended if access to a vascular radiology suite is unavailable.

A recent report has demonstrated the absence of crossing vessels lateral to the UPJ, and for this reason the **Acucise incision should allow be performed laterally** (6). Although a straight lateral incision should significantly decrease the incidence of post-operative bleeding after endopyelotomy for primary UPJ obstruction, the possibility of bleeding still exists and patients should be closely observed.

CONCLUSIONS

Although Acucise endopyelotomy does not provide the identical success rates as open pyeloplasty, this endourologic procedure is currently the preferred approach given its decreased morbidity, reduced operative time, shorter hospitalization, and overall decreased costs. Moreover, failure of this minimally invasive approach does not preclude performance of a successful open operative repair. Acucise endopyelotomy is currently our first choice for managing the majority of patients with ureteropelvic junction obstruction.

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TECHNIQUE OF LAPAROSCOPIC PYELOPLASTY

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ABSTRACT

Pyeloplasty remains the gold standard therapy in the treatment of ureteropelvic junction obstruction. Laparoscopic pyeloplasty provides a minimally invasive alternative to open pyeloplasty without compromise of treatment success or durability. Presented is the surgical technique of laparoscopic pyeloplasty.

Key words: ureteropelvic junction, obstruction, laparoscopy, pyeloplasty
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INTRODUCTION

A ureteropelvic junction (UPJ) obstruction is an impediment to urine flow at the junction of the ureter and renal pelvis that leads to progressive dilation of the collecting system. The condition can be primary or secondary and may not present until later in life. The "gold standard" therapy has been the open pyeloplasty with success rates consistently greater than 90% for all types (1). Endoscopic incision either in an antegrade or retrograde fashion provides a minimally invasive alternative, however has success rates of only 70-89% even in well-selected patients (2,3). Patients at high risk for failure include those with a large redundant renal pelvis, the presence of crossing vessels, or poor renal function (< 20%). In these cases, pyeloplasty has a clear advantage.

The first laparoscopic pyeloplasty was performed by Schuessler et al. (4) in 1993 as an alternative to standard open pyeloplasty performed through a flank incision. Initially there was some skepticism surrounding the technical feasibility, success and durability of the procedure. Recent studies however have shown overall success rates over 95% for primary obstructions (5).

INDICATIONS AND PATIENT PREPARATION

Radiographic evidence of a UPJ obstruction in conjunction with recurrent urinary tract infections, pain, deterioration of renal function or calculus formation are unequivocal indications.

In equivocal cases, a nuclear medicine examination with lasix washout may be helpful. A urine culture is obtained pre-operatively and any infection treated with appropriate antibiotics. The presence of calyceal stones previously was a relative contraindication, however pyelolithotomy can be safely performed in the same setting. If the patient has a stone in the renal pelvis, the stone should be removed percutaneously and the patient subsequently re-evaluated for UPJ obstruction. A mild bowel preparation with clear liquids and laxative is given one day pre-op and the patient is typed and screened.

TECHNIQUE

The patient is brought to the operating suite and cystoscopy with retrograde pyelography is performed to delineate ureteral anatomy and exclude distal stricture or filling defects due to calculus or

tumor. A ureteral double pigtail stent is then placed and correct position confirmed with fluoroscopy. We perform this portion with flexible cystoscopy with the patient supine so that minimal re-positioning is required for the next portion of the procedure. A Foley catheter is placed just prior to proceeding to the laparoscopic portion of the procedure.

Patient Positioning

The patient is moved to the flank position with the ipsilateral side rotated up approximately 20-degrees. An axillary roll is placed, pressure points are padded and the table is flexed slightly at the hips. The patient is secured to the table using wide cloth tape at the lower extremities, hips and shoulders. This allows for the patient to be rotated from a relatively horizontal position to the flank position by simply rotating the table. The surgeon and assistant stand on the contralateral side of the table and the scrub nurse

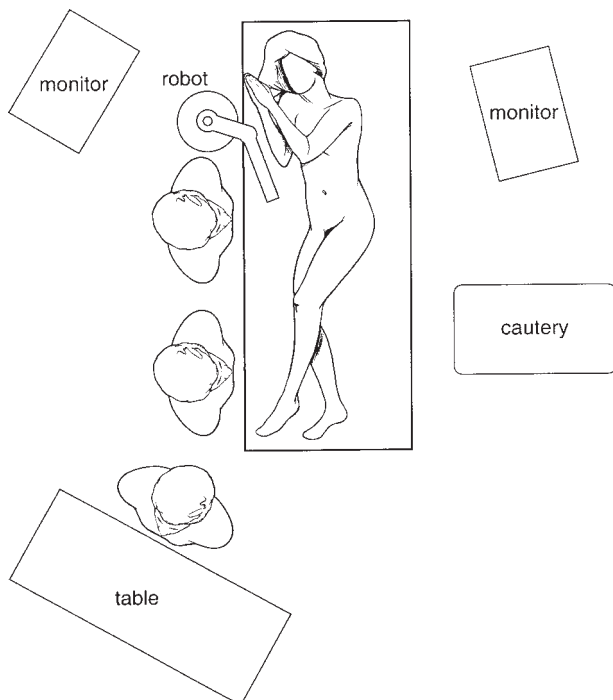


Figure 1 – Proper positioning for laparoscopic pyeloplasty. The patient is placed in a slight flank position with the hips and shoulders rotated 15 to 20-degrees. The patient is secured so that the table can be rotated to the full flank position after trocar placement.

at the feet (Figure-1). The abdomen and flank is prepped and draped in the usual sterile fashion.

Insufflation and Trocar Placement

Although both retroperitoneal and transperitoneal approaches have been described, the author's preference is transperitoneal due to familiarity and ease of exposure of the UPJ. Open port placement at the umbilicus or placement of the Veress needle can be performed with the patient in the horizontal position. Correct placement in the peritoneum is confirmed by aspiration with no withdrawal of air, urine, blood or fecal matter and maintenance of a low pressure (10-mm Hg) with slow insufflation. Following this step, three midline 10-12 mm trocars are placed

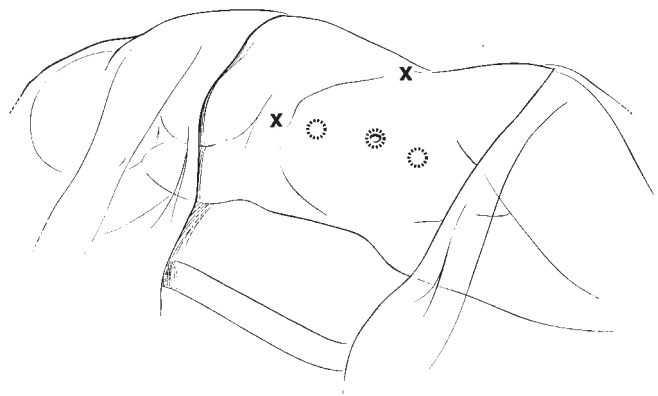


Figure 2 – Three midline 10-12 mm trocars are placed. Accessory trocars (X) can be placed in the mid axillary line at the level of the umbilicus for retraction of adjacent organs. For right-sided procedures, a midline accessory port can be placed just below the xiphoid for retraction of the liver.

as outlined in Figure-2. Although smaller trocars can be used, this configuration allows for passage of the camera as well as any instrument through any of the ports. Accessory trocars can be placed lateral to the rectus fascia at the level of the umbilicus for use by the assistant in retraction of adjacent organs. For right-sided repairs, a small midline trocar just below the xiphoid can be used for retraction of the liver.

Mobilization of the Colon

The patient is rotated from the horizontal to the flank position. Frequently, the hydronephrotic

kidney can be identified posterior and lateral to the colon. The posterior peritoneum overlying the kidney is divided from the upper pole to a distance approximately 3 cm below the lower pole. Care must be taken so as to not divide the lateral attachments of Gerota's fascia allowing the kidney to "flop" medially. The reno-colic ligaments are divided allowing the colon to passively move medially and provide clear exposure to the UPJ (Figure-3).

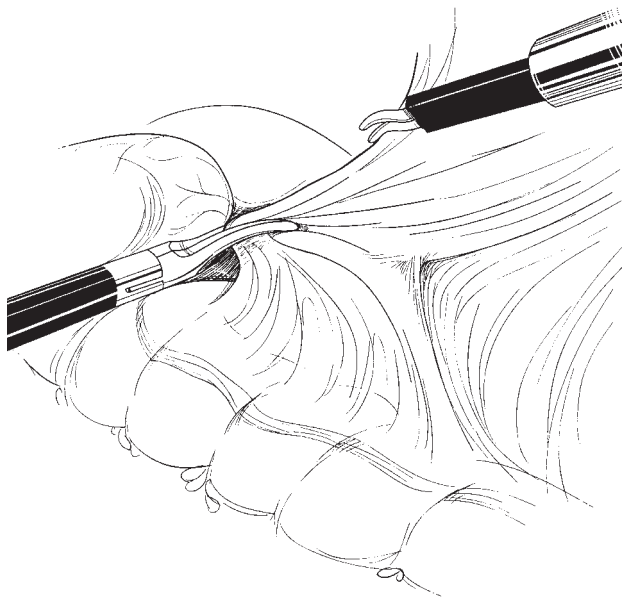


Figure 3 – The posterior peritoneum is divided. The colon is then mobilized medially by division of the renocolic ligaments. The UPJ is frequently seen at this point as a fluid filled sack.

Identification of the Ureter

The ureter is identified by following the psoas muscle to a point just medial to the lower pole of the kidney. The ureter can be distinguished from the gonadal vessels by peristalsis and by the presence of the internal stent. If a stent had previously been placed, this part of the case may be difficult due to marked peri-ureteral inflammatory reaction. Care should be taken to not strip the peri-ureteral tissues (and blood supply) except at the level of the UPJ. Once the ureter has been identified, it is freed in a cephalad direction toward the UPJ.

A significant number of patients will have a crossing vessel, which may be inadvertently injured if not identified. At this point, the surgeon must commit to one of three following types of repairs: 1)- Anderson-Hynes dismembered pyeloplasty, 2)- Foley Y-V plasty or 3)- Fengerplasty (Heinke-Michuliz repair). Pyelolithotomy (discussed later) is performed if stones are present prior to proceeding to surgical repair.

Regardless of repair performed, the surgeon needs to ensure that the repair can be made without tension. Maneuvers to help decrease the distance between UPJ and ureter are the following: 1)- continued dissection of the UPJ and ureter (while maintaining its blood supply), 2)- freeing the kidney outside the capsule so that may be mobilized caudally and/or 3)- a nephropexy can be performed by suturing the renal capsule at the lower pole to the psoas muscle.

Anderson- Hynes Repair

An Anderson Hynes repair can be used with any type UPJ obstruction and is the technique of choice with a crossing vessel as the ureter can be divided and transposed anteriorly. To facilitate this repair the pelvis is dissected (Figure-4) so as to allow for optimal visualization and enough mobility to allow for a tension free anastomosis with the ureter. The scissors are used to divide the ureter at the UPJ. In the presence of a crossing vessel, the ureter is transposed anteriorly. With a large redundant pelvis, a reduction needs to be performed prior to final repair. The ureter is then spatulated on its lateral aspect (facing the medial aspect of the kidney). Although free hand intra-corporeal suturing can be performed, we have found this portion of the case facilitated by use of an intra-corporeal suturing device (Endostitch, US Surgical, Norwalk, CT). Three interrupted sutures (4-0 vicryl) are initially placed to properly align the repair. The first interrupted stitch is placed from extraluminal to intraluminal at the apex of the incision of the ureter and then from intraluminal to extraluminal on the most dependent portion of the UPJ (Figure-4). The ureter is then secured at the most cephalad portion anteriorly and posteriorly in a tension free fashion to the corre-

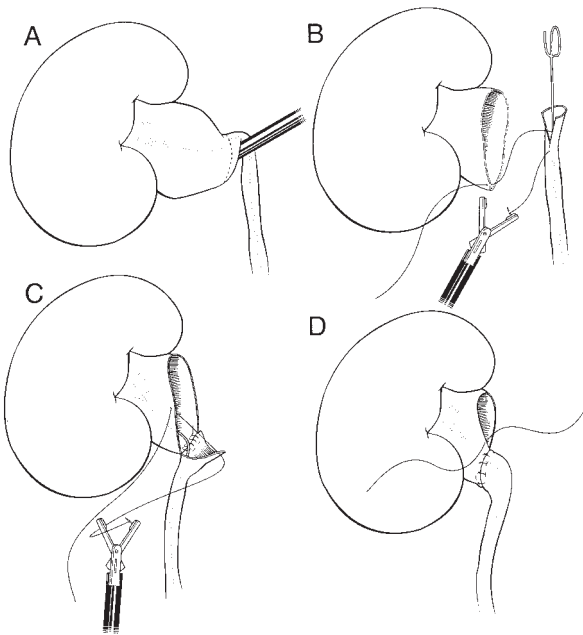


Figure 4 – Dismembered pyeloplasty.

- A) UPJ obstruction due to a crossing vessel. The UPJ is dissected for optimal visualization.
- B) The UPJ is divided and the ureter transposed anteriorly if a vessel is present. The repair is started by suturing the apex of the incision in the ureter to the most dependent portion of the UPJ.
- C) A second interrupted suture is placed at the most cephalad portion of the ureter (posterior aspect) and the gaps closed with additional interrupted sutures. This step is repeated for the anterior aspect of the repair.
- D) The remaining portion of the repair is closed with a running stitch.

sponding site on the pelvis. The repair is inspected and any gaps closed with interrupted sutures. The cephalad portion of the defect is closed with a running repair (Figure-4).

Foley Y-V Plasty

A Foley Y-V plasty repair can be used in the absence of a crossing vessel and is optimal for UPJ obstruction with a high insertion. The advantages of this repair are that it significantly reduces operative time and has less risk of devascularization of the UPJ. The success of the Y-V plasty depends on proper placement of the incision ensuring a broad-based flap of pelvis. Following incision the apex of the flap is advanced and secured with an interrupted suture ensuring no tension. The remain-

ing gaps are then closed in an interrupted fashion (Figure-5).

Heineke-Mikulicz Repair

A Fengerplasty is technically the simplest repair and can be used with a short stricture in the absence of a crossing vessel or high insertion. With this type of repair, abnormal ureter is identified and an incision created using scissors for a distance of approximately 7 mm above and below the stenosis. The incision is then closed in a transverse fashion using interrupted sutures to bring the caudal and cephalad portions of the incision together. The remaining gaps are then closed in an interrupted fashion (Figure-6).

Pyelolithotomy

Pyelolithotomy can be performed in the same setting for treatment of calyceal and non-ob-

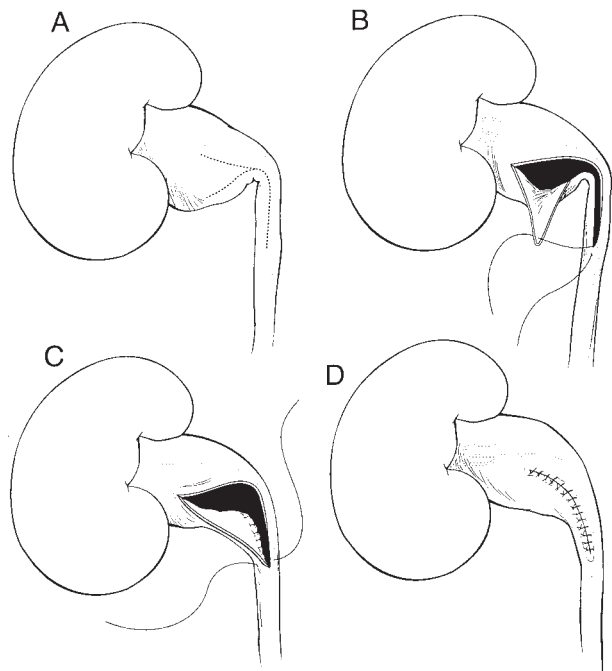


Figure 5 – FOLEY Y-V PLASTY

- A) The UPJ is inspected and a broad-based flap is mapped out.
- B) The incision is created as illustrated.
- C) The tip of the flap is advanced distally on the ureter and secured with an interrupted suture. The posterior aspect of the repair is then performed with interrupted sutures.
- D) The anterior aspect of the V is repaired to complete the procedure.

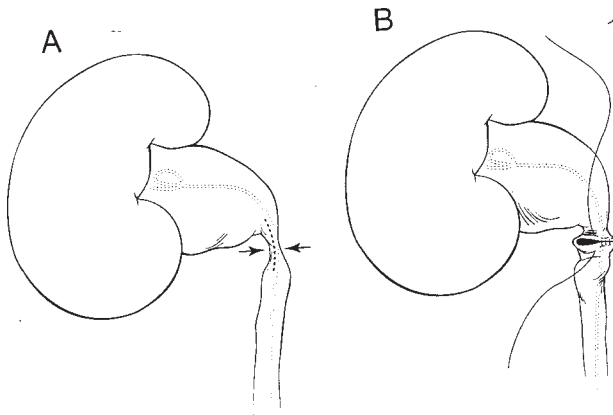


Figure 6 – Heineke-Mikulicz Repair

A) An incision is created as illustrated extending above and below the UPJ.

B) The incision is then closed transversely in an interrupted fashion.

structuring renal stones. Review of the pre-operative intravenous urography (IVU) and a plain film just prior to the procedure is helpful in delineating the exact number and location of the stones. For pyelolithotomy, an incision is created in the renal pelvis as needed for the proposed repair (i.e. Anderson Hynes, Y-V plasty). Many times the stones can be seen and grasped under direct vision. If not readily seen or located in peripheral calyces, a flexible cystoscope is passed through the upper port site and manipulated into the renal collecting system. A tipless basket (Cooke Urologic; Spencer, Indiana) or grasper is used for stone removal. If the stones are large then lithotripsy may be necessary. One should not proceed to repair until a stone free status is ensured.

At the end of the laparoscopic pyeloplasty, a 5 mm closed suction drain is placed at the posterior axillary line and positioned just posterior to the repair site and sutured in place. Trocar sites are closed and the patient is transferred to the recovery room.

POST-OPERATIVE CARE AND DRAIN MANAGEMENT

Strict outputs from the Foley catheter and retroperitoneal drain are recorded. If there is mini-

mal output from the retroperitoneal drain, the Foley is typically removed on post-operative day number two. The retroperitoneal drain is removed shortly thereafter if there is no increase in output. If there is persistent urine drainage from the retroperitoneal drain, the patient is sent home and educated on recording the outputs. The drains are removed when the above criteria are met.

FOLLOW-UP

The ureteral stent is removed in 4-6 weeks and an IVU is obtained two to three months post-operatively if the patient is without symptoms. Most failures will present in the first year

COMPLICATIONS

Complications related to laparoscopic pyeloplasty and their management are similar to those with open pyeloplasty. Intra-operative complications include bleeding that might require transfusion, injury to adjacent organs (bowel, liver, spleen and pancreas), conversion to an open procedure, adhesion formation, incisional hernia, infection or deep venous thrombosis. Postoperative complications include urinoma secondary due to persistent leakage and inadequate drainage.

COMMENTS

Laparoscopic pyeloplasty is a challenging but safe operation in the hands of an experienced laparoscopist. The advantages to the patient are optimal cosmetics, less post-operative morbidity leading to shorter hospitalization, less discomfort, and more rapid convalescence. Studies thus far indicate the approach is as efficacious as its open surgical counterpart when applied for the treatment of UPJ obstructions.

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EDITORIAL COMMENTS: CURRENT TECHNIQUES FOR TREATING URETEROPELVIC JUNCTION OBSTRUCTION

EDITORIAL COMMENT - I

The previous section deals with the newest modalities available for the treatment of ureteropelvic junction obstruction. With an emphasis on minimally invasive techniques, each article tries to provide a compelling argument for their particular method.

The paper by Gettman and Segura nicely summarizes the accepted technique of antegrade endopyelotomy. The authors discuss the use of the cold knife for the incision as well as laser and electrosurgical energies. There are the accepted risks of bleeding as with other incisional techniques. The antegrade approach gives the surgeon the best visualization and control of vessels that might be encountered of any of the minimally invasive techniques while also providing some of the best long term patency results. A relative disadvantage any antegrade technique is the presence of a draining nephrostomy tube.

The Acucise technique of endoureterotomy has been established as a safe and effective minimally invasive maneuver for the treatment of obstructed UPJ segments. Of the three methods discussed here, it is the least invasive although some control over exact site of incision is lost. In experienced hands the risk of severe bleeding is less than 1%. The Acucise technique is not without shortcomings however. Ureters with high insertions will do not do well with this method and there is also a risk of stent misplacement as there is not complete control using fluoroscopy alone.

In the paper by Jarret we are given the impression that laparoscopic pyeloplasty is a viable alternative to other minimally invasive therapies. In fact when all is well patients can often go home by 23 hours with an internal stent. Unfortunately the intracorporeal knot tying is quite difficult despite the Endostitch device. Though advances in laparoscopic urology are important, this operation in its current state is not a procedure for the general practicing urologist. It is also difficult to accept the argument that it is less invasive than an antegrade endopyelotomy.

A modality not presented in this series of papers is ureteroscopic endopyelotomy. Developments in ureteroscopic technology including the smaller quartz fibers for laser energy delivery and endoluminal ultrasound have lead to yet another minimally invasive technique for treating UPJ obstruction. Bagley (1) has been at the forefront of this approach and reports an 81% success rate. Identifying a crossing vessel using the ultrasound can guide the decision on where to make the incision with more accuracy. As with the Acucise technique there is still a risk of stent misplacement.

The financial aspects are also important to review. At one cost extreme there is the laparoscopic pyeloplasty. In general for the laparoscopic procedures to be financially justified, one expects that every extra hour operating should save a day in the hospital. At the other extreme it has been shown that the Acucise procedure can be performed in a relatively inexpensive radiology suite and patients can be discharged within six hours. Naturally cost is only one aspect of the choice of approach. As with all of these techniques, patient selection is the ultimate preoperative challenge. The poorly functioning or severely distended kidney is a poor candidate for almost any technique. To be well versed in many different techniques for the treatment of the obstructed UPJ can only help the patient.

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EDITORIAL COMMENT - II

Open operative intervention for ureteropelvic junction (UPJ) obstruction provides a widely patent, dependently positioned, well-funneled ureteropelvic junction. While the procedure has stood the test of time and offers a success rate exceeding 95%, several alternatives to standard operative reconstruction are now available that can provide this result in a less invasive manner. For all of these newer approaches, the advantages include a significantly reduced length of hospital stay and post operative recovery. However, for many of these procedures the success rate does not approach that of standard open pyeloplasty. Furthermore, while open operative intervention can be applied to almost any anatomical variation of UPJ obstruction, consideration for any of the less invasive alternatives must take into consideration individual anatomy including, but not limited to, the degree of hydronephrosis, overall and ipsilateral renal function, and in some cases, the presence of crossing vessels or concomitant calculi.

Three papers in this month's Brazilian Journal of Urology address many of these issues, and at the same time, provide detailed descriptions of three of the more widely accepted and utilized minimally invasive alternatives to standard open pyeloplasty.

Percutaneous endopyelotomy was first described over 15 years ago by Whitfield and Wickham as a percutaneous pyelolysis (1), and popularized in the United States by Smith (2) who coined the term "endopyelotomy". As noted by Gettman and Segura, in their paper regarding the technique of percutaneous endopyelotomy, this approach has provided success rates that generally exceed those of the Acucise balloon, but still do not compare to open operative reconstruction. The disadvantage compared to retrograde fluoroscopic and endoscopic techniques is the more invasive manner in which the ureteropelvic junction is accessed, that is, percutaneously rather than in a retrograde fashion via the ureter. As such, the length of hospitalization is marginally increased over that associated with the retrograde procedures. However, a clear indication for the percutaneous approach is the presence of upper tract calculi, which can then be man-

aged simultaneously. Again, the presence of crossing vessels need not be a major consideration as these can be identified during the endopyelotomy and avoided.

The technique is well described by these authors and has become a standard part of the urologic armamentarium. We have used a modification that involves placement of the endopyelotomy stent prior to the actual endopyelotomy incision, and have found that this tends to further define the ureteropelvic junction itself. With the stent in place, a Collins' knife or Bugbee electrode is used on a pure cutting current to cut down onto the stent in a fashion analogous to a ureteral meatotomy. In addition to further defining the site and orientation for the actual endopyelotomy incision, placement of the stent prior to actual incision has allayed our concern regarding potential disruption of the UPJ when trying to place a stent in an antegrade fashion following the incision itself.

Drs. Delvecchio and Preminger, describe their technique for use of the Acucise cutting balloon. This technique gained rapid acceptance in the United States because, as noted by Drs. Delvecchio and Preminger, only standard cystoscopic equipment is needed along with real-time fluoroscopy. The technique is readily learned with a short "learning curve" and the results are acceptable, though certainly do not approach those of open pyeloplasty. Contraindications to this technique include the presence of concomitant calculi which are not addressed with this procedure, and a long segment of stenosis, that is, greater than 2 cm in length.

An area of controversy is the presence of crossing vessels. While such vessels may not functionally impact on the overall success of the technique, many investigators feel they do present a risk of hemorrhage during this fluoroscopically guided procedure, and as such may represent a contraindication.

As initially described, the technique includes placement of a 14/7 French endopyelotomy stent at the completion of the procedure, and this is left in place for six weeks. As noted by these authors, most centers have reduced the time of stenting to four weeks

or even less. Furthermore, when large stents cannot easily be placed, especially in those patients who have not been pre-stented, equivalent results can generally be obtained with an 8 French stent.

The authors suggest that a true lateral incision should significantly decrease the incidence of post-operative hemorrhage, as vessels generally do not cross lateral to the UPJ. However, the risk of hemorrhage remains significant and is being reported with increasing frequency (3). As such, at our center, this technique has all but been replaced with direct vision ureteroscopic endopyelotomy utilizing a Holmium laser. The advantage of the ureteroscopic approach is that it allows direct visualization of the UPJ and assurance of a properly sited, full thickness endopyelotomy incision. If any vessels are encountered, these are easily visualized and avoided during the procedure. Another advantage of the ureteroscopic approach is a decrease in cost compared to use of the Acucise cutting balloon, at least when ureteroscopic equipment and a Holmium laser is already available. Even without the Holmium, equivalent results can be obtained with a small ureteroscopic Bugbee electrode using a pure cutting current.

Dr. Jarrett, in the last of these papers, describes the technique and results of a laparoscopic pyeloplasty performed at an experienced center. A laparoscopic approach, in the hands of such surgeons, can provide an excellent alternative both to less invasive and more invasive procedures. In contrast to endourologic management, this approach does allow an anatomic repair similar to that achieved with open

pyeloplasty. In comparison to open surgical intervention however, the hospital stay with a laparoscopic approach is generally shorter and the length of disability significantly reduced. Because an anatomic repair can be accomplished, the success rate approaches that of open pyeloplasty, and can exceed 95%. A laparoscopic approach is contraindicated in the setting of a particularly long segment of obstruction such that the proximal ureter and pelvis can not be brought together without tension. Another contraindication is the association of multiple caliceal stones, which may be difficult to access laparoscopically. With the increasing application of laparoscopic procedures in urology, laparoscopic pyeloplasty has the best chance of truly replacing standard open operative pyeloplasty.

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EDITORIAL COMMENT - III

The groups from Mayo Clinic, Duke University, and Johns Hopkins review their experience with treatment techniques for ureteropelvic junction (UPJ) obstruction.

With their vast experience at the Mayo Clinic, Drs. Gettman and Segura emphasize that the key to success is selecting patients properly. This not only applies to their discussion about percutaneous endopyelotomy but also to the other techniques. They note that for a poorly functioning kid-

ney and/or a massively dilated renal pelvis, surgery is often indicated. For percutaneous endopyelotomy, the Mayo Clinic group does not routinely assess preoperatively whether an accessory vessel or high insertion is present. They use a cold knife technique under direct vision rather than the Acucise® cutting balloon catheter. They note the critical anatomic work by Sampaio and colleagues regarding the location of crossing vessels and, therefore, make their incision laterally; it should be noted that these ana-

tomic studies show that the incision should be made lateral in reference to the kidney which is, in many cases, postero-lateral in relationship to the patient's torso. The overall success rate of eight reported studies is 90 percent for percutaneous endopyelotomy.

The technique or retrograde endopyelotomy utilizing the Acucise cutting balloon as detailed by DelVecchio and Preminger reflects the continued advancement in technologies with decrease in invasive procedures for the patient. The reduced profile balloon now allows retrograde ureteral access without preprocedural ureteral stenting. They also mention that the cutting wire is to be positioned laterally; again, however, it needs to be noted that this is lateral in relationship to the kidney, not necessarily the torso of the patient. Done properly the success rate approaches that of percutaneous endopyelotomy. Over 90% of failures occur within the first year. As with percutaneous endopyelotomy, an 8F ureteral stent is left in place for 6 weeks.

As reported by Jarrett, the technique of laparoscopic pyeloplasty adds one more advancement in decreasing morbidity and maintaining successful treatment of UPJ obstruction. The specific surgical technique used laparoscopically depends on whether or not a crossing vessel is present and whether or not

a high insertion is present. As with all new techniques, long-term success awaits further follow-up.

In summary, urologic techniques for dealing with UPJ obstruction continue to evolve resulting in decreased hospitalization and morbidity for the patient. Retrograde incision with the low profile Acucise® cutting balloon catheter offers low morbidity, short hospitalization, and high success rate for the majority of patients. For those patients in whom retrograde ureteral access cannot be accomplished or who have calculi in the pelviocalyceal system, percutaneous endopyelotomy offers high success and relatively low morbidity. Laparoscopic pyeloplasty will likely replace open surgery for those patients where neither retrograde Acucise® endopyelotomy nor percutaneous endopyelotomy is optimal.

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VOIDING DYSFUNCTION IN CHILDHOOD

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ABSTRACT

Objectives: Voiding dysfunction (VD) in children with no neurological disease can be related to the delayed maturation of the voiding reflex. The purpose of this work was to assess the clinical and radiological finds and the impact of the treatment on the VD in childhood.

Design: Fifty-seven children (aged 5 to 12 years) with VD were submitted to urinalysis, urine culture, creatinine, plain film (lumbosacral spine), renal ultrasonography, voiding cystourethrogram (VCUG) and urodynamic study (UD). Oxybutynin chloride (OC) or dicyclomine hydrochloride (DHCl) were used if indicated.

Results: Symptoms such as nocturnal enuresis (88%), urgency with urinary incontinence (84%), daytime urinary incontinence (61%) and intestinal constipation (51%) were common. Twenty-eight patients (49%) had recurrent urinary tract infection (UTI). Detrusor instability occurred in 62% of the 21 patients who performed UD. Thirty-six children underwent pharmacological treatment, 24 (67%) used OC and 12 (33%) used DHCl. Improvement or resolution of symptoms were obtained in 94% of those taking OC and in 67% of those with DHCl ($p < 0.05$).

Conclusion: In cases of VD we can establish pharmacological treatment based on clinical and laboratorial findings. However, when this was not successful or in those with recurrent UTI, the performance of UD, VCUG and ultrasonography (US) are imperative.

Key words: bladder, unstable bladder, oxybutynin, enuresis, infancy

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INTRODUCTION

Voiding dysfunction occurs in children neurologically normal (1,2) and can be related to the delayed maturation of the voiding reflex (1,3) Yeung et al. (4) studied newborn babies through continuous urodynamic examination and found detrusor instability in 5% of cases while 50% presented with vesico-sphincteric dyssynergia. This called in question a phase denominated as autonomic bladder, which characterizes normal neurological maturation of the voiding control in a child (3,5). The etiology of the voiding dysfunction is still unknown and its incidence may vary from 2 to 25% of children in toilet training (6-8). Frequency, urgency and enuresis (3,9-11) are the main symptoms of the voiding

dysfunction. Approximately 50% of urinary infection cases are related to detrusor instability (11) and 34% to vesicoureteral reflux (VUR) (11). Occult spina bifida (7) may occur in 38% of cases of voiding dysfunction. The value of this finding, though, is still controversial (12). VUR and urinary infection may cease successfully after voiding dysfunction treatment.

The aim of this study is to analyze clinical, radiological and treatment aspects of voiding dysfunction in childhood.

METHODS

Fifty-seven patients with voiding dysfunction were studied between June 1992 and De-

ember 1996. There were 36 girls (63%) and 21 boys (37%), ranging in age from 5 to 12 years old (average 8 years old).

The evaluation included clinical history, physical and laboratory examination (urinalysis, urine culture, serum urea and creatinine), lumbosacral spine radiography, VCUG, abdominal US and urodynamic examination. Either oxybutynin chloride (dose of 0.3 to 0.7 mg/kg taken orally, every 12 hours) or dicyclomine hydrochloride (dose of 0.5 mg/kg/ taken orally, once a day) were used in pharmacological treatment of vesical dysfunction. The results were considered good for resolution of the symptoms and moderate for cases of improvement. The results of the pharmacological treatment were analyzed by means of the X^2 (chi-square) test.

RESULTS

Symptoms such as nocturnal enuresis (88%), urgency with urinary incontinence (84%), daytime urinary incontinence (61%) and intestinal constipation (51%) were common. Neurological examination was normal in all patients.

Of the 28 patients (49%) with recurrent UTI, 17 (26%) presented signs of pyelonephritis. The urinary tract was evaluated by means of ultrasonography in 38 children (67%) whereas 50 children (87%) underwent VCUG. The main radiological findings were "spinning top" deformity in 22% (11 out of 50), vesicoureteral reflux in 28% (14 out of 50), bladder trabeculation in 16% (8 out of 50). Occult spina bifida was found in 9 cases (16%). Uninhibited contractions were found in 13 (62%) of the 21 patients (37%) who performed urodynamic study. Of the 36 (63%) children who underwent pharmacological treatment, 24 (67%) used OC and 12 (33%) used DHCl during 26 months (5-60 months) on average. Either considerable improvement or resolution of symptoms were observed in 23 children (94%) taking OC, in contrast with 67% of the cases treated with DHCl, with statistically significant difference ($p < 0.05$).

DISCUSSION

Detrusor instability is a benign condition, which occurs, in neurologically normal children. It is mainly characterized by the presence of nocturnal enuresis and urgency with incontinence, in addition to frequency and daytime urinary incontinence. Some cases may be asymptomatic (9).

In our study, nocturnal enuresis (88%), followed by urge incontinence (84%), was observed as the main symptoms. According to the literature, the incidence of enuresis is around 40% whereas urgency with incontinence varies from 17% to 40% (20,23). Persson-Jünemann et al. (18) observed detrusor instability in 68% of cases of nocturnal enuresis. Sixty-two percent of children showed uninhibited contractions (detrusor pressure > 15 cm of H_2O) in the urodynamic study. The literature, though, reports a variation from 31% to 52% of cases (20,21,23). Therefore, if one takes into consideration the urodynamic examination alone in order to confirm the diagnosis of instability, 38% to 69% of patients would not present such diagnosis as they did not show uninhibited contractions. We believe that the introduction of pharmacological treatment to the vesical dysfunction may be based on clinical symptomatology and laboratorial findings, reserving the urodynamic study either to those cases on which the treatment was not successful or to those with functional alteration of the urinary tract.

The incidence of UTI observed in our cohort of patients (49%) is similar to the one presented in the literature, varying from 36% to 50% of cases with voiding dysfunction (20,23).

The VCUG performed in 87% of patients detected VUR in 28%, "spinning top" deformity (radiographic image of dyssynergic contraction of the external sphincter in a girl with an unstable bladder) (9) in 22%, and bladder trabeculation in 16%. Aubert (3) considers the irregularity of the vesical wall as radiological lesion specific to the voiding dysfunction. The probable cause for this vesical alteration could be the increase of intravesical pressure produced by the vesico-sphincteric dyssynergia (3,20), which is one of the possible etiological

factors, responsible for the manifestation of VUR (13). The vesical hyperpressure regime could cause wall bladder ischaemia, decreasing the protective factor of the vesical mucosa. This factor along with the urine flow inversion in the urethra could perpetuate urinary infection (4).

The literature reports that the incidence of “spinning top” deformity is 68% in cases of vesical immaturity, which is a higher percentage when compared to our series. VUR could be associated with detrusor instability in 30% to 47% of the cases (6,20). Surgical treatment in patients with vesicoureteral reflux and detrusor instability shows poor results (9). An effective clinical treatment of detrusor instability might lead to the resolution of 20% to 30% of cases of VUR (9,11).

Intestinal constipation is often associated with vesical dysfunction and UTI. Since it seems that fecal accumulation induces uninhibited detrusor contractions, the treatment of constipation by dietary manipulation, stool softeners and laxatives are indicated (10).

Occult spina bifida was radiologically detected in 16% of cases. These results are lower than those reported in the literature (38%) (19). However, the meaning of this finding is not clear. Ritchey et al. (19) proclaim a conventional treatment for such cases and only recommend surgery when a neurological lesion and occult spina bifida occur simultaneously to tethered cord.

The urodynamic study was performed in 37% (21/57); only 62% (13/21) presented with detrusor instability and none of the cases presented with vesico-sphincteric dyssynergia. Szabó and Borbás (20) observed expressive indication of detrusor instability in 40% of urodynamic studies. These data suggest that urodynamic studies should be reserved to the cases resistant to clinical treatment or to those presenting alterations in the lower urinary tract (bladder trabeculation and VUR). Significant loss of compliance (17) may occur in severe vesico-sphincteric dyssynergia, causing VUR and renal scarring, which characterizes Hinman’s syndrome (10,14). Prolonged sphincteric hypertony may cause vesical atony, “lazy bladder” (10,14).

In our series we observed that significantly better results were obtained when OC (94%) was used instead of DHCl (67%). In the literature, different authors describe similar results varying from 78 to 90% success (3,23) when using OC. Malone-Lee et al. (15) suggest the use of OC, regardless of age, beginning with 2.5 mg twice a day, despite the fact that the half life of the drug lasts 3 hours, which would suggest the necessity of a larger fractionation and therefore its disadvantages. In our experience, satisfactory results were obtained, beginning with 0.3 mg/kg/day, twice a day and increasing them gradually, if necessary, until the effective dose was reached. Side effects of the drug (constipation, dry mouth, mood change, heat intolerance) might occur but can be reversed when the medication is discontinued or the dosage is decreased. In cases resistant to the pharmacological treatment, Mauroy et al. (16) suggest the use of electrical therapy and reports 90% of efficacy. The use of intravesical oxybutynin is limited to cases of vesical neurogenic dysfunction in intermittent catheterization regime, either because oxybutynin is orally ineffective or because of its side effects (2).

In cases where the obstruction may cause detrusor instability in boys, infravesical obstruction should be ruled out. Maximum flow rate and ultrasound may be used (postvoid residual urine volume and bladder wall thickness). Amaro et al. (1), studying 167 normal male children, observed that maximum flow rate is 15 ml/s until the pre-adolescence on average, and after that it is similar to the urinary flow of an adult (20 ml/s). In this way, having established a parameter of normality of the urinary stream, one can, together with the information from the ultrasound, avoid the manipulation of these children with urodynamics, ruling out a possible infravesical obstruction (1).

Therefore, in cases of voiding dysfunction with no complicating factors, we can establish the pharmacological treatment based on clinical symptoms and laboratorial findings. However, in cases on which the pharmacological treatment was not successful, or in those presenting with recurrent urinary tract infection, the performance of urodynamic

study, cystourethrography and ultrasound are imperative.

Vesical dysfunction is a condition that can lead to serious psychological damage. Also, its association with recurrent urinary infections and vesicoureteral reflux may be harmful to the urinary tract. Thus, its early recognition and treatment may promote resolution of symptoms and will prevent long term complications.

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LONG TERM HISTOMORPHOMETRIC EVALUATION OF THE VILLOUS AND ILEAL GOBLET CELLS AFTER ILEOCYSTOPLASTY IN FEMALE RATS

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ABSTRACT

Objective: The aim of the present study was to evaluate the long-term changes in the number and the height of villous and the number of goblet cells in rats submitted to ileocystoplasty.

Material and Methods: Thirty-six female Wistar rats weighing 172-230g were submitted to ileocystoplasty with an ileal segment of 2.5 cm long. An additional 1-cm ileal segment was used as control. Periods of observation were 4, 12 and 40 weeks, thus constituting 3 experimental groups (GEI, GEII and GEIII) of 12 animals each. Suitable sections of control ileum and of the ileal tissue incorporated into the bladder were treated with hematoxylin-eosin (HE) and alcian blue orange (pH 2.5) for goblet cells staining. The number and the height of villous were determined in 10 microscopic fields (HE) and the number of goblet cells were determined in 10 microscopic fields stained with alcian blue orange.

Results: There was a progressive shortening and atrophy of the villous. The villous become progressively smaller in number ($p < 0.05$). The number of goblet cells was significantly higher in the ileal graft than in the control ileum ($p < 0.05$). The number of goblet cells was 65.7% higher in the 4-week group, 89.2% higher in the 12-week group and 49.1% higher in the 40-week group.

Conclusions: There was a progressive villous atrophy and an increase in the number of the goblet cells of the ileal segment after ileocystoplasty with the maximal density 12 weeks after surgery followed by a decrease after 40 weeks.

Key words: bladder, ileum, bladder augmentation, goblet cells, hystomorphometry, ileocystoplasty

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INTRODUÇÃO

As alterações na mucosa de segmentos do sistema digestivo utilizados na reconstrução do sistema urogenital, mostraram diversos graus de hipotrofia, até atrofia e urotelização; perda das microvilosidades, com modificações da arquitetura da mucosa e portanto dos fenômenos absorptivos hidroeletrólíticos; alterações do número de células caliciformes, com presença de muco aumentado, diminuído ou inalterado, conforme o segmento digestivo, o modelo e o tempo experimental (1-7).

Não existe ainda segmento do sistema digestivo considerado ideal para ampliação ou substitui-

ção da bexiga urinária, persistindo as controvérsias em relação ao uso do estômago, íleo ou cólon (8,9).

Em estudo anterior, foram avaliadas as alterações da mucosa do segmento ileal na ileocistoplastia em ratas, por 4 e 12 semanas e observou-se diminuição das vilosidades e aumento do número de células caliciformes ileais, com aumento do muco (7). Decidiu-se então realizar outro experimento com tempo maior de observação, para saber o que ocorre com as vilosidades e as células caliciformes ao longo do tempo.

O objetivo do presente estudo, foi comparar pela histomorfometria, as alterações encontradas a longo prazo, na mucosa do segmento ileal após ileocistoplastia em ratas.

MATERIAL E MÉTODOS

Foram utilizadas 36 ratas da linhagem OUTB EPM-1, com 172 a 230 gramas, distribuídas em 3 grupos, com 12 animais cada.

Para cada grupo experimento (GE) correspondeu um grupo controle (GC). Portanto, foram analisados 6 grupos: GE I, GC I, GE II, GC II, GE III e GC III.

Em cada animal, no início da operação, retirou-se um segmento ileal de aproximadamente 1,0 cm, que serviu como controle.

Depois de 18 horas de jejum, as ratas foram pesadas, sorteadas e receberam anestesia intraperitoneal, com pentobarbital sódico a 3%, na dose de 30 mg Kg de peso. Os animais foram imobilizados sobre uma prancha, em decúbito dorsal e após depilação da região central do abdome, receberam anti-sepsia com clorhexidine a 2%.

Após laparotomia mediana longitudinal de 3 cm, com exposição do íleo distal, era isolado um segmento pediculado de 3,5 cm (distante 1,0 cm do ceco), do qual se retirou 1,0 cm proximal, como controle de cada rata. O trânsito intestinal íleo-ileal era refeito

com anastomose término terminal, com pontos separados, em plano único, com de fio de polipropileno 7-0. Na bexiga urinária, aberta 0,5 cm no sentido sagital, era anastomosada a extremidade distal do segmento ileal pediculado com fio de poliglecaprone-25, 5-0, com pontos separados em plano único. O segmento ileal pediculado isoperistáltico, era fechado em sua extremidade proximal com pontos separados de polipropileno 7-0. Após revisão da cavidade abdominal, a parede era fechada em 2 planos, com polipropileno 4-0. As ratas permaneceram em gaiolas para 2 animais até recuperação anestésica, quando eram reconduzidas ao biotério.

Depois de 4, 12 e 40 semanas, as ratas eram novamente anestesiadas e reoperadas para retirada em monobloco da bexiga urinária, com o segmento ileal. A anestesia era aprofundada e a eutanásia consumada. As peças eram abertas longitudinalmente e fixadas em líquido de Bouin. Antes de 48 horas eram retiradas do líquido e processadas pelas técnicas histológicas usuais, e coradas pelos métodos de hematoxilina-eosina (HE) para estudo das vilosidades e pelo Alcian Blue (pH = 2,5) Orange-G, para o estudo das células caliciformes (sialomucinas).

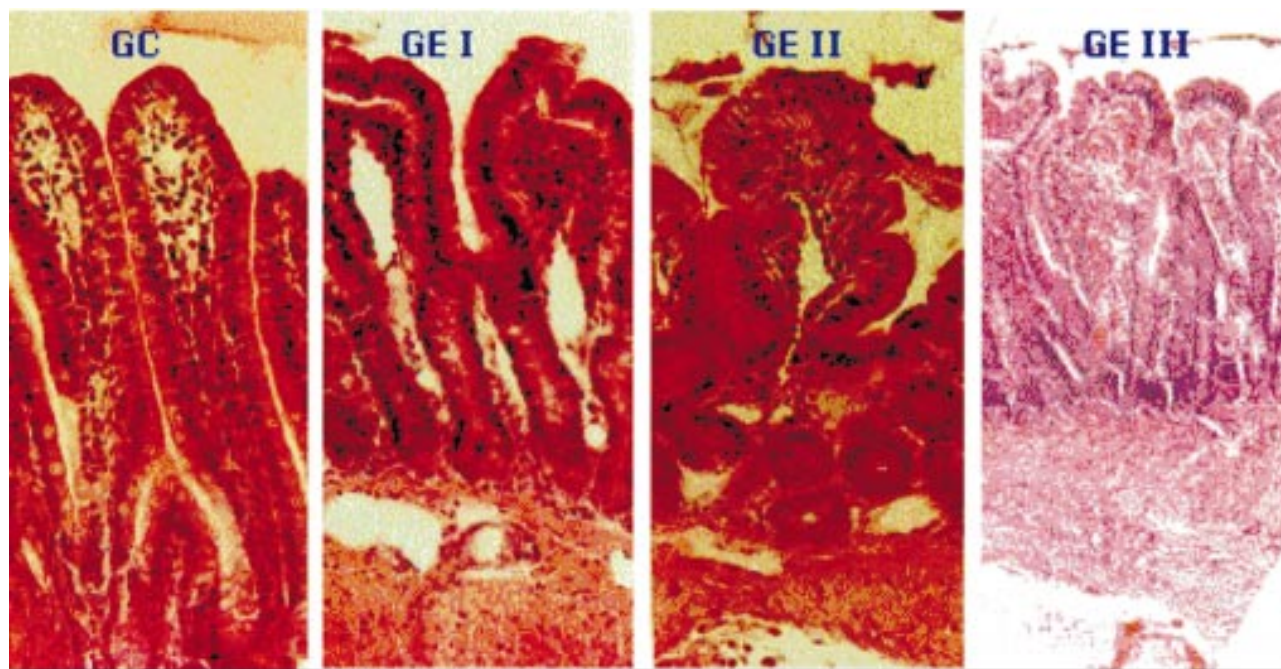


Figura 1 – Fotomicrografias de corte longitudinal de parte da mucosa de segmento ileal mostrando diminuição progressiva do número e altura das vilosidades, de forma comparativa, em rata de GC, de GE I, GE II e GE III (HE, X280).

A média das contagens dos números de vilosidades e de células caliciformes e das medidas das alturas das vilosidades era obtida em 10 campos ou em 10 vilosidades tomadas aleatoriamente. Para todos os testes estatísticos, fixou-se 5% ($p < 0,05$), o nível para rejeição da hipótese de nulidade.

RESULTADOS

Todos os animais ficaram bem adaptados às novas condições morfofuncionais da operação, e apresentaram ganho de peso. Observou-se macroscopicamente, no momento da reoperação, um aumento volumétrico do segmento ileal pediculado usado para ampliação da bexiga urinária. O muco era sempre aumentado nos grupos de 4 e 12 semanas e diminuído no de 40 semanas. Na análise microscópica, as vilosidades da mucosa do segmento ileal pediculado na ileocistoplastia eram digitiformes e uniformes nos controles, enquanto que nos experimentos apresentaram um achatamento progressivo e algumas deformações (Figura-1).

Em relação à histomorfometria da mucosa, as lâminas coradas em HE demonstraram que as características básicas morfológicas exibidas nos 3 grupos controles, foram mantidas nos grupos experimentais, com algumas diferenças. O número e a altura das vilosidades, diminuíram progressivamente, do tempo 0 até 40 semanas, conforme resultados obtidos pela análise de variância por postos de Kruskal-Wallis (Figuras-1 e 2). A contagem das células caliciformes que foi realizada nas lâminas coradas em Alcian Blue (pH 2,5) Orange-G, apresentou um aumento significativo, que foi maior nos experimentos de 4 e 12 semanas, em relação a de seus controles, e no de 12 semanas, em relação ao de 4 semanas. Nos animais de 40 semanas, houve diminuição do número de células caliciformes em relação aos experimentos de 4 e 12 semanas, e aumento em relação aos seus controles.

Quanto ao teste de comparações múltiplas, pela análise de variância por postos de Kruskal-Wallis, a diferença entre as médias de contagens das células caliciformes foi significativa entre animais

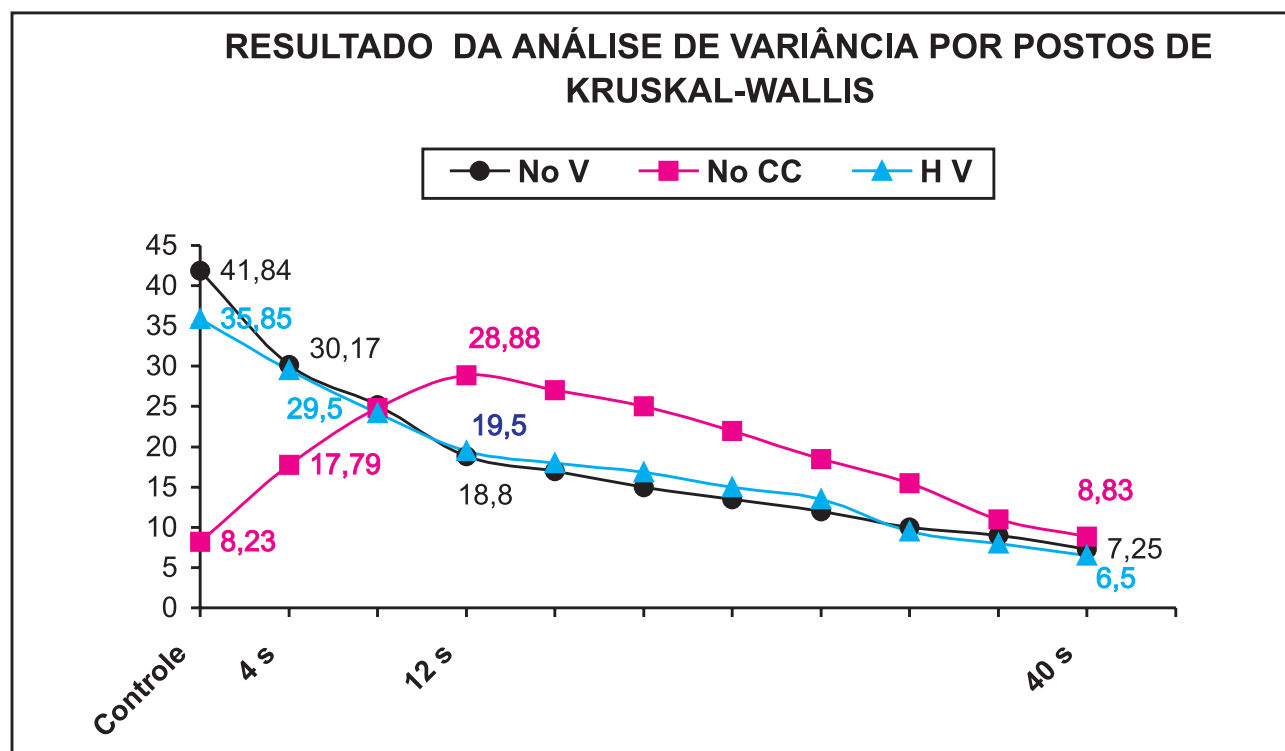


Figura 2 – Gráfico do número médio de vilosidades ileais (No. V), de células caliciformes (No. CC) e da altura das vilosidades ileais (HV), na ileocistoplastia em ratos, observadas nos diversos períodos de tempo.

de 4 e 12 semanas ($4 < 12$), não foi significativa entre os animais de 4 e 40 semanas ($4 > 40$), e foi significativa entre os de 12 e 40 semanas ($12 > 40$) (Figuras-2 e 3).

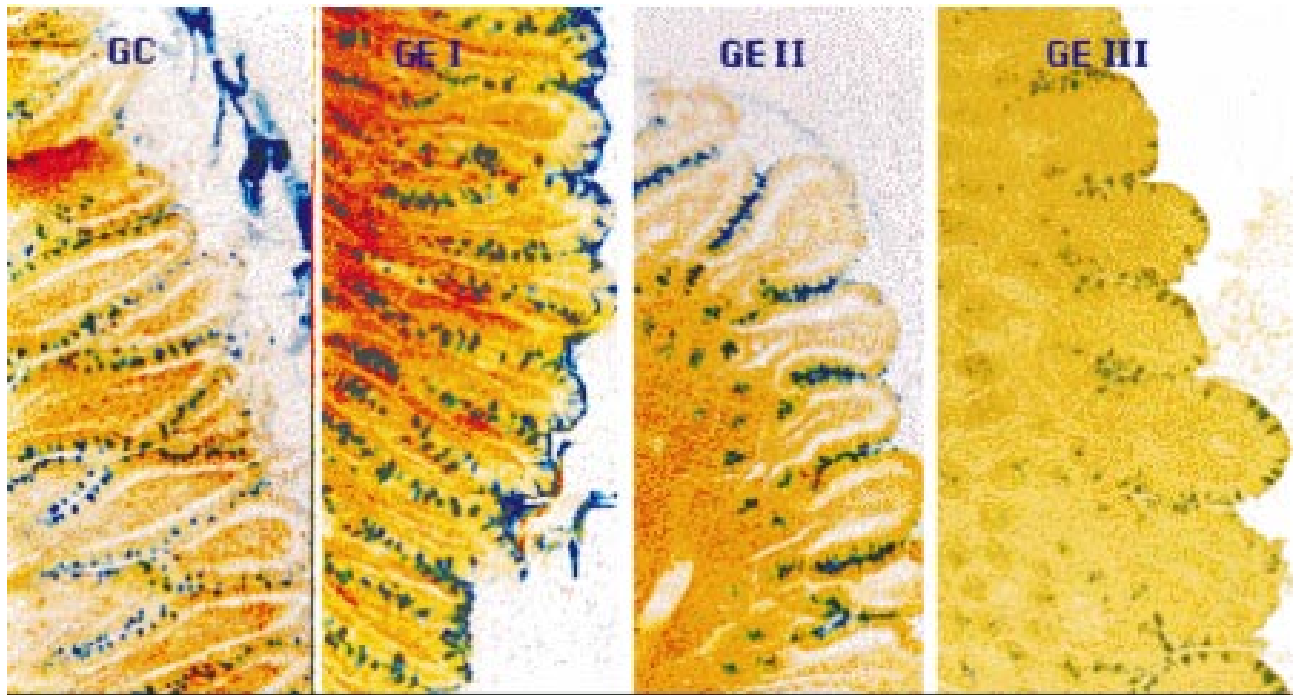


Figura 3 – Fotomicrografias de corte longitudinal de parte da mucosa de segmento ileal mostrando aumento progressivo do número das células caliciformes (mucopolissacarídeos), destacadas em azul, de forma comparativa em rata de GC, de GE I, e GE II; e diminuição no GE III, em relação aos GE I e GE II, e aumento quando comparada ao GC (Alcian blue, pH = 2,5, orange-G, X100).

DISCUSSÃO

Os estudos experimentais com o segmento ileal pediculado e desfuncionalizado para a reconstrução do aparelho urogenital tiveram início em 1888, sendo que a primeira ileocistoplastia em humanos foi realizada em 1898 (6). Muitos autores estudaram as alterações histomorfométricas da mucosa desses segmentos incorporados ao trato urinário e constataram redução do número e da altura das vilosidades (1-7).

Na clínica, constata-se um aumento da quantidade de muco presente na urina desses pacientes e, com o passar do tempo, há uma redução de sua produção (10,11).

O aumento da produção de muco poderia estar relacionado a um maior estímulo às células caliciformes, por algum agente presente na urina, ou

ao crescimento da população dessas células.

Na literatura, em trabalhos experimentais e clínicos, os autores reportaram aumento do número de células caliciformes, embora sem análise morfo-

métrica e sem coloração especial para sialomucinas (1,5,6,11,12). Apenas um estudo revelou diminuição da quantidade de células caliciformes (1). A utilização do alcian blue (pH = 2,5) orange-G, permitiu a coloração das sialomucinas presentes nas células caliciformes ileais.

A quantidade de células caliciformes encontrou-se aumentada em todos os momentos do experimento, sendo mais intensa nas 12 primeiras semanas e a partir daí, reduzindo-se gradativamente (Figura-2). Com 40 semanas, a quantidade de células caliciformes diminuiu, aproximando-se dos valores do grupo controle (Figura-2).

A atrofia progressiva da mucosa ileal foi evidente em todos os momentos analisados. Essa atrofia, diminuiu a superfície de absorção da mucosa, minimizando os efeitos metabólicos que

ocorrem quando a urina está em contato com o íleo (13,14).

O muco ileal, representado pelas sialomucinas, representa um mecanismo de defesa imunológico importante (12).

Ele é produzido pelas células caliciformes, sendo rico num peptídeo denominado "trefoil", que é resistente à protease. O "trefoil peptide" apresenta uma função semelhante a um fator de crescimento e é responsável pela integridade do epitélio ileal, além de representar uma barreira imunológica (15).

Dessa forma, é provável que o aumento do número de células caliciformes e da produção de muco, represente um mecanismo de defesa imunológico.

Segmentos de íleo desfuncionalizados e em desuso, também apresentam atrofia da mucosa (6). Portanto, é possível que as alterações que ocorrem na mucosa ileal na ileocistoplastia sejam conseqüentes apenas à desfuncionalização e não ao contato com a urina. Tal assunto está sendo objeto de estudo em outra pesquisa em andamento.

CONCLUSÕES

No presente estudo, pode-se concluir que na ileocistoplastia em ratas ocorre atrofia da mucosa ileal e aumento inicial do número de células caliciformes, com diminuição progressiva após 12 semanas, embora mesmo com 40 semanas, seu número seja superior ao do controle.

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RESUMO

AVALIAÇÃO TARDIA DA HISTOMORFOMETRIA DAS VILOSIDADES E DAS CÉLULAS CALICIFORMES ILEAIS NA ILEOCISTOPLASTIA EM RATAS

Objetivo: Avaliar os efeitos tardios ocorridos na mucosa de segmento ileal incorporado à bexiga.

Material e Métodos: Trinta e seis ratas foram submetidas a ileocistoplastia e distribuídas em 3 grupos experimentais, estudados em 4, 12 e 40 semanas. Foram analisados o número e altura das vilosidades ileais e o número das células caliciformes ileais produtoras de muco (sialomucinas), coradas pelo alcian blue (pH = 2,5) orange-G.

Resultados: Os resultados histomorfométricos mostraram que há diminuição progressiva do número e da altura das vilosidades. O número de células caliciformes evoluiu em percentuais de +65,7%, +89,2% e +49,1%, nos grupos de 4, 12 e 40 semanas respectivamente (p 0,05), em relação aos seus controles.

Conclusões: Na ileocistoplastia em ratas ocorre atrofia progressiva da mucosa ileal e aumento inicial do número de células caliciformes, com diminuição após 12 semanas, que se acentua com 40 semanas.

Unitermos: bexiga, íleo, ampliação vesical, células caliciformes, histomorfometria, ileocistoplastia.

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DEVELOPMENTAL CHANGES OF GLYCOSAMINOGLYCANS IN THE HUMAN FETAL BLADDER WALL

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ABSTRACT

Objectives: Glycosaminoglycans (GAGs) play key roles in the normal physiology and pathology of the bladder. There is little data, however, on GAG composition in the human fetal bladder wall. In the present study we aimed at establishing the composition of GAGs in the bladder wall of human fetuses at different gestational ages.

Methods: Bladder samples consisting of the dome and front wall were obtained from 4 fresh, macroscopically normal human fetuses aged 13 to 32 weeks postconception (WPC). GAGs in delipidated tissue samples were extracted by papain digestion and cetylpyridinium chloride/ethanol precipitation. The concentration of total GAG was assessed by a hexuronic acid assay and expressed as μg hexuronic acid per mg dry tissue, while the proportions of sulfated GAG species were determined by agarose gel electrophoresis.

Results: At 13 WPC bladder GAG concentration is about $2.2 \mu\text{g}/\text{mg}$. It then decreases slowly, and at 32 WPC the value is $1.8 \mu\text{g}/\text{mg}$. Proportions of sulfated GAGs from 13 to 21 WPC are stable, with 40% chondroitin sulfate, 50% dermatan sulfate, and 10% heparan sulfate. At 32 WPC, however, the proportions of chondroitin and dermatan sulfate are 48 and 42%, respectively.

Conclusion: Overall, the extracellular matrix of the vesical wall does not undergo dramatic compositional changes between the 13th and 32nd WPC. Still, the lower GAG concentration and the change in the proportions of GAG species at the 32nd WPC suggest that major developmental modifications in the vesical wall, which certainly bear on the mechanical properties of the bladder, occur by this period.

Key words: bladder, fetus, glycosaminoglycans, development

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INTRODUÇÃO

Glicosaminoglicanos (GAGs) são heteropolissacarídeos complexos que possuem quantidades diversas de grupamentos carboxila e sulfato. Os GAGs portanto têm alta densidade de grupamentos aniônicos, e in vivo esses polissacarídeos existem sob a forma de glicoconjugados denominados proteoglicanos, cuja parte protéica contém quantidades variáveis de domínios de adesão. Os proteoglicanos têm, dessa forma, grande capacidade de interações específicas com o meio circundante, e suas funções fisiológicas são basicamente decorrentes dessa propriedade. Essas funções incluem principalmente: (1) retenção seletiva de íons e moléculas difusíveis; (2)

organização estrutural da matriz extracelular; (3) regulação da interação célula-matriz extracelular e célula-célula; (4) modulação do efeito de citocinas; e (5) regulação da atividade de proteases (1-3).

Os GAGs desempenham diferentes e importantes funções na fisiologia da bexiga. Em virtude de sua bem conhecida interação com o colágeno e outros componentes da matriz extracelular (4), pode-se inferir que os GAGs têm participação marcante nas propriedades de complacência da parede vesical, embora tal fato não tenha sido ainda apropriadamente investigado. Uma função que vem sendo bem estudada, e que tem implicações clínicas imediatas, é participação dos GAGs na permeabilidade do urotélio. Resultados de diversos trabalhos, utilizando tanto

métodos morfológicos como bioquímicos, têm mostrado que a camada de glicocálix sobre o urotélio é enriquecida em GAGs (5,6). Outros experimentos revelaram que essa camada não apenas impede a difusão de componentes da urina para dentro da parede da bexiga (7), mas também dificulta a aderência de bactérias ao urotélio (8,9). Baseados nessas propriedades, tem-se correlacionado alterações de GAG do urotélio com a cistite intersticial (10,11). É importante notar que essas alterações limitam-se, provavelmente, à composição de GAGs, pois não foram detectadas diferenças morfológicas em relação ao tecido normal (6).

Existem poucos trabalhos sobre a composição de proteoglicanos e GAGs na bexiga de humanos, e estes utilizam apenas tecido de adultos (12,13). Embora alguns estudos tenham sido feitos sobre as alterações com o desenvolvimento do colágeno em humanos (14) e em animais (15,16), dados semelhantes sobre proteoglicanos e GAGs, os quais forneceriam informações funcionais importantes sobre esses componentes, são inexistentes. Essa questão foi abordada no presente trabalho, no qual se investigou a concentração e composição bioquímica de GAGs em bexigas provenientes de fetos humanos de diferentes idades gestacionais.

MATERIAL E MÉTODOS

As amostras consistiram da bexiga de 4 fetos masculinos com idade gestacional variando entre 13 e 32 semanas pós-concepção (SPC), segundo o método de medida do pé mais longo (17). Os fetos estavam macroscopicamente bem preservados e não apresentavam sinais externos de malformações congênitas. Após dissecação, a cúpula e a parede anterior da bexiga foram removidas e imediatamente fixadas em acetona. As amostras foram então delipidadas por meio de duas trocas de 24 horas cada em clorofórmio:metanol (2:1, v/v), e depois secas a 60°C. A parede vesical foi analisada por inteiro, sem se fazer distinção entre urotélio, lâmina própria, e camada muscular.

A extração de GAGs seguiu um protocolo previamente descrito (18). Resumidamente, cerca de 30 a 100mg de tecido delipidado e seco foram incu-

badadas com papaína bicristalizada (Sigma) em tampão acetato 100mM, pH 5,0, contendo cisteína 5mM e EDTA 5 mM, por 24 horas a 60°C. Após centrifugação, cloreto de cetilpiridínio (CPC) foi adicionado ao sobrenadante para precipitar os GAGs. As amostras foram centrifugadas e o complexo CPC-GAG no pellet foi dissociado com NaCl 2M. Os GAGs foram por fim precipitados ao se adicionar 2 volumes de etanol absoluto às amostras, que foram então mantidas a 4°C por 24 horas. Após uma série de centrifugações e lavagens do pellet, obteve-se a preparação final de GAGs totais, a qual foi utilizada nas análises subsequentes.

A quantificação de GAGs totais foi feita por meio da dosagem de ácido hexurônico, utilizando o método do carbazol (19), no qual as amostras purificadas de GAG são primeiramente tratadas com H_2SO_4 a 100°C. A concentração de GAG no tecido vesical foi expressa em microgramas de ácido hexurônico por miligrama de tecido delipidado e seco.

A quantidade relativa dos GAGs sulfatados (condroitim sulfato, dermatan sulfato, e heparan sulfato) foi determinada por eletroforese em gel de agarose a 0,5% em tampão 1,3-diaminopropano 50 mM, pH 9,0 (20). Após corrida a 80V, o gel foi fixado em brometo de N-Cetil-N,N,N-trimetilamônio 0,1%, corado em azul de toluidina 0,1%, e a proporção dos GAGs foi determinada por densitometria das bandas seguida de integração dos picos usando o programa Scion Image (Scion Corp, Maryland, USA). A identificação das bandas na placa de agarose foi feita com base na comparação com a migração de padrões de GAG comerciais (Sigma) e na susceptibilidade à degradação por GAG-liases (18).

RESULTADOS

As amostras de bexiga fetal estudadas indicam que a concentração de GAG total nesse tecido diminui ligeiramente entre a 13ª e a 32ª SPC (Figura-1). Nesse período, a concentração de GAG, expressa como microgramas de ácido hexurônico por miligrama de tecido delipidado e seco, passa de 2.2 a 1.8 em valores médios.

Os GAGs sulfatados majoritários na parede da bexiga fetal, como mostrado pela eletroforese em

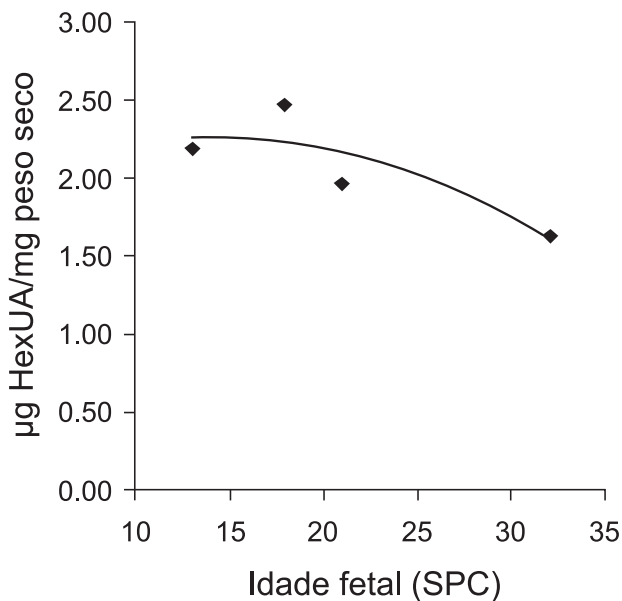


Figura 1 – Concentração de glicosaminoglicanos totais na parede vesical de fetos humanos. As amostras consistiram da cúpula e parte anterior da bexiga, e incluem toda a extensão da parede. A concentração foi determinada pelo método do carbazol e é expressa em microgramas de ácido hexurônico (HexUA) por miligrama de tecido delipidado e seco. A idade gestacional foi calculada pelo método do pé mais longo e é dada em semanas pós-concepção (SPC).

gel de agarose, são o dermatan sulfato e o condroitin sulfato, havendo, além disso, em torno de 10% de heparan sulfato (Figura-2). O conteúdo relativo desse último GAG sofre poucas alterações entre a 13^a e a 32^a SPC. De maneira similar, as proporções dos outros GAGs se mantêm estáveis nas amostras de 13 e 21 SPC, nas quais se observa uma predominância do dermatan sulfato (49-51%) quando comparado ao condroitin sulfato (40-41%). Na amostra de 32 SPC, no entanto, essa relação se inverte, e o conteúdo relativo do condroitin sulfato (48%) passa a ser maior que o do dermatan sulfato (42%).

DISCUSSÃO

Os resultados obtidos no presente trabalho mostram que, de uma maneira geral, a composição de GAGs na parede vesical não sofre grandes alterações no período estudado, que se situa entre a 13^a e a 32^a SPC. Nesse mesmo período, estruturas de tecido conjuntivo associadas ao testículo, por exemplo, apre-

sentam modificações muito mais marcantes (observações não publicadas). Por outro lado, nossos resultados indicam que as modificações mais acentuadas na composição de GAGs ocorre mais para o final do período analisado, em torno da 32^a SPC. Nessa idade gestacional, a concentração de GAGs é menor do que em idades mais iniciais, e há uma inversão nas proporções do dermatan e condroitin sulfato. Esses 2 GAGs estão associados principalmente aos proteoglicanos decorina/biglican e versican, respectivamente, os quais têm distribuição predominantemente intersticial (3).

A imunomarcagem de elastina e de colágenos tipo I e III em bexigas normais e não complacentes sugere que a lâmina própria é um componente fundamental para essa propriedade mecânica (21). Como decorina/biglican e versican ocorrem tipicamente na lâmina própria de epitélios, as modificações em concentração e composição de GAGs em fases mais tar-

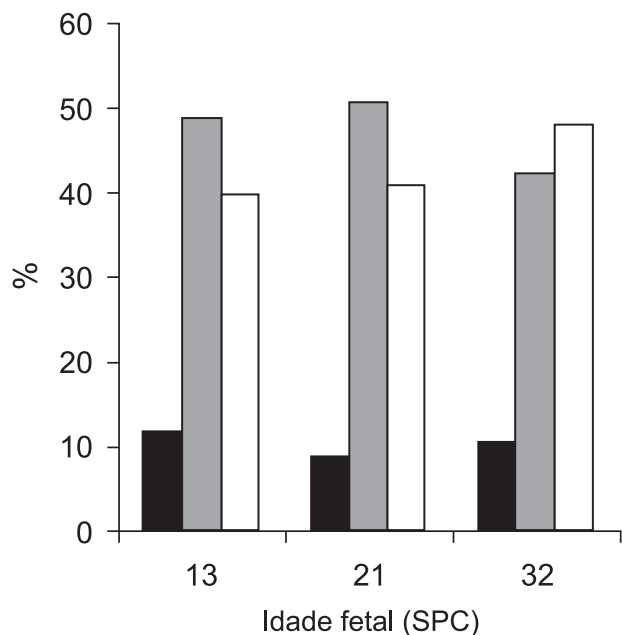


Figura 2 – Concentração relativa dos diferentes tipos de glicosaminoglicanos (GAG) sulfatados na parede vesical de fetos humanos. Após extração e purificação, os GAGs totais foram submetidos a eletroforese em gel de agarose, e as proporções do heparan sulfato (barras pretas), dermatan sulfato (barras cinzas), e condroitin sulfato (barras brancas), expressas como porcentagem do total de GAGs sulfatados, foram determinadas por densitometria das bandas. SPC, semanas pós-concepção.

dias do período fetal, como mostrado por nossos resultados, estão provavelmente relacionadas de maneira estreita com as propriedades de complacência da parede vesical.

Outros estudos utilizando a mesma técnica de imunohistoquímica revelaram que o síndecan-1, um proteoglicano de heparan sulfato, predomina no urotélio (22). Dessa forma, a ausência de variação na concentração relativa do heparan sulfato, no período fetal estudado, sugere que a camada de GAGs do urotélio está presente desde idades gestacionais iniciais.

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RESUMO

COMPOSIÇÃO DE GLICOSAMINOGLICANOS DURANTE O DESENVOLVIMENTO DA PAREDE VESICAL EM FETOS HUMANOS

Objetivos: Os glicosaminoglicanos (GAGs) desempenham papel fundamental na fisiologia normal e patológica da bexiga. Existem poucos dados, entretanto, sobre a composição de GAGs na parede da bexiga fetal de humanos. O presente estudo teve por objetivo estabelecer a composição de GAGs na parede vesical de fetos humanos de diferentes idades gestacionais.

Métodos: As amostras consistiram da cúpula e parede anterior de bexigas de 4 fetos macroscopicamente normais e com idade entre 13 e 32 semanas pós-concepção (SPC). Os GAGs em amostras delipidadas de tecido foram extraídos por digestão com papaína e precipitação com cloreto de cetilpiridínio/etanol. A concentração de GAG total foi determinada pela dosagem de ácido hexurônico, e foi expressa como μg de ácido hexurônico por mg de tecido seco, enquanto que as proporções de GAGs sulfatados foram determinadas por eletroforese em gel de agarose.

Resultados: Com 13 SPC a concentração de GAG na bexiga é de $2.2 \mu\text{g}/\text{mg}$. Esse valor então decresce lentamente, e com 32 SPC é de $1,8 \mu\text{g}/\text{mg}$. As proporções dos GAGs da 13^a à 21^a SPC são estáveis, com 40% de condroitin sulfato, 50% de dermatan sulfato, e 10% de heparan sulfato. Com 32 SPC, entretanto, as proporções são 48 e 42%, respectivamente.

Conclusões: A matriz extracelular da parede vesical não sofre grandes mudanças de composição entre a 13^a e a 21^a SPC. No entanto, a concentração de GAG mais baixa, e a alteração nas proporções dos GAG na 32^a SPC sugerem que modificações importantes na parede vesical com o desenvolvimento, que certamente se relacionam com as propriedades mecânicas da bexiga, ocorrem nesse período.

Unitermos: bexiga, feto, glicosaminoglicanos, matriz extracelular
Braz J Urol, 26: 97-101, 2000

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UROLOGICAL SURVEY

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ENDOUROLOGY AND LAPAROSCOPIC SURGERY

Percutaneous nephrostomy as adjunct management in advanced upper urinary tract infection

Watson RA, Esposito M, Richter F, Irwin Jr. RJ, Lang EK

Urology, 54: 234-239, 1999.

Nefrostomia percutânea como auxiliar no manuseio de infecção importante do tracto urinário superior

Objetivo: Avaliar a importância clínica da nefrostomia percutânea no tratamento de casos de piodrose.

Pacientes e Métodos: De 1977 a 1996, 315 pacientes (181 homens, 134 mulheres), entre 17 e 88 anos de idade, foram submetidos à nefrostomia percutânea para tratamento de hidronefroses infectadas. Todos os pacientes apresentavam obstrução do trato urinário superior associada à infecção. Em adição ao procedimento da nefrostomia era iniciada imediata antibioticoterapia. Antes do início da antibioticoterapia era coletada a urina, ou por micção espontânea ou por cateterismo uretral. As primeiras amostras de urina, coletadas da nefrostomia, também eram prontamente enviadas para cultura. O controle das culturas de urina da nefrostomia e vesical era realizado entre 48 e 96 horas após o procedimento.

Resultados: As causas de obstrução foram: litíase (187 casos); neoplasia (67 casos); obstrução por material necrótico (24 casos) e de etiologia não esclarecida (37 casos). O nível de melhora variou entre 83,8% (no grupo de etiologia não esclarecida da obstrução) até 97,3% (no grupo de obstrução por litíase). O nível de melhora, em 35 pacientes tratados clinicamente, sem nefrostomia, foi de 57%. Microorganismos adicionais foram identificados nas culturas de urina das nefrostomias de 116 (36,8%) dos 315 pacientes, levando a uma mudança clínica significativa, ou adição de novos antibióticos e/ou agentes antifúngicos em 84 (73%) dos 116. Muito frequentemente foi encontrada disparidade importante entre os resultados de culturas obtidas das nefrostomias e aqueles obtidos das amostras de urina com origem na bexiga.

Conclusões: Este estudo retrospectivo confirma as vantagens da drenagem percutânea do trato urinário superior, como um tratamento adjuvante importante de piodroses.

Comentário Editorial

Os autores demonstraram o valor da nefrostomia percutânea na drenagem do trato urinário superior, mesmo em casos difíceis, associados à septicemia. Em particular, o trabalho focaliza que as culturas de urina das nefrostomias percutâneas frequentemente identificam patógenos que diferem daqueles detectados em culturas de urina da bexiga, determinando a mudança dos antibióticos para o tratamento desses casos. O trabalho também comenta outras vantagens do uso da nefrostomia percutânea, como a redução da pressão intra-renal, melhorando o acesso dos antibióticos ao parênquima renal e a filtração glomerular. Outra observação importante foi que em todos os casos, apesar da instituição prévia de antibioticoterapia endovenosa, antes da execução das nefrostomias, as culturas de urina aspiradas através de punções renais, raramente foram estéreis. Admite-se que, talvez o material purulento, e sob pressão no sistema coletor antes da realização da nefrostomia, pode significativamente impedir o acesso de antibióticos sistêmicos ao parênquima renal. Outras vantagens do procedimento podem ser destacadas, como o reduzido nível de complicações, evitando alternativas cirúrgicas de maior porte e risco, o uso da anestesia local, o baixo custo, a criação do acesso percutâneo que poderá ser usado posteriormente como nefroscopia, para a litotripsia, endopielotomia ou dilatação ureteral. Enfim, o trabalho faz uma revisão objetiva da real necessidade da nefrostomia percutânea no tratamento de casos de obstrução infectada do trato urinário superior.

Complications of laparoscopic procedures in urology: experience with 2,407 procedures at 4 german centers

Fahlenkamp D, Rassweiler J, Fornara P, Frede T, Loening SA
J Urol, 162: 765-771, 1999

Complicações de procedimentos laparoscópicos em urologia: experiência com 2.407 procedimentos em 4 centros na Alemanha

Objetivo: Avaliar as complicações dos procedimentos laparoscópicos realizados nos 4 maiores centros de laparoscopia da Associação Urológica Alemã.

Materiais e Métodos: 2.407 laparoscopias ou retroperitonioscopias foram realizadas de 1992 até maio de 1998 em 4 centros, incluindo 776 varicocelectomias, 259 pesquisas de testículo não palpável, 481 linfadenectomias pélvicas, 351 nefrectomias ou heminefrectomias, 139 ressecções de cisto renal, 58 procedimentos ureterais, 44 adrenalectomias, 41 nefropexias, 41 drenagens de linfocele, 40 linfadenectomias retroperitoneais para-aórticas e 187 outras operações. As complicações foram avaliadas e listadas de acordo com a especificidade anatômica e agrupadas com relação aos passos cirúrgicos durante a laparoscopia.

Resultados: Um total de 107 complicações (4,4%) ocorreram. A taxa de reintervenção foi de 0,8% e a de mortalidade de 0,08%. A taxa de complicação dependeu da dificuldade do procedimento e teve como médias 1,0; 3,9 e 9,2 % para operações fáceis, difíceis e muito difíceis, respectivamente. A maioria foi de lesões vasculares (1,7%) e viscerais (1,1%), seguidas de complicações de cicatrização e infecção (0,8%). Somente 0,2% das complicações foram associadas à técnica de acesso (inserção do trocar), enquanto que a maioria ocorreu durante a dissecação (2,9%). A taxa de complicação foi de 13,3% para os primeiros 100 procedimentos e subsequentemente teve como média 3,6%.

Conclusões: A análise crítica da experiência de várias instituições, especialmente para a avaliação das complicações da laparoscopia urológica, é importante para o desenvolvimento desta técnica cirúrgica. A taxa de complicações gerais é comparável a de outras especialidades. Futuros desenvolvimentos técnicos na inserção do trocar, na dissecação tecidual e no controle de sangramento, associados a um programa de treinamento contínuo das equipes podem reduzir a taxa de complicações.

Comentário Editorial

Os autores agruparam a experiência em quase 2.500 procedimentos laparoscópicos e a taxa de complicações resultante. Algumas conclusões práticas podem ser retiradas. Quanto mais difícil o procedimento, maior a taxa de complicações. Conforme se progride, dos procedimentos mais simples para os mais difíceis, as complicações aumentaram em 9 vezes. Entretanto, conforme a experiência cresce, a incidência de complicações reduz-se acentuadamente e após 100 casos, há uma redução de 4 vezes. A experiência abrange não só maior familiaridade em se obter um pneumoperitônio ou com as técnicas de dissecação laparoscópica, mas também maior conhecimento no uso da instrumentação. Com relação a isso, o uso da corrente monopolar para eletrocoagulação é causa do maior número de problemas relacionados aos instrumentos. Os autores citam vários métodos para se diminuir os problemas com a eletrocoagulação. Grande importância é colocada pelos autores quanto ao treinamento constante em laparoscopia, tendo criado um curso didático e de treinamento em laboratório. Está se tornando cada vez mais evidente que a laparoscopia não é uma técnica que se aprende durante um único curso de procedimento orientado de 2 ou 3 dias. A tática de treinamento escalonado, com procedimentos progressivamente mais complexos, além de ser mais prudente, aumenta a segurança e consegue reunir um maior número de urologistas com interesse pelos procedimentos laparoscópicos.

Marcelo Lopes de Lima

IMAGING

Contrast-enhanced sonography of vesicoureterorenal reflux in children: preliminary results

Mentzel H-J, Vogt S, Patzer L, Schubert R, John U, Misselwitz J, Kaiser WA.
AJR, 173: 737-740, 1999

Ultra-sonografia com contraste no refluxo vesico-uretero-renal: resultados preliminares

Objetivos: Avaliar a ultra-sonografia(US) com contraste como alternativa para uretrocistografia miccional na detecção de refluxo.

Métodos: Foram investigadas 46 crianças com suspeita de refluxo, idade variando de 3 semanas a 14 anos(média de 4 anos e 6 meses), O total de 92 unidades uretero-renais foi examinado pela uretrocistografia miccional e US com contraste. Após o exame ultra-sonográfico do trato urinário, a bexiga foi sondada e cheia com solução salina. Posteriormente, o eco-contraste foi instilado e o exame por US, repetido. A documentação foi feita em vídeo e câmara laser. Refluxo foi diagnosticado quando se observou a presença de microbolhas no ureter ou na pelve renal. Além disso, a uretrocistografia miccional foi realizada e as crianças que não conseguiram urinar foram excluídas (8 unidades uretero-renais).

Resultados: Os achados obtidos com o eco-contraste e a uretrocistografia foram concordantes em 78 unidades uretero-renais(92.9%). Ausência de refluxo por um dos métodos ,foi observado em 67 unidades(79.8%). Usando-se a cistografia como referência, a sensibilidade do US com contraste foi de 91.7%; a especificidade 93.1%, e a acurácia 92.9%.O valor preditivo de positividade foi de 68.8%, e o valor preditivo de negatividade 98.5%

Conclusão: O US com contraste é altamente sensível para a detecção do refluxo vésico-ureteral. Desse modo, a sua utilização pode reduzir o número de investigações radiográficas.

Comentário Editorial

Embora a cistografia radioisotópica ter-se mostrado uma alternativa útil para a detecção do refluxo, a uretrocistografia miccional continua sendo o método de escolha para esta avaliação. Ambos os métodos porem , expõem a criança à radiação ionizante. A procura de meios não invasivos se faz, desta maneira, necessária, principalmente se considerarmos a incidência do refluxo em crianças com infecção urinária (20 a 50%) e a eventual necessidade do enchimentos vesicais cíclicos durante a uretrocistografia que aumentariam ainda mais o tempo de fluoroscopia e conseqüentemente a exposição à radiação. Este estudo mostra resultados satisfatórios com a utilização do eco-contraste intra-vesical tendo como referência os resultados da uretrocistografia miccional; seria interessante, todavia, uma complementação com a medicina nuclear com o intuito de detectarmos eventuais falsos negativos do exame radiológico. O exame US possibilita um exame da bexiga mais duradouro, permitindo inclusive a detecção de refluxos em crianças com uretrocistografias normais, a quem o autor chama de “falsos positivos”, os quais na realidade seriam reais e, portando, falsos negativos do exame radiográfico. Se consideramos que O US com eco-contraste tem a limitação de não estudar a uretra fica fácil entendermos que esse exame poderá ser realizado como método inicial; se positivo então estaria indicado a uretrocistografia para a avaliação da uretra e uma adequada graduação do refluxo. Grande utilidade em potencial deve ser no seguimento de crianças com refluxo e nos controles pós-operatórios.

The abdominal compartment syndrome: CT findings

Pichardt PJ, Shimony JS, Heiken JP, Buchman TG, Fisher AJ
AJR, 173: 575-579, 1999

A síndrome do compartimento abdominal: achados da TC

Objetivo: Esta síndrome é uma condição potencialmente fatal e resulta de uma elevação patológica da pressão intra-abdominal. Foram avaliados os exames de TC pré-operatórios de 4 pacientes comprovadamente portadores da síndrome do compartimento.

Métodos: Por um período de um ano, 4 pacientes foram examinados com TC abdominal, e com hipóteses diagnósticas que não incluíram esta síndrome. Os pacientes tinham idades entre 17-51 anos (média 37 anos). A síndrome desenvolveu-se em 2 pacientes com complicações de pancreatite aguda e em 2 com trauma abdominal fechado. Dos 4, apenas um paciente apresentou laparotomia exploradora antes da cirurgia descompressiva.

Resultados: Os principais achados do TC abdominal foram: a) maciça coleção retroperitoneal (hemorragia, exsudado ou ambos); b) compressão extrínseca da VCI e c) sinal da “barriga arredondada”. Nestes pacientes as coleções retroperitoneais predominavam em volume sobre a doença peritoneal. Três dos 4 pacientes sobreviveram e tiveram alta hospitalar após resposta dramática à descompressão cirúrgica.

Comentário Editorial

Cerca de 14% dos pacientes submetidos à cirurgia abdominal conseqüente a traumatismo abdominal severo, desenvolvem esta síndrome. Esse fato ocorre devido à isquemia visceral e à coagulopatia associadas ao recebimento pelo paciente de grande volume de fluídos. O artigo, segundo os autores, atrai a atenção devido a quase inexistência de relatos dessa síndrome em pacientes sem esses antecedentes. A existência de extensa hemorragia retroperitoneal em pacientes com ruptura renal traumática não é infreqüente e o radiologista deve estar atento para à análise criteriosa da morfologia da VCI, das paredes viscerais (que se espessam e tornam-se impregnáveis por contraste) e da configuração do abdome (abdome arredondado). Este último achado é considerado como sendo de alta sensibilidade e especificidade para o diagnóstico dessa síndrome. Cuidados do cirurgião ao “fechar o abdome” e do radiologista são essenciais para a indicação da cirurgia descompressiva a qual deve ser realizada dentro de um período de 24 horas.

Adilson Prando

BENIGN PROSTATIC HYPERPLASIA

Prediction of alpha-blocker response in men with benign prostatic hyperplasia by magnetic resonance imaging

Mimata H, Nomura Y, Kasagi Y, Satoh F, Emoto A, Li W, Douno S, Mori H.
Urology, 54: 829-833, 1999

Previsão da resposta a alfa-bloqueador em homens com hiperplasia prostática benigna através da imagem por ressonância magnética

Objetivo: Demonstrar que a ressonância magnética (RM) pode ser uma alternativa à biópsia prostática na avaliação objetiva da terapêutica medicamentosa na hiperplasia benigna da próstata (HPB).

Métodos: Vinte e oito pacientes receberam alfa-bloqueador (tamsulosin) como tratamento sintomático da HPB. Após período de 4 a 6 semanas de tratamento analisou-se o fluxo urinário máximo e o escore

internacional de sintomas prostáticos (I-PSS). Os pacientes foram também avaliados através da RM, sinal T2, comparando a intensidade do sinal na próstata e na medula óssea da cabeça do fêmur. Em 16 pacientes foi realizada, também, biópsia prostática.

Resultados: O fluxo urinário máximo apresentava-se significativamente maior nos pacientes que, após tratamento, exibiam sinal baixo ou de iso intensidade, ao contrário dos que exibiam sinal de alta intensidade. Os portadores de sinal iso ou de baixa intensidade à RM eram detentores de maior quantidade de músculo liso. Esse grupo demonstrou 53,3% de melhora no fluxo urinário máximo, comparado com 15,4% nos portadores de alta intensidade de sinal.

Conclusão: O estudo radiológico por RM pode predizer a histologia da próstata e, assim, orientar o uso de alfa bloqueador no tratamento da HPB.

Comentário Editorial

No presente artigo, como no artigo semelhante **MRI can predict response to drug therapy for benign prostatic hyperplasia**, Mimata H, Nomura Y, Kasagi Y, Satoh F, Emoto A, Li W, Douno S, Mori H., *Urology*, 54: 773-775, 1999, os autores verificaram que pacientes, em cujas próstatas predomina o tecido muscular liso em relação ao epitélio glandular, respondem bem ao tratamento com alfa bloqueador. Dessa forma, é interessante reconhecer esse fato, para que a indicação terapêutica da HPB, seja a mais adequada. Estudos histológicos demonstraram que na próstata do jovem, antes da instalação da hiperplasia benigna, a relação estroma/glândula é 2:1, e com o aparecimento da HPB, passa a ser 5:1. Dessa maneira, de modo prático, a possibilidade de se atingir o objetivo, ou seja, conseguir resposta adequada com o tratamento com alfa bloqueador, é muito grande. Assim, a ressonância magnética seria uma alternativa à biópsia da próstata na confirmação do predomínio de músculo liso e, dessa maneira, orientar a prescrição de alfa bloqueadores no tratamento da HPB.

Nelson Rodrigues Netto Jr.

PEDIATRIC UROLOGY

Relationship among pediatric voiding dysfunction and vesicoureteral reflux and renal scars

Soygür T, Arikan N, Yesilli C, Gögüs O
Urology, 54: 905-908, 1999

Relação entre disfunção miccional, refluxo vesico-ureteral e cicatrizes renais

Objetivos: Analisar a correlação entre disfunção vesical não neurogênica, refluxo vesico-ureteral (RVU) e cicatriz renal, considerando o refluxo unilateral ou bilateral.

O refluxo vesicoureteral é um problema comum no grupo pediátrico. Embora o refluxo unilateral seja devido à insuficiência primária da junção uretero-vesical, o refluxo bilateral pode ser resultante da disfunção miccional.

Métodos: Entre 1993 e 1998, 80 crianças, das quais, 52 meninas e 28 meninos, com idade variando de 3,8 a 14 anos, mediana de 5,7 anos, foram avaliadas por refluxo vesico-ureteral. Dezoito pacientes com anomalias associadas e quadro de disfunção vesical neurogênica foram excluídos do estudo. Foram realizadas investigações urológica, neurológica e urodinâmica completas em todos os pacientes.

Resultados: Dos 62 pacientes, 25 (40,3%) tinham RVU unilateral e 37 (59,6%) RVU bilateral. A disfunção miccional foi encontrada em 7 (28%) com refluxo unilateral e em 27 (72,9%) com refluxo bilateral ($p < 0,01$). Dois pacientes (25%) dos 8 com refluxo unilateral e cicatriz renal tinham disfunção miccional, porém, sem infecção do trato urinário, 10 (55,5%), dos 18 pacientes com refluxo bilateral e lesão renal, tinham disfunção miccional, sem infecção do trato urinário ($p < 0,01$).

Conclusões: No RVU bilateral a prevalência de disfunção miccional é alta. O primeiro passo, no manuseio, deverá ser a avaliação detalhada da função vesical para escolher o tratamento adequado e prevenir a deterioração da função renal.

Comentário Editorial

Este trabalho vem reforçar a necessidade de uma avaliação cuidadosa em crianças com refluxo vesico-ureteral. A associação entre refluxo vesico-ureteral e disfunção miccional está bem definida, com frequência que varia de 15% a 50%. A história da micção é o ponto primordial na suspeita clínica entre essas duas enfermidades, sendo que há necessidade do estudo urodinâmico completo para poder diferenciar o refluxo primário do secundário. O reconhecimento desta associação tem implicação direta no sucesso do tratamento, pois muitos casos de falha no manuseio clínico ou mesmo cirúrgico são devidos a problemas de instabilidade vesical ou de incoordenação vesico-esfincteriana.

A long continent ileovesicostomy using a single piece of bowel

Casale, AJ

J Urol, 162: 1743-1745, 1999

Ileovesicostomia continente longa usando apenas um segmento de intestino

Objetivo: Em 1981, Mitrofanoff apresentou um procedimento para criar um estoma urinário continente, permitindo o cateterismo intermitente. Desde então, vários outros métodos têm sido introduzidos, incluindo a ileovesicostomia de Yang-Monti. O comprimento dessas ileovesicostomias é limitado pela circunferência do segmento intestinal usado, tornando inadequado em alguns casos. Desenvolvemos um procedimento para dobrar o comprimento da ileovesicostomia de Yang-Monti usando um segmento simples de intestino.

Material e Métodos: Um segmento de 3,5 cm de íleo acompanhado pelo mesentério é isolado. O intestino é dividido em dois segmentos com 80% de sua circunferência, deixando a alça intestinal intacta sobre o mesentério. Cada anel do segmento é, portanto, dividido adjacente ao mesentério, porém, em lados opostos, permitindo que o intestino seja dobrado e reconfigurado numa simples faixa longa que pode ser, então, tubularizado. O suprimento sanguíneo para o tubo é excelente e localizado no centro do íleo reconfigurado. Se necessário, a porção terminal pode ser seccionada ou amplamente espatulada.

Resultado: O procedimento foi empregado em 8 pacientes. A ileovesicostomia criada de um segmento ileal de 3,5 cm, atinge comprimento de 10 a 14 cm e aceita cateter Foley 12F. Um tubo longo pode ser criado através de um segmento do íleo alongado.

Todos os pacientes estão secos e realizam cateterismo facilmente.

Conclusões: Essa técnica de ileovesicostomia permite a criação de um tubo intestinal longo e fácil de cateterizar. O comprimento longo do tubo aumenta a aplicação do princípio de estoma continente para mais pacientes e permite que a reconstrução seja realizada no local adequado, e sem tensão.

Comentário Editorial

O princípio de Mitrofanoff trouxe importante contribuição para o sucesso da reconstrução do trato urinário continente, permitindo maior adaptação e integração social, principalmente em crianças. Desde então,

várias modificações surgiram na confecção do tubo que permita a cateterização, incluindo ureter, parede do estômago, íleo e parede vesical. A utilização do apêndice cecal vem sendo tradicionalmente mais aceita pela sua vascularização própria, com tecido muscular flexível e adequada circunferência. Recentemente, a utilização do segmento ileal descrita por Monti trouxe uma contribuição importante, quando o apêndice é curto ou mesmo ausente. Por outro lado, a utilização do apêndice, parece ser mais adequada no tratamento de incontinência fecal, de acordo com Malone. A modificação simples proposta pelo autor parece ser uma opção bastante atraente, principalmente pelo fato de que com um pequeno segmento intestinal pode-se conseguir até 14 cm de comprimento, ideal para crianças obesas, evitando anastomoses termino-terminais, o que teoricamente poderia dificultar a cateterização.

Osamu Ikari

UROLOGICAL NEUROLOGY AND FEMALE UROLOGY

A three-year follow-up of tension-free vaginal tape for surgical treatment of female urinary stress urinary incontinence

Ulmsten U, Johnson P, Rezapour M
Br J Obstet Gynaecol, 106: 345-350, 1999.

Três anos de seguimento utilizando o “tension-free vaginal tape” (TVT) para o tratamento da incontinência urinária de esforço na mulher

Objetivo: Estudar os resultados a longo prazo do TVT no tratamento da incontinência urinária de esforço na mulher.

Pacientes e Métodos: Cinquenta mulheres com idade média de 57 anos (± 11 anos) foram incluídas em um estudo prospectivo incluindo história e exame físico e pélvico, teste com absorventes, cistometria e perfil pressórico uretral estático e avaliação de qualidade de vida com escala visual analógica. Em todas as pacientes a cirurgia foi realizada com a técnica padrão e sempre que possível anestesia local. Cura completa foi definida como ausência de perda no teste com absorventes (inferior a 10g/24h), melhora da qualidade de vida superior a 90% e ausência de dificuldade miccional pós-operatória ou resíduo vesical acima de 100 ml. Cura parcial foi definida como ausência de perdas e satisfação entre 75% e 90%. O não preenchimento dos critérios acima foi definido como falha.

Resultados: Quarenta e duas pacientes (84%) eram multíparas e 8 (16%) nulíparas. A cirurgia foi realizada com anestesia local e ambulatorialmente em todas as pacientes exceto uma. O tempo cirúrgico médio foi de 29 minutos (variando de 16 a 47 minutos). Quarenta e cinco pacientes (90%) urinaram sem dificuldade em 24 horas e nenhuma apresentou retenção urinária por tempo superior a 14 dias (tempo máximo de sondagem de demora, 12 dias). Não ocorreram complicações hemorrágicas ou infecciosas. O total de 43 (86%) pacientes ficaram completamente curadas, seis (12%) tiveram melhora significativa e 1 (2%) não obteve melhora. Estes resultados se mantiveram pelos 3 anos de seguimento.

Conclusões: Os autores consideram o TVT um procedimento eficaz e seguro, realizado ambulatorialmente e com anestesia local, para o tratamento da incontinência de esforço na mulher.

Comentário Editorial

O primeiro autor do artigo é o idealizador e principal proponente do TVT para o tratamento de incontinência urinária na mulher. Os autores apresentam os resultados após 3 anos de seguimento, incluindo pacientes inicialmente relatados.(1). O fato de uma técnica obter sucesso total ou parcial em 98% das pacien-

tes inspira respeito, ainda mais quando consideramos as vantagens adicionais, como o tempo cirúrgico reduzido, e a realização ambulatorial em quase todas as pacientes. Apesar dos resultados iniciais serem favoráveis (1-3), sempre com índices de sucesso acima de 85%, a técnica ainda é recente e mais estudos são necessários para que tenhamos avaliação dos resultados a longo prazo. Dificilmente poderíamos considerar 3 anos como seguimento de longo prazo, especialmente quando lembramos dos resultados a longo prazo com as suspensões endoscópicas. O índice de complicações nestas séries iniciais foi baixo, geralmente envolvendo perfurações inadvertidas da bexiga, durante o período de aprendizado. O uso de um trocarte calibroso às cegas, através do espaço retropúbico, causou pelo menos uma complicação vascular grave, que exigiu cirurgia aberta (3). Vale ressaltar que existe uma enorme pressão de mercado sobre o TVT, e uma palavra de cautela é necessária.

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Sacral nerve stimulation for treatment of refractory urinary urge incontinence

Schmidt RA, Jonas U, Oleson KA, Janknegt RA, Hassouna MM, Siegel SW,
van Kerrebroeck PEV, for the sacral nerve stimulation study group
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Eletro-estimulação de raiz nervosa sacral para o tratamento de urge-incontinência refratária.

Objetivo: Avaliar a eletro-estimulação da raiz nervosa sacral para o tratamento da urge-incontinência refratária.

Pacientes e Métodos: Variáveis primárias para inclusão foram obtidas dos diários miccionais, história e exame físico e avaliação urodinâmica. As pacientes que satisfizeram os critérios de inclusão (idade maior que 16 anos, refratariedade a outros tratamentos, apto do ponto de vista anestésico-cirúrgico, capacidade vesical mínima de 100 ml e com trato urinário superior normal, ausência de doença neurológica, incontinência urinária de esforço ou dor pélvica primária) foram submetidas à colocação percutânea do eletro-estimulador sacral por um período de teste que variou de 3 a 7 dias (155 pacientes). Apenas pacientes que apresentaram melhora superior a 50% em relação aos episódios de urge-incontinência foram randomizados. Em um grupo era colocado, através de cirurgia, o eletro-estimulador (52 pacientes) e em outro a colocação era retardada por 6 meses (42 pacientes). Os indivíduos do grupo em que a colocação do eletro-estimulador era retardada, foram avaliados com 3 e 6 meses, quando então foram submetidos à colocação do eletro-estimulador. Após a colocação do eletro-estimulador os pacientes foram avaliados após 1, 3 e a seguir a cada 6 meses. Para determinar a eficácia do tratamento um segundo teste era utilizado, consistindo em desligar o eletro-estimulador pelo menos durante três dias e os sintomas reavaliados.

Resultados: Após 6 meses de implantação os episódios de incontinência diurna, intensidade dos episódios e número de absorventes foram reduzidos de forma significativa quando comparados ao grupo com colocação retardada (todas as variáveis; $p < 0,0001$). Dos 34 pacientes avaliáveis após 6 meses, e inicialmente submetidos à eletro-estimulação, 16 (47%) obtiveram total resolução dos sintomas e 10 (29%) demonstraram redução maior que 50% dos episódios de incontinência. A eficácia manteve-se durante 18 meses, com retorno

dos níveis iniciais de incontinência em todos os pacientes quando a eletro-estimulação foi desativada. Não houve disfunção miccional detectada pelo estudo urodinâmico com a eletro-estimulação de nervos sacrais. As complicações incluíram dor no local do gerador de impulsos para eletro-estimulação em 15,9%, dor no local do implante em 19,1% e migração do eletrodo em 7% dos pacientes. Revisões cirúrgicas foram necessárias em 32,5% dos pacientes devido a complicações. Não há relato de dano nervoso permanente.

Conclusão: A eletro-estimulação de nervo sacral é um método seguro e eficaz para o tratamento de urge-incontinência refratária.

Comentário Editorial

Este é um estudo que chega em hora oportuna, um vez que se inicia nos Estados Unidos a comercialização da eletro-estimulação da raiz sacra, e em breve deve chegar em nosso meio. Este é um grupo muito especial de pacientes, onde todos os tratamentos conservadores falharam, sendo este procedimento a última opção antes de considerar medidas extremas (ampliação vesical, enervação vesical). Ainda não existe explicação consistente para o mecanismo de ação da eletro-estimulação sacral no tratamento da urge-incontinência, e a hipótese mais aceita é que a eletromodulação do assoalho pélvico tenha um efeito inibitório sobre o detrusor, atuando na via aferente ou eferente das raízes sacras (1). O problema é ainda mais complexo, pois ocorrem alterações na produção de urina, com aumento da secreção do hormônio antidiurético (ADH) (2). Considerando este grupo especial de pacientes, a cura parcial ou total em 64% dos pacientes é um resultado extraordinário, embora não considerando os pacientes onde a estimulação temporária, através do eletrodo percutâneo, foi inefetiva em 57 de 155 (36%) dos pacientes inicialmente avaliados. Do ponto de vista metodológico o estudo não merece crítica. Como o paciente é capaz de sentir a eletro-estimulação, não é possível construir um verdadeiro grupo controle com o gerador desligado ou com redução da amplitude ou frequência da eletro-estimulação. A leitura do artigo fica confusa, uma vez que não é clara a resposta clínica dos pacientes no grupo de colocação após 6 meses (no qual ocorreu um abandono dos pacientes da ordem de 50% até o final do seguimento). Além disso, a necessidade de revisão cirúrgica em um terço dos pacientes é excessiva, e médicos e pacientes devem ficar atentos para esse fato. A justificativa dos autores é que o procedimento é recente e que com o aumento da experiência das equipes a taxa deve baixar. Outro ponto que deve ser ressaltado, é que a colocação do eletrodo permanente requer laminectomia sacral posterior. É prudente que os urologistas envolvidos no tratamento desses pacientes e interessados na utilização dessa tecnologia tenham perfeita integração com as equipes de neurocirurgia e/ou ortopedia para evitar.

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