Hindawi Publishing Corporation
Mediators of Inflammation
Volume 2007, Article ID 45794, 5 pages
doi:10.1155/2007/45794

Clinical Study

Proinflammatory and Oxidative Stress Markers in Patients with Periodontal Disease

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Received 31 January 2007; Revised 23 May 2007; Accepted 25 May 2007

Objective. To evaluate the involvement of proinflammatory and oxidative stress markers in gingival tissue in individuals with chronic periodontitis. *Subject and methods*. Eighteen subjects were divided in two groups: experimental (age 52.9 ± 5.0) and control (age 51.1 ± 9.6). The activities of enzymatic antioxidants such as catalase, glutathione peroxidase (GPx), glutathione S-transferase (GST), glutathione reductase, nonenzymatic antioxidants: total glutathione and reduced glutathione, oxidized glutathione (GSSG), thiobarbituric acid reactive substances (TBARS), and myeloperoxidase activity (MPO) were evaluated in gingival tissues from interproximal sites. Statistical differences between groups were determined by independent Student *t* test and $P < .05$. *Results*. Individuals with periodontal disease exhibited a significant increase in the activities of MPO, GPx, GST, and also in TBARS and GSSG levels in gingival tissue compared to the control group ($P < .05$). *Conclusion*. The results of the present work showed an important correlation between oxidative stress biomarkers and periodontal disease.

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1. INTRODUCTION

The inflammatory and immune reactions induced by the bacterial plaque represent the main characteristics of periodontitis, and this disease represents a particularly cogent example of problem arising from the phenomenon [1].

Studies have demonstrated that periodontal disease affects between 10% and 15% of the world's population, representing the greatest cause of tooth loss [2].

There is strong evidence that this disease affects a specific, predisposed group of the population that presents an exacerbated inflammatory/immune response to the periodontopathogenic bacteria that accumulate on the teeth and around the gingival tissue, which in turn may lead to tissue damage [1, 3].

The exact mechanism of periodontitis development, including the prior agents or mediators involved, is not clear. Periodontitis manifests itself as a multifactor phenomenon, including the generation of reactive oxygen species (ROS) [4].

The strong evidence linking ROS to the pathological destruction of the connective tissue during periodontal disease rests on the presence of neutrophils infiltration as the main event in the host's response to bacterial invasion [1, 5, 6]. Furthermore, hydroxyl radical ($^{\bullet}OH$) is most active in damaging important molecules such as DNA proteins and lipids, while hydrogen peroxide (H_2O_2), even not being considered a potent ROS, is capable of crossing the nuclear membrane and also damaging the DNA [7]. Quantitatively, the main source of superoxide anion ($O_2^{\bullet -}$) and other ROS responsible for initiation reactions is the respiratory chain. However, its presence in the periodontal tissue results first and foremost from the activation of phagocytes (neutrophils and macrophages), such as antibacterial agents [1, 5, 8]. It has been suggested that superoxide anion is involved in bone reabsorption which has been corroborated by studies that have demonstrated the presence of this anion in reabsorption zones adjacent to the osteoclasts [9].

The hydroxyl radical is able to initiate a classical chain reaction known as lipid peroxidation leading to the vasodilation production and rat bone reabsorption [8]. An example of the damage caused by hydrogen peroxide is that it can stimulate the phosphorylation of the NF-$_K$B-I$_K$B complex activating the NK-$_K$B and facilitating nuclear translocation

and downstream of proinflammatory cytokines, including interleukin-2 (IL-2), interleukin-6 (IL-6), interleukin-8 (IL-8), β-interferon, and tumor necrosis factor-α (TNF-α) that are very important in the pathogenesis of periodontal disease [10–12].

ROS production is inevitable in all aerobic organisms including humans, who necessarily posses a complex system of antioxidant defense [8, 13]. If the homeostasis is interrupted in favor of ROS, an oxidative stress situation is created [13].

The aim of this study was to evaluate the involvement of proinflammatory and oxidative stress markers in individuals with chronic periodontal disease.

2. SUBJECTS AND METHODS

2.1. Experimental design

This case-control study was carried out between May–September, 2003 in a single centre (Peridontologic Centre, Florianopolis, Santa Catarina, Brazil). Eighteen subjects were divided into 2 groups: experimental group (E), comprising individuals with chronic periodontitis, age 52.9 ± 5.0 (4 men and 5 women), with the following inclusion criteria: presence of chronic inflammation (pain, redness, heat, swelling), diagnosed according to bleeding on probing, at least 5 or 6 sites with probing depth ≥ 5 mm, attachment loss ≥ 3 mm, and extensive radiographic bone loss [14]. Control group (C), was composed of healthy individuals, age 51.1 ± 9.6 (4 men and 5 women) with no prior history of periodontal disease. The probing depth in this latter group did not exceed 3 mm [14].

For both groups, the following items were considered as exclusion criteria: infection, cardiovascular and/or neurological illness, renal insufficiency and/or diabetes; pregnancy; smoking; use of antibiotics and/or hormonal or nonhormonal anti-inflammatory drugs 6 months prior to tissue collection.

In the day of the surgical procedures, the patients showed no complication.

This study was in agreement with the ethical principles of the World Medical Association Declaration of Helsinki (1964). Permission for this study was obtained from the Ethical Committee for Human Research of the Federal University of Santa Catarina (Project no. 210/2002) and the study included only individuals that agreed to participate after reading and signing a free and informed consent form, except those with difficulty in understanding and communicating, with physical handicap, or both, which could have compromised the sample collection.

2.2. Assessment of periodontal disease

All of the surgical procedures were assessed and performed by a periodontist, according to the necessity for each treatment. The patients with chronic periodontitis (experimental group) were submitted a pocket depth reduction technique from palatal/lingual, buccal, and interproximal sites [15]. The biopsies were obtained from inflammatory granulation tissues, connective and epithelium tissues.

The samples collected from the control group were obtained from quarantined mucosa during the surgical procedures of impacted third molars removed following orthodontic recommendation or after the reopening of dental implants.

All samples from the experimental and control groups were removed during the surgical and were immediately frozen in liquid nitrogen ($\cong -170^{\circ}$C) subsequently latter laboratory analysis.

The determinations of the inflammatory parameters were made as scheduled on different days. On the day of the experiments, the samples were deathward at room temperature to determine the different parameters: CAT, GPx, GST, GR, MPO activities, and the contents of TG, GSH, GSSG, and TBARS.

2.3. Assessment of antioxidants enzymes

The method described by Aebi was employed to measure the catalase activity (CAT) by measuring the decay of a freshly prepared 10 mM hydrogen peroxide solution at 240 nm [16].

Glutathione peroxidase (GPx) was measured at 340 nm through the glutathione/NADPH/glutathione reductase system by the dismutation of *tert*-butyl hydroperoxide [17].

Glutathione S-transferase (GST) activity was determined at 340 nm using CDNB (1-chloro-2, 4-dinitrobenzene) as substrate and a 0.15 M GSH concentration [18].

Finally, glutathione reductase (GR) activity was assayed at 340 nm by measuring the rate of NADPH oxidation [19]. Results were expressed as $\text{mmol}^{-1}\text{g}^{-1}$(CAT) and $\mu\text{mol}\ \text{min}^{-1}\text{g}^{-1}$ (GPx, GST, and GR).

2.4. Nonenzymatic antioxidants

Nonprotein thiols, mostly present as the reduced form of glutathione (GSH), were measured at 412 nm according to Beutler using Elmann's reagent (DTNB: 2-dithionitrobenzoic acid) [20]. Immediately after thawing, acid extracts were obtained by adding tissue portions to 12% trichloroacetic acid (1 : 4 w/v), which were then centrifuged at 15 000 g for 5 minutes at 5°C. Supernatants from the acid extracts were added to a buffer containing 0.25 mM DTNB in 0.1 M Na_2PO_4, pH 8.0, and the formation of the thiolate anion was immediately determined. Total glutathione (TG) was also measured at 412 nm in acid extracts according to the enzymatic method of Tietze [21]. Oxidized glutathione (GSSG) was also determined by calculating the difference (in equivalents of GSH) between total glutathione and reduced glutathione contents. Results were expressed as $\mu\text{mol}\ \text{g}^{-1}$.

2.5. Myeloperoxidase activity

Myeloperoxidase activity was measured according to the method developed by Rao et al., and was estimated by colorimetric measurement at 450 nm on an Elisa plate reader [22]. Results were expressed as mU/mL.

Table 1: Biomarkers of oxidative stress in gingival tissue of healthy control and individuals with periodontal disease. The results are represented by means ± SEM of controls (healthy individuals) and patients with periodontal diseases (E). CAT = Activities of Catalase, GPx = glutathione peroxidase, GST = glutathione S-transferase, GR = glutathione reductase, MPO = myeloperoxidase, TG = total glutathione, GSH = glutathione.

	Control	Experimental	P
CAT (mmol $min^{-1}g^{-1}$)	1.64 ± 0.46	2.00 ± 0.30	.523
GPx (μmol $min^{-1}g^{-1}$)	0.80 ± 0.11	2.09 ± 0.34	.006***
GST (μmol $min^{-1}g^{-1}$)	4.28 ± 0.89	10.81 ± 0.63	.001***
GR (μmol $min^{-1}g^{-1}$)	0.28 ± 0.04	0.22 ± 0.06	.481
MPO (mU/mL)	222.20 ± 54.00	556.44 ± 76.77	.003***
TG (μmol g^{-1})	0.44 ± 0.11	0.63 ± 0.09	.171
GSH (μmol g^{-1})	0.38 ± 0.08	0.46 ± 0.06	.459
SSG (μmol g^{-1})	0.06 ± 0.01	0.17 ± 0.04	.019***
TBARS (nmol g^{-1})	113.07 ± 16.59	188.80 ± 20.73	.015***

*** ($P < .001$) mean statistical differences between controls and experimental group.

2.6. Lipoperoxidation assay

Thiobarbituric acid-reactive substance (TBARS) contents were determined to assess endogenous lipid oxidation in gingival tissue according to Ohkawa et al. [23] and Bird and Draper [24]. After thawing, gingival portions were immediately added to 12% trichloroacetic acid (1 : 4 v/v) and were then centrifuged at 15 000 g for 5 minutes at 5°C. Supernatants were added to 50 mM Tris-HCl pH 7.0, vortexed for 20 seconds, added to 0.67% (w/v) 2-thiobarbituric acid, maintained in boiling water for 60 minutes, cooled at 5°C for 30 minutes, and then analyzed spectrophotometrically at 535 nm. Concentrations were expressed as nmol TBARS/g wet tissue using $\in_{535} = 153\,mM^{-1}cm^{-1}$.

All the biochemical parameters described above were measured in duplicate, except for the TBARS determinations, which were measured in triplicate.

3. STATISTICAL ANALYSIS

The results were expressed as mean ± SEM. Statistical differences between groups were determined by independent Student t test analysis. For all analyses, $P < .05$ was used to assess overall differences.

4. RESULTS

4.1. Antioxidant enzyme activities

These results show that there were no significant differences in catalase activity in the experimental group (E) compared to the control group ($P = .523$). However, a significant increase in GPx activities in the experimental group when compare to the control group ($P = .006$) was detected (see Table 1). Furthermore, in the experimental group, a significant increase of glutathione S-transferase (GST) values compared to the control group ($P = .001$) was also observed (see Table 1). The analysis of glutathione reductase (GR) revealed no differences between the studied groups ($P = .481$) (see Table 1).

4.2. Myeloperoxidase activity

The myeloperoxidase activity revealed a significant increase of this inflammatory biomarker in the experimental group ($P = .003$) (see Table 1).

4.3. Nonenzymatic antioxidant defenses

In relation to the total glutathione (TG) and the reduced glutathione (GSH) contents, no differences in the values of the experimental group compared to the control group were found ($P > .05$) (Table 1). However, the values obtained for oxidized glutathione (GSSG) showed a significant increase in the experimental group when compared to the control group ($P = .019$) (see Table 1).

4.4. Measurement of tissue lipoperoxidation

Lipoperoxidation was measured through TBARS contents, which were significantly a higher increase in the experimental group ($P = .015$) (see Table 1).

5. DISCUSSION

Few studies have considered the effect of the imbalance between oxidants and antioxidants in patients with periodontitis, which in turn predisposes such individuals to the damaging effects of ROS in the periodontium [25]. Ellis and collaborators analyzed gingival tissues from patients with severe periodontal disease and showed that the activity of catalase was decreased [26]. In the present study, the activity of catalase was not different when the experimental and control groups were compared. One possible explanation for these different responses is that the patients with periodontal disease were in distinct stages of the disease. In this regard, it is well known that the antioxidant responses found in different pathologies depend on the severity or extension suffered by the patients, and long-term chronic conditions may have jeopardized the antioxidant defenses [8].

The analysis of the enzyme glutathione peroxidase revealed a significant increase in the experimental group.

A GPx increase in gingival samples from dogs and humans with periodontal disease has already been described [6, 27]. The GPx increase may represent possible antioxidant compensation in detoxification reactions of organic peroxides produced during oxidative stress in gingival tissue [28].

Furthermore, glutathione S-transferase (GST) also revealed a significant increase in its activities in the experimental group. Since GST has a direct role in the neutralization of hydroperoxides derived from the lipoperoxidation processes, increases in GST activities are probably related to the oxidative stress caused by the periodontal inflammatory process [8, 29]. GST comprises a group of enzymes that are also able to detoxify a variety of compounds including xenobiotics derived from pathogenic microorganisms, catalyzing their conjugation with GSH [30]. Hence, increases in GST activities are excellent indicators of endogenous detoxification from exogenous sources [31].

The enzyme glutathione reductase (GR) has an important accessory antioxidant function related to glutathione peroxidase and glutathione S-transferase. GR intervention continuously regenerates GSH from GSSG in the presence of NADPH, therefore preventing cellular loss of GSH [32]. However, in the current study, no differences in GR activities were detected in gingival tissue between the two groups.

The ubiquitous tripeptide glutathione (GSH) acts directly as a generic ROS scavenger or as a cofactor of GPx and GST, either by catalyzing the reduction of hydrogen peroxide and lipid hydroperoxides or by the conjugation/excretion processes of the so-called Phase II reactions [31]. Total and reduced glutathione revealed a tendency to increase, but the values were not significantly different in patients with periodontitis compared to the controls.

Despite GSH, these results suggest a de novo synthesis of glutathione, which is extremely necessary for the homeostasis of cells [31]. Some periodontopathogenic bacteria deplete GSH, and this may explain the amount of this antioxidant was not elevated in the gingival tissue of patients with periodontitis combined with an increase of the GPx activity in the affected tissue [33, 34]. A similar result was obtained in gingival tissue and blood, but lower levels of GSH were detected in the crevicular gingival fluid of patients with chronic periodontitis, when compared to normal subjects [27, 35].

On the other hand, a significant increase in GSSG concentrations was detected in the experimental group, which is a clear biomarker of oxidative stress detected in inflammatory processes linked to periodontitis. Nevertheless, Chapple et al. (2002) found less GSSG in gingival cervical fluid of patients with chronic periodontitis [35]. Consistent with the results for GSSG, tissue lipoperoxidation, measured as TBARS contents in the gingival tissue, also displayed a significant increase ($P = .015$) in individuals affected by periodontitis, and oxidative stress, in the gingival tissue associated with periodontal disease [36].

The systemic depletion of antioxidants clearly indicates that in chronic periodontitis the antioxidant system is affected by a relatively strong oxidation insult, which can also deplete nutritional antioxidants such as vitamin E and C in plasma and also vitamin E in red cell membrane [27].

Moreover, myeloperoxidase activity in gingival tissue showed a significant increase in patients with periodontal disease when compared to the control group, an indicative of a chronic inflammatory process also reflected at a systemic level. These results were similar to the measurements obtained from the analysis of crevicular gingival fluid in humans with periodontal disease [37].

Oxidative stress processes and alterations in the immune system are closely related and have been described in different diseases, thus both the aspects also seem to be linked to the pathogenesis of periodontal disease, and can also be detected in the plasma of patients with periodontitis [8, 27, 35]. However, the extent to which ROS overgeneration influences the initiation and progression of periodontal diseases is still unknown.

In conclusion, in spite of the limited number of samples examined in the present study, the results indicate a relationship between proinflammatory and oxidative stress biomarkers and periodontal disease.

ACKNOWLEDGMENT

This work was supported by grants from the Conselho Nacional de Pesquisa e Desenvolvimento Científico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, from Brazil for fellowship support).

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Interdisciplinary Perspectives on Infectious Diseases

Special Issue on Climate Change and Infectious Disease

Call for Papers

Virtually every atmospheric scientist agrees that climate change—most of it anthropegenic—is occurring rapidly. This includes, but is not limited to, global warming. Other variables include changes in rainfall, weather-related natural hazards, and humidity. The Intergovernmental Panel on Climate Change (IPCC) issued a major report earlier this year establishing, without a doubt, that global warming is occurring, and that it is due to human activities.

Beginning about two decades ago, scientists began studying (and speculating) how global warming might affect the distribution of infectious disease, with almost total emphasis on vector-borne diseases. Much of the speculation was based upon the prediction that if mean temperatures increase over time with greater distance from the equator, there would be a northward and southward movement of vectors, and therefore the prevalence of vector-borne diseases would increase in temperate zones. The reality has been more elusive, and predictive epidemiology has not yet allowed us to come to conclusive predictions that have been tested concerning the relationship between climate change and infectious disease. The impact of climate change on infectious disease is not limited to vector-borne disease, or to infections directly impacting human health. Climate change may affect patterns of disease among plants and animals, impacting the human food supply, or indirectly affecting human disease patterns as the host range for disease reservoirs change.

In this special issue, Interdisciplinary Perspectives on Infectious Diseases is soliciting cross-cutting, interdisciplinary articles that take new and broad perspectives ranging from what we might learn from previous climate changes on disease spread to integrating evolutionary and ecologic theory with epidemiologic evidence in order to identify key areas for study in order to predict the impact of ongoing climate change on the spread of infectious diseases. We especially encourage papers addressing broad questions like the following. How do the dynamics of the drivers of climate change affect downstream patterns of disease in human, other animals, and plants? Is climate change an evolutionary pressure for pathogens? Can climate change and infectious disease be integrated in a systems framework? What are the relationships between climate change at the macro level and microbes at the micro level?

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Guest Editors

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Advances in Urology

Special Issue on
The Changing Concepts of Vesicoureteral Reflux in Children

Call for Papers

Vesicoureteral reflux (VUR) is considered an enigma of pediatric urology practice, where the management of this salient disease evolved from surgical intervention to observation. Bladder physiology and dysfunction has become the culprit behind VUR, making the diagnosis of primary reflux a historical diagnosis. However, recently the introduction of Deflux and other injectable materials revolutionized the management of VUR in pediatric population. Subsequently, from the moment a child is diagnosed with reflux, pediatric urologists are faced with challenging questions both by parents and peers:

- Do antibiotics have a role in management of VUR?
- If the management of reflux is conservative, do we really need to have this pathology diagnozed? and which radiological modality is better?
- What are the current surgical modalities to treat reflux in 2008?
- What if reflux is not treated, does it cause higher risk of infections in girls at puberty?
- What can the literature tell us? More specifically, do we have enough objective data in the literature on the research and outcome of VUR that will help pediatric urologists make a decision?

Voiding cystourethrogram is recognized as a disturbingly invasive test in pediatrics and sedation, for this test is becoming a routine for children undergoing this test in some centers.

This special issue on the changing concepts of vesicoureteral reflux in children will be focused on addressing most of these questions in an attempt to provide a state-of-the-art foundation for decision making when a urologist is faced with a child who harbors VUR.

The ideal list of topics to be covered is as follows:

- Bladder dynamics, voiding dysfunction and reflux
- Endoscopic treatment: technique
- Intravesical ureteral reimplantation: surgical technique
- Extravesical ureteral reimplantation: surgical technique
- Antibiotics and vesicoureteral reflux
- Diagnostic approach to reflux in 2007
- Outcome of surgical versus medical management of VUR
- Update on reflux nephropathy and ESRD 2nd to VUR
- Relation between Deflux volume and reflux resolution
- Reflux treatment evolution
- Design of study
- VCUG and radiation
- Sedation and VCUG
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Publication Date	October 1, 2008

Guest Editors

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Advances in Urology

Special Issue on
Comprehensive Management of Upper Tract Urothelial Carcinoma

Call for Papers

Urothelial carcinoma of the upper urinary tract is relatively uncommon, representing only 5% of all urothelial cancers. The 5-year cancer-specific survival for upper tract urothelial carcinoma in the United States is roughly 75% with grade and stage serving as the most powerful predictors of survival. Nephroureterectomy with excision of the ipsilateral ureteral orifice and bladder cuff en bloc remains the gold standard treatment for upper tract urothelial carcinoma, but endoscopic and laparoscopic approaches, are rapidly evolving as standards of care depending on grade and stage of disease. Several controversies remain in management of upper tract urothelial carcinoma including patient selection for endoscopic versus laparoscopic approaches, management strategies of the distal ureter, the role of lymphadenectomy in upper tract urothelial carcinoma, and the value of chemotherapy in upper tract disease.

Aims of this special edition will be to critically review and evaluate controversies in management of upper tract urothelial cancer including: endoscopic management of upper tract urothelial carcinoma, laparoscopic nephroureterectomy and management of the distal ureter, the role of lymphadenectomy in management of upper tract urothelial cancer, and the emerging role of chemotherapy in upper tract disease.

- Endoscopic management of upper tract urothelial carcinoma
- Laparoscopic nephroureterectomy and management of the distal ureter
- Role of lymphadenectomy in management of upper tract urothelial cancer
- Role of chemotherapy in management of upper tract urothelial carcinoma

Authors should follow the Advances in Urology manuscript format described at the journal site http://www.hindawi.com/journals/au/. Prospective authors should submit an electronic copy of their complete manuscript through the journal Manuscript Tracking System at http://mts.hindawi.com/, according to the following timetable:

Manuscript Due	May 1, 2008
First Round of Reviews	August 1, 2008
Publication Date	November 1, 2008

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Advances in Urology

Special Issue on Practice Management and Health Policy

Call for Papers

The explosion of better health care technology coupled with the government's inability to adequately pay for these services has caused a major dilemma. Because of this, many different reimbursement paradigms have been suggested to replace the current fee for service system. This movement in part also stems from the Institute of Medicine's (IOM) 1998 report "*To Err is Human*" which reported that approximately 98 000 people die annually in the United States because of preventable medical mistakes. This has raised public awareness of medical errors and sparked new ideas from payers and consumers in order to improve health care quality and outcomes. In 2001, the IOM's subsequent report recommended aligning reimbursement policies with quality improvement thus increasing awareness of pay-for-performance (P4P), a reimbursement system based on rewarding physicians for the quality, rather than quantity, of provided care. With P4P initiatives currently underway in both the private and public sectors, there has been increased attention towards refining healthcare delivery through improved efficiency, application of core business principles to ambulatory care, and improving patient satisfaction.

The scope of this special edition is two fold: one is to focus on the importance of practice management and to present and discuss research in this area along with commentary on the implementation of electronic medical records, practice mergers, and methods to improve practice efficiency. The second objective is to provide the reader with health policy updates from nationally recognized experts and organizations regarding many of the rapidly evolving issues involving urologists.

The list of topics to be covered includes, but is not limited to:

- Office efficiency in the urology practice
- The impact of physician work effort both in the operating room and in the office: what is the best balance?
- Merging physician practices: lessons learned
- Update from MEDPAC on current health policy trends as related to reimbursement in the United States (Ron Castellanos)
- Leverage advocacy: promoting new models for health policy in urology (UROPAC: Sam Sheppard)
- The ramifications of the pay for performance reimbursement paradigm on clinical practice patterns for common urologic conditions
- The impact of electronic medical records on physician practice
- Update on AUA efforts in the area of physician quality reporting and the development of urology specific quality measures

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Manuscript Due	June 1, 2008
First Round of Reviews	September 1, 2008
Publication Date	December 1, 2008

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Advances in Urology

Special Issue on Management of Small Renal Masses

Call for Papers

This special issue aims at summarizing distinct aspects of the management of small renal masses nowdays, focusing on its epidemiology, pathological aspects, prognosis, and mostly the different treatment strategies.

During the last two decades, we all have observed an astonishing increase in the detection of small renal masses, which, generally speaking, we assume to be under 4 cm although there is not a clear cut-off for the definition of a small renal mass. The increase in longevity and medical attention demanded by the population and mainly due to the popularization of sonography among different colleagues, even as a first visitation test in many offices, are some of the classical reasons to justify this phenomenon, but maybe not the unique ones.

All these have led the evolution from radical to partial nephrectomy as the gold standard technique for the treatment of these masses, based on the high percentage of benign masses within this cohort and also the same oncological data when renal cell carcinoma is reported among both techniques.

Then laparoscopy came into scene and partial nephrectomy was finally adopted as a difficult technique but with improved quality of life issues compared to open partial nephrectomy and with the same oncological outcome. While we were attending the slow generalization of this approach, or maybe due to its intrinsic difficulty, we are now receiving many other minimally invasive techniques trying to compete with the previous surgical procedures, namely, radiofrequency, cryoablation, HIFU, and so forth. But, is it necessary to treat all these masses? It is clear that approximately 25% of these masses are not malignant, and there is growing evidence that not all these masses will kill our patients.

This special issue will be focused on the characterization of the present small renal masses and the different management possibilities. We invite authors to present personal experiences, reviews, and opinions around the issue.

The list of topics to be covered is as follows:

- Epidemiology of renal masses
- Incidental diagnosis and clinical symptoms: prognosis aspects
- Histological characterization of small renal masses
- Necropsy studies: incidence of silent renal masses
- Concept of renal adenoma: useful or old term
- Radiology of small renal masses
- Familial syndromes coupling with small renal masses
- Genetic counselling in renal masses
- Potential role of percutaneous biopsy in small renal masses
- Size as a prognostic factor in renal masses
- Multifocality and renal masses
- Watchful waiting in front of a small renal mass
- Importance and limits of ischeamia in renal partial surgery: experimental and clinical research
- Open partial nephrectomy
- Laparoscopic partial nephrectomy
- Cryoablation
- Radiofrequency
- HIFU

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Manuscript Due	April 1, 2008
First Round of Reviews	July 1, 2008
Publication Date	October 1, 2008

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Advances in Urology

Special Issue on Penile Reconstructive Surgery

Call for Papers

The aim of this special issue is to summarize various congenital and acquired penile anomalies, focusing on recent surgical techniques and their outcomes.

Penile reconstruction presents a great challenge. During the last few decades, many operative procedures and their modifications for the treatment of both congenital and acquired anomalies have been published. One of the most common congenital anomalies is hypospadias. Repair of this anomaly has become easier with the Snodgrass principle for distal and buccal mucosa graft combined with genital flaps for proximal forms. However, the complication rate has not been minimized to a satisfactory outcome. Lengthening of the epispadiac penis presents the main aim in epispadias repair with a dilemma regarding correction of curvature, internal rotation, plication or graft techniques. The current management of patients with intersex, now named disorders of sex development, has resulted in updated etiological and outcome data as well as refined surgical procedures. Ambiguous genitalia play a role in gender differentiation and surgical treatment should be based on answers obtained from the psychosexual questionnaire of this population.

The degree of curvature, type of deformity, erectile dysfunction, and penile length are all characteristics that are assessed when choosing the best surgical intervention in Peyronie's disease. The majority of procedures are usually plagued with some loss of length. The application of radical geometrical principles in creating and fashioning of the graft of an appropriate size leads to precise correction with adequate penile lengthening. A wide variety of medications, devices, and surgical interventions are available to patients with erectile dysfunction. Although technological improvement of penile prosthesis leads to their rising popularity, strict indications and rigorous surgical principles for implantation should always be respected (followed) in order to avoid unnecessary surgery and possible complications with severe psychological consequences.

Modern technology results in frequent injuries which include penile trauma. Generally, reconstruction is very demanding and selected surgical options depend on etiology and severity of injury. Last but not least, penile carcinoma is an aggressive disease with significant treatment-associated psychosexual morbidity. Despite high control rates with radical surgical approaches, organ-sparing surgery should be considered in order to achieve a better psychosexual life.

We invite authors to present personal experiences, reviews, and opinions surrounding the following issues:

- Hypospadias repair
- Epispadias repair
- Intersex
- Peyronie's disease
- Penile prosthesis
- Penile cancer

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First Round of Reviews	August 1, 2008
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