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Research in surgery

Pesquisa em cirurgia

Aldo Cunha Medeiros, ECBC-RN[1].

We must agree that research represents the backbone for the development of surgery. Research in surgery, developed by a multidisciplinary team of researchers and support team, focused on the prevention and relief of human suffering due to surgical disease. The way to achieve this vision is through the use of patient-centered outcome research. Patient-centered researchers use data critical evaluation to identify the best evidence to guide patient care in the real world. Researchers are interested in how various procedures influence the patient's health in terms of functional capacity and quality of life. Once best practices are identified, research surgeons or academic surgeons, whether in basic or clinical research, work with common sense to sooner or later make them a reality for all surgical patients.

However, the reality in our country is that incentives for research are scarce, one of the causes that makes the great majority of Brazilian surgeons exclusively dedicated to the care activity, both in public and private hospitals, university or do not. It must be recognized that in order to perform relevant, good-quality and scientifically-based research, it takes time, a lot of teamwork, and no financial return most of the time. Three magic words are essential for the activity of research: interest, appreciation for what one does and dedication.

Developing the interest for research in surgery

The interest in surgical research has been a decisive factor in the surgical advances observed over time, since it represents the key to the progress of surgical sciences. How to stimulate interest in research? This is the critical issue that needs to be answered in order to get the best possible participation. One must believe that mixing interest in research with the results coming from it shows the benefits of research in the surgical sciences and patient care. In addition, emphasizing the importance of the interest in scientific research in meetings of Surgery Services and in Brazilian and International Surgery Congresses represents the best way to position its prominence among all participants. Knowing that research is the basis for evidence-based medicine makes it obvious that interest in research and its results facilitates the understanding and application of evidence-based principles. In this sense, then, interest in research becomes paramount.

Research groups or, in a broader context, Departments and Surgery Services, increasingly need to act in an integrated manner in their research efforts, working in collaboration with other departments, services and medical schools. Senior researchers in surgery services should insist on encouraging the youngest and provide expertise in research design, study methodology, primary and secondary data collection, and complex data analysis, and work on the use of techniques to innovate and translate research results into real-world process of surgical activity. To support the vision of new surgeons, next generation research training is of paramount importance. It is perfectly feasible to associate care and research activities from medical residency to the battle for survival in working life. It is difficult but possible and it should be stimulated.

Surgery Services need to have as premises: VISION – leadership in the prevention and relief of human suffering due to surgical disease; MISSION – to advance the care of the surgical patient through multidisciplinary research, focused on results and to train the next generation of surgeons and researchers. VALUES – to develop a teaching culture combined with research in the hospital staff and in the faculty of the university surgical departments; to transform research innovation

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into improvement of procedures and surgical procedures; to ensure education and research in surgery for the next generation. These premises pass through ethics.

Research in experimental surgery

The laboratory of experimental surgery continues to be important and even indispensable in medical schools, a key factor in the evolution of surgery (since the time of Claude Bernard, Alfred Blalock and many others), both to test new surgical techniques, new materials and medications, and for surgical training and learning. The essential character of the laboratory of experimental surgery in medical schools has been increasingly important in the information technology century, for is high the speed with which new procedures, equipment and biocompatible materials for potential use in surgery are presented. The emergence of videoendoscopic surgery, robotics and other technologies has made it increasingly important to use experimental surgery laboratories to better understand the pathophysiological mechanisms of diseases, to undertake therapeutic trials with new drugs, to study biological markers and to evaluate these new techniques with perspectives of applicability in the human species[1]. All this has triggered, throughout history, ethical, bioethical, philosophical and religious reflections directed to research in vertebrate animals[2].

The use of animals in experimental surgery

The use of laboratory animals in scientific research is a dilemma that has caused some of the greatest conflicts in bioethics debate. The principle of ethical experimentation with animals, known as the three Rs principle, proposes a *reduction* of the number of animals used in each experiment, *refinement* of experimental techniques to avoid unnecessary pain and suffering, and *replacement* by alternative methods whenever possible. Undoubtedly, this is a concern of experimental work advisors and academic surgeons, who have used technological refinements in the design of experimental models, resulting in a reduction in the number of animals and experimental groups. In this context, researchers should, before thinking about the real need for a biological model with animals, ensure the relevance of the study before deciding to propose a project involving animals. However, the reduction in the number of animals in surgical investigation should not compromise the detection and interpretation of biological effects and should not lead to the repetition of experiments. The design of the study and the calculation of the sample size, the control of variables, the statistical hypothesis tested, the choice of the statistical test used for data analysis and interpretation of the results contribute to refinement, enabling more information without increasing the number of animals used[3].

Ethics in the research

Essentially, ethics in surgical research refers to the application of reasonable behavior to the best moral care with people and animals, as well as to the development and implementation of good laboratory practices in the detailed execution of experimental studies. To perform sound and acceptable surgical research, the surgeon researcher must adhere to the discipline ethic. Performed with the most appropriate scientific methodology available, good research involves a series of steps – the design of a project with the objective of answering the relevant question, the ideal care with the experimental subjects and the appropriate interpretation of data. The completion of these stages of surgical research allows science and ethics to collaborate intimately, resulting in better results. Brazil currently has its own legislation that establishes rules for research on human beings (Resolution 466/2012) and on animals (Law Nº 11,974/2008 and respective Normative Resolutions).

Without research, the many breakthroughs found in surgery would not have been possible the way we see them today. Research allows unprecedented information, more precise knowledge, elements of new and innovative discoveries and possibilities of better treatments. Without research we would not be able to help the thousands, millions of patients who have benefited so far from conquering the evolution of the diseases that affect them. Without research, stagnation in medicine and surgery would reign at

all times. Patients and doctors would not have the same knowledge and possibilities in the treatment of diseases. Research, then, is essential to medicine in general and even more so for surgery. Discovery and validation are two of the most critical developments that emphasize the importance of research. Research can be considered the force that drives the innovators and discoverers who want to advance the understanding of the disease in the surgical world[4].

Developing ideas for new research in surgery

Where do the research ideas come from? What are the factors that stimulate the research idea? When the neophyte researcher comes from a *stricto-sensu* graduate program and is driven by the interest in research and the multiplier effect of the know-how acquired, it is natural that in his home institution he be stimulated to develop studies in the same line of research of the advisor. Ideally, one should choose one or more lines of research, avoiding working in studies at random. Following a line, it is very likely that a paper will render the proposed question not completely answered, generating new questions and new chain searches. Those who are interested in this activity are always attentive to the questions not fully answered in the works they read, in the discussions in research forums, congresses in surgical area, discussions in formal rounds or informal meetings, where naturally arise new ideas and the viabilization of cooperation for further investigation. It is critical that an environment and research group be created in the surgery services or departments, which will be important in generating ideas and bringing them to light. It is an important, pleasurable activity that contributes to learning how to think and to generate knowledge[5].

Writing and publishing results of research in surgery

There is nothing more rewarding for the investigator than seeing the product of his/her research accepted for publication and published in an indexed journal. It is necessary to recognize the essential elements of research, to gather and report the data in a coherent and intelligent way, as critical elements in the submission for the success of the publication. Writing a research article is a demanding process that young surgeons are often ill-equipped to tackle, which is very natural and predictable. The help of more experienced researchers in the writing of scientific work is always important and welcome. It consists of many complex tasks and unavoidable difficulties that confront each researcher. Residence programs should give more attention to cultivating writing skills, especially in the scientific arena. Residency Programs oblige the residents to present a course completion work, which, if done with patient or animal data, must have been compulsorily approved by a Commission or Ethics in Research Committee, and by law publication of results is mandatory. Unfortunately, such works are rarely published. The Journal of the Brazilian College of Surgeons, currently with high international visibility, indexed in several national and international indexers, is available to all surgeons to disseminate their research.

Those who want to join surgical research groups in hospitals or experimental surgery labs must demonstrate not only that they can give good answers to relevant questions, but also that they can and should report their results clearly and effectively so they are useful for their peers.

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Epidemiology of urolithiasis consultations in the Paraíba Valley

Epidemiologia dos atendimentos por urolitíase no Vale do Paraíba

Guilherme Ricardo Nunes Silva[1]; Luiz Carlos Maciel[1].

ABSTRACT

Objective: *to know the epidemiological profile of patients with urolithiasis in the Paraíba Valley region, identifying its prevalence and spatial distribution.* **Method**: *we conducted a cross-sectional study, by residence location in the Paraíba Valley, on morbidity data due to urolithiasis obtained from the DATASUS, covering the period between 2010 and 2012. We aimed at identifying the general, male and female prevalence of urolithiasis, the distribution by age, type of visit, year season and spatial distribution.* **Results**: *there were 1,901 visits for urolithiasis in the 35 municipalities of the Paraíba Valley in the three years studied, 52.3% of them of female patients. Of the total, 70.1% of the visits were emergency ones. The feminine visits (67.2%) were mostly also urgent (p <0.01). The overall prevalence for urolithiasis was 31.7/100,000. Male prevalence was 30.7/100,000, and the female, 32.7/100,000 (p>0.05). The prevalence ratio was 0.9 men for every woman. The age group with the highest prevalence was between 30 and 39 years, with 23.1%. Warm seasons concentrated 51.6% of cases, while 48.8% occurred in the cold ones (p>0.05).* **Conclusion**: *women are more affected by urolithiasis than the male in the Paraíba Valley region, an unprecedented in the literature. There was no relationship between the year season and the disease. We identified municipalities where preventive actions of urinary lithogenesis are required.*

Keywords: *Urology. Urolithiasis. Epidemiology.*

INTRODUCTION

Urolithiasis is one of the most frequent diseases of the urinary tract in the world, displaying an increase in incidence and prevalence in all age groups and genders in the last decades, especially in industrialized countries[1-3]. It determines large costs for the health care systems in the world. In 2000, the estimated treatment cost of urolithiasis was more than two billion dollars in the United States[4]. In 2012, the Brazilian Unified Health System (SUS) has spent more than 32.5 million reais on hospital visits and admissions due to urolithiasis in Brazil[5].

The epidemiological and lithogenic factors of urolithiasis involve ethnicity, gender, age, nutritional and dietary aspects, climate, occupation and physical activity, and it is known to be more common in diabetic, hypertensive and obese patients[2,3,6]. The peak incidence occurs between 20 and 50 years, decreasing after 70 years, being uncommon in children under ten years. Whites are three times more likely to develop urolithiasis that blacks, while Hispanics and Asians have intermediate risk. By mainly affecting people in the economically active group, it is a major cause of absenteeism, affecting the patients' professional productivity. Studies suggest that the incidence of symptomatic urolithiasis increases during the summer, since the increase in temperature and exposure to sunlight are important risk factors for urinary lithogenesis, by favoring a greater risk of dehydration, resulting in increased urinary concentration and increased possibility of formation of urinary calculi and its clinical manifestations[2,6-8].

Historically, urolithiasis has been two to three times more common in men than in women, reaching the men-woman ratio of 3-2[2,6,7]. However, alterations in food consumption patterns, fluid intake and obesity in men and women can cause changes in urolithiasis incidence and prevalence. In the United States the prevalence of urolithiasis is one in every 11 people, and the possibility of the male and female population develop urinary calculi during life is 12% and 6%, respectively[6,9]. Recent studies suggest that this epidemiological relationship between male and female is changing. An annual increase of women calls with complaints related to urolithiasis in emergency units was found, with decreasing male predominance in this disease. The incidence of urolithiasis in the United States,

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for example, is currently 1.3 men for every woman[9-11]. Currently there are no epidemiological studies on the profile of patients seen due to urolithiasis in Brazil.

Changes in the incidence and prevalence of urolithiasis may reflect underlying changes in the disease's risk factors. By identifying changes in its epidemiological pattern, new avenues for the prevention and better care for patients with this disease can be elucidated. This study aims to evaluate the epidemiological profile of the patients treated for urolithiasis in the Paraíba Valley region.

METHODS

This is a cross-sectional study with urolithiasis morbidity data by residence location in the 35 municipalities of the Paraíba Valley region, State of São Paulo, in the period between 2010 and 2012. We obtained data from the National Health System DATASUS database. We excluded the coastal municipalities (Caraguatatuba, Ubatuba, Ilhabela and São Sebastião) from the study because they are geographically separated from the others by the Serra do Mar (Sea Hills).

We considered the population living in the municipalities in the years 2010 to 2012, with the diagnoses N20 to N23 (kidney and ureter calculi, lower urinary tract calculi, urinary tract calculi in diseases classified elsewhere, unspecified renal colic) of the International Statistical Classification of Diseases and Related Health Problems, tenth revision (ICD-10)[12].

We analyzed the data to identify the overall prevalence of symptomatic urolithiasis per 100,000 inhabitants, the prevalence by gender, the age group of patients treated, the type of care (elective or emergency), the season when hospitalizations occurred and the spatial distribution of urolithiasis visits by municipality in which the patient lived. The months considered representatives of the seasons summer (January, February and March), autumn (April, May and June), winter (July, August and September) and spring (October, November and December) are in agreement with data obtained at the Information Access Portal of the National Institute of Meteorology (INMET), for the three years.

We analyzed data using spatial statistics, being geo-referenced and analyzed by area to provide the Global Moran indices (I), with the TerraView software, provided by the National Institute for Space Research (INPE). The Global Moran index is a first order measure of spatial autocorrelation, which indicates the degree of spatial association in the set of information through the product relative to the average. After assembly of the thematic maps with the urolithiasis general, male and female prevalence, we evaluated the expected spatial distribution by Local Empirical Bayesian Method. This performs a softening of rates by municipality, assuming that the knowledge and uncertainties about the real risk value of an event in each area within a given region may be represented by a probability distribution[13]. With the achievement of the expected rates by the local empirical Bayes method, we then compared these with the actual prevalence rates found.

RESULTS

During the study period, urolithiasis complaints were responsible for 1,901 calls from residents in the 35 municipalities of the Paraíba Valley, ranging from one to 562. Of these, 665 (35%) occurred in 2010, 612 (32.2%) in 2011 and 624 (32.8%) in 2012. The average was 54.3 attendances, with a standard deviation of 107.8. During the three years, 52.3% (995) of visits were from female patients. Of the 906 calls by male patients, 73.3% (664) were on an emergency basis. In females, of the 995 urolithiasis calls, 67.2% (668) were urgent ($p<0.01$).

The prevalence of symptomatic urolithiasis in Paraíba Valley, obtained indirectly by the number of visits resulting from this disease, was 31.7/100,000. Regarding gender, the prevalence was 30.7/100,000 in men and 32.7/100,000 in women ($p>0.05$). The relationship found between the male and female prevalence was 0.9 men for every woman affected with the disease. During the period, the age group with the highest number of patients was between 30 and 39 years, with 439 calls, equivalent to 23.1% of the total demand in the three years. Of the total demand due to urolithiasis, 45.1% occurred in patients aged between 30 and 49 years.

In the summer, there were 517 due to urolithiasis, corresponding to 27.2% of the total. In the fall, there were 460 (24.2%). In winter, the number of urolithiasis treatments was 461 (24.2%). Finally, in the spring, there were 463 (24.4%) calls. In the warm seasons (spring and summer) calls summed 51.6% (980) (p>0.05). The global Moran index (MI) and the p-value were I_M=0.01 (p=0.43) for urolithiasis calls per 100,000 inhabitants. Table 1 brings the general and by-gender prevalence of symptomatic urolithiasis of all 35 studied municipalities.

Applying the estimated Bayesian Local Empirical method, we found differences in the actual general prevalence from that expected. The I_M and its p-value were respectively 0.08 and 0.13. We computed the same estimate of the Bayesian Local Empirical method for the prevalence of symptomatic urolithiasis by gender. In men, the I_M was 0.17, and its p-value, 0.07. For females, the I_M was 0.11, and p=0.1.

Table 1. *Overall and by gender/100,000 prevalence of symptomatic urolithiasis in residents of the 35 municipalities of the São Paulo State Paraíba Valley between 2010 and 2012.*

Variables	Overall	Male	Female
Aparecida	10.5	9.9	11.0
Arapeí	40.3	79.8	0
Areias	9.0	18.2	0
Bananal	13.0	19.7	6.4
Caçapava	10.9	12.6	9.3
Cachoeira Paulista	41.8	53.8	30.2
Campos do Jordão	43.0	31.2	54.3
Canas	15.0	14.8	15.2
Cruzeiro	47.4	46.1	48.7
Cunha	139.3	132.0	147.0
Guaratinguetá	51.8	55.3	48.5
Igaratá	45.1	73.4	15.4
Jacareí	34.5	38.8	30.3
Jambeiro	6.1	0	12.7
Lagoinha	27.6	26.9	28.3
Lavrinhas	35.2	20.0	50.6
Lorena	33.4	35.8	31.1
Monteiro Lobato	16.0	0	33.5
Natividade da Serra	40.1	28.8	52.4
Paraibuna	17.2	18.8	15.6
Pindamonhangaba	27.1	26.9	27.4
Piquete	9.5	4.9	13.8
Potim	16.8	14.9	19.3
Queluz	14.5	11.4	17.7
Redenção da Serra	34.5	16.6	54.2
Roseira	34.4	27.3	41.7
Santa Branca	12.1	0	24.1
Santo Antônio do Pinhal	20.5	10.2	31.0
São Bento do Sapucaí	76.4	75.9	76.9
São José do Barreiro	16.4	16.3	16.5
São José dos Campos	29.4	28.1	30.7
São Luíz do Paraitinga	60.9	62.7	59.1
Silveiras	11.4	11.3	11.6
Taubaté	27.3	22.5	31.9
Tremembé	22.5	9.1	37.5

Source: *DATASUS.*

DISCUSSION

This study on the epidemiology of urolithiasis has identified the profile of the distribution of the disease in Paraíba Valley and its prevalence by gender, age, type of service and the season with the most calls. Urolithiasis is historically more prevalent in men than in women. In a review of the specific aspects of male and female genders that are related to the genesis of urolithiasis, Seitz *et al*.[3] stressed that urinary osmolality in men is higher than in women. Furthermore, the antidiuretic response to vasopressin is different between genders, being greater in males, which can influence the urinary concentration and therefore result in a higher chance of urinary stone formation. For years urolithiasis researchers have realized the trend of change in its incidence and prevalence, especially by the gradual increase in the care of women, with consequent reduction of the relationship between male/female care[3,11,14-17].

The prevalence of urolithiasis found in our region is different from all the other identified in similar studies. We found a prevalence in which the female gender is the majority, an unprecedented event. In

Table 2, we compare the prevalence of urolithiasis between male and female found in several studies on its prevalence.

Regarding the type of call, it became clear that the most common call is the urgent one, given that, when symptomatic, urolithiasis usually presents with intense pain and signs that compromise quality of life[6,18]. Women were more prevalent, both in elective and in emergency care ($p<0.01$).

We found that 45.1% of patients treated during the study period were aged between 30 and 49 years, in agreement with the literature[3,15]. According to Trinchieri *et al*.[19], the overall incidence of urolithiasis increases about 0.4% per year, 0.6% in males and 0.2% in females. According to their study, the annual increase in urolithiasis is probably a result of interaction between environmental factors such as dietary habits and lifestyle, particularly the increase in the consumption of animal protein.

When analyzing calls for urolithiasis by season, it became clear that most of the visits occurred in the summer, in which there is greater risk of dehydration due to the increased average temperature, which predisposes to increased urinary concentration and greater chance of urinary calculus formation. However, when comparing the attendances in the warm seasons (spring and summer) with the cold ones (fall and winter), there was no statistical significance ($p>0.05$). In a study on the influence of geographical variation in the prevalence of urolithiasis, Soucie *et al*.[20] concluded that the ambient temperature and the intensity of sunlight are important factors in the genesis of urolithiasis. They observed that the risk of a person developing urinary calculi is almost twice higher in the residents of states nearby the equator, and therefore warmer and with higher incidence of sunlight, when compared with those closer to the north pole, with lower average temperatures and lower sunlight incidence.

The prevalence of symptomatic urolithiasis in Paraíba Valley in the three years studied was 31.7/100,000, fewer than the one found in Florida, in 2004, by Strope *et al*.[11], of 169.9/100,000. In the same study, the prevalence of symptomatic urolithiasis in males and females were, respectively, 105.5 and 64.4/100,000. In our study, the prevalence was 30.7/100,000 for males and 32.7/100,000 for females. No municipality in the studied region showed a higher overall prevalence than that found by Strope *et al*.[11], however the municipality of Cunha had a higher male prevalence than the one found in that study, and as the female prevalence, again Cunha and also São Bento do Sapucaí had a prevalence higher than that found in Florida (Table 1).

Upon spatial analysis, the municipalities with the highest prevalence of urolithiasis in the Paraíba Valley were evident. When considering both genders, there was a cluster of municipalities represented by Sao Luiz do Paraitinga, Cunha, Guaratinguetá, Campos do Jordão and Sao Bento do Sapucaí. For the prevalence in males, the predominant cluster of municipalities was formed by São Luiz do Paraitinga, Cunha and Guaratinguetá. For females, the municipalities belonging to the higher prevalence cluster were Redenção da Serra, Natividade

Table 2. *Urolithiasis male/female prevalence ratio. Adapted from Seitz et al.[3].*

	Male/female prevalence ratio	
Daudon *et al*.[14]	2.3 (2001)	France
Knoll *et al*.[15]	2.4 (1977)	Germany
	2.7 (2006)	
Nowfar *et al*.[16]	1.6 (1998)	United States
	1.2 (2003)	
Lieske *et al*. [17]	3.1 (1970)	United States
	1.3 (2000)	
Our study	0.9 (2015)	Brazil

da Serra, Sao Luiz do Paraitinga, Cunha, Guaratinguetá, Campos do Jordao and São Bento do Sapucaí. These clusters represent municipalities where intervention is important for reducing urolithiasis incidence and prevalence. After evaluation of the municipalities by the Empirical Bayesian Local method, it was possible to see differences in the spatial distribution of the general, male and female symptomatic urolithiasis, which may mean an underreporting of urinary calculi cases or even bad filling of health services forms by staff, not respecting the patient's municipality of residence.

In conclusion, the epidemiological and spatial analysis of urolithiasis in the Paraíba Valley has identified that in the area in question, the women seem to be more affected than men are. We did not detect a relationship between the season and disease. It was possible to identify cities with the highest prevalence rates, where an intervention is required to reduce the occurrence of urolithiasis. For the epidemiological evaluation of urolithiasis in Brazil to be possible, further studies in other Brazilian regions are needed.

RESUMO

Objetivo: conhecer o perfil epidemiológico dos pacientes com urolitíase, na região do Vale do Paraíba, identificando sua prevalência e distribuição espacial. **Métodos:** estudo transversal com dados de morbidade por local de residência decorrente de urolitíase no Vale do Paraíba, relativos ao período compreendido entre 2010 e 2012, obtidos do DATASUS. Os dados foram analisados para identificar a prevalência geral, masculina e feminina da urolitíase, a distribuição por idade, tipo de atendimento, estação do ano e sua distribuição espacial. **Resultados:** ocorreram 1901 atendimentos por urolitíase nos 35 municípios do Vale do Paraíba nos três anos estudados, sendo 52,3% dos pacientes do sexo feminino. Do total, 70,1% dos atendimentos foram em caráter de urgência. Os atendimentos femininos, na sua maioria (67,2%), também foram de urgência ($p<0,01$). A prevalência geral encontrada para a urolitíase foi 31,7/100.000 habitantes. A prevalência masculina foi 30,7/100.000 e a feminina de 32,7/100.000 ($p>0,05$). A relação de prevalência encontrada foi 0,9 homens para cada mulher. A faixa etária com o maior número de pacientes atendidos foi entre 30 e 39 anos, com 23,1% do total. Nas estações quentes ocorreram 51,6% dos atendimentos, enquanto nas frias 48,8% ($p>0,05$). **Conclusões:** foi possível identificar que na região do Vale do Paraíba o sexo feminino é mais acometido pela urolitíase do que o masculino, fato inédito na literatura. Não se encontrou relação entre a estação do ano e a doença. Foram identificados municípios onde ações de prevenção da litogênese urinária são necessárias.

Descritores: Urologia. Urolitíase. Epidemiologia.

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Comparison between polypropylene and polypropylene with poliglecaprone meshes on intraperitoneal adhesion formation

Estudo comparativo entre tela de polipropileno e poliglecaprone com tela de polipropileno na formação de aderências intraperitoneais

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R E S U M O

Objetivo: comparar a formação de aderências intraperitoneais em ratos, com o uso de tela de polipropileno e tela composta de polipropileno e poliglecaprone. **Métodos**: vinte ratos Wistar machos, foram alocados em dois grupos. No grupo 1 os ratos receberam tela de polipropileno no lado direito e tela de polipropileno e poliglecaprone no lado esquerdo. No grupo 2 inverteu-se a posição das telas. Analisou-se a presença ou não de aderências após 30 dias, sendo incluídas apenas aderências sobre as telas. Os resultados foram submetidos à análise estatística, adotando-se como nível de significância p≤0,05. **Resultados**: todas as telas se apresentaram com aderências. Verificou-se que, na tela de polipropileno, a porcentagem de superfície coberta por aderências variou entre 10,5 a 100%, com média 34,07±24,21% enquanto que na tela de polipropileno e poliglecaprone a porcentagem de tela coberta por aderências variou entre 8,5 a 100%, com média 44,7±32,85% (p=0,12). **Conclusão**: ambas as telas dão origem às aderências, não havendo vantagem de aplicação no reparo intraperitoneal de uma em relação à outra.

Descritores: Hérnia. Aderências Teciduais. Telas Cirúrgicas. Estudo Comparativo.

INTRODUCTION

Incisional hernia or eventration is a protrusion of abdominal contents through a weakened area on the abdominal wall, as a result of trauma or a surgical incision. It is a common complication of abdominal surgeries, occurring in 2% to 35% of laparotomies[1-3] and causing significant morbidity and mortality. A considerable number of patients presents with bowel strangulation (2%) and incarceration (6-15%)[4].

The repair of incisional hernias is surgical, with many techniques described. The advent of the use of prosthesis could significantly reduce the recurrence rate when compared with the primary correction[4]. Through laparoscopic approaches, the meshes reached the abdominal cavity. Thus, by being in contact with abdominal structures, they have brought complications such as adhesions, fistulae and intestinal obstructions[5,6]. A systematic review by Castro *et al*.[7] reports that 4.7% of patients that had undergone laparoscopy required enterectomies, a condition capable of raising mortality to 2.8-7.7%[8].

Peritoneal adhesions are present in 90% of patients undergoing abdominal surgery and can cause complications such as intestinal obstruction, infertility, chronic pelvic and abdominal pain, besides difficulties on reoperation[9]. A study by van Goor[10] draws attention, also, to longer periods of hospitalization, duration of surgery, and the need for conversion of laparoscopy to laparotomy. The most commonly used surgical mesh is the polypropylene mesh, because of its flexibility, stimulation of cell growth, satisfactory inflammatory response, ease of handling and low cost. However, this prosthesis induces the formation of adhesions when in contact with intra-abdominal contents[11], justifying the search for meshes that would provoke less complications, while maintaining tissues' resistance and tensile strength[12].

Within this context, several prostheses have been developed, differing in aspects such as composition material, pore size, weight, elasticity, tissue reaction, absorption and biocompatibility[13]. A review by Araújo *et al*.[14] recommends the use of composite meshes for intraperitoneal use. Among these meshes,

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figures the Ultrapro®, a partially absorbable prosthesis, composed of equal parts of polypropylene and poliglecaprone, incorporating high tensile strength, with good biocompatibility, despite the light weight[15].

The objective of this study is to compare the formation of intraperitoneal adhesions between the meshes made of polypropylene and polypropylene associated with poliglecaprone.

METHODS

The project was submitted to the Ethics Committee for Use in Animals of the Biological Sciences Department at the Federal University of Paraná (UFPR), under registry number 23075.006274/2014-48, having been approved.

The sample consisted of 20 male Wistar rats, aged between 100 and 120 days old each, and weighting 316 to 400 grams, with an average weight of 360.5±19.32 grams. The animals were allocated at the Vivarium of the Discipline of Surgical Technique and Experimental Surgery of UFPR during the experiment, with free access to food and water.

We randomly divided the sample into two groups, with ten rats each. We inserted both meshes in each animal on the ventral wall on the intraperitoneal face, so that each rat would be its own control. In Group 1, the polypropylene mesh was disposed on the peritoneal surface, to the right side of the midline incision, and the polypropylene with poliglecaprone mesh was placed on the left side. In Group 2, we inverted the disposition of the meshes. After 28 days of the procedure, we euthanized the rats.

The animals underwent anesthesia with 0.1ml/100g weight of a composite solution of ketamine (50mg) and xylazine (20mg), complemented with inhalatory isoflurane. We performed a midline, 4cm, xifo-pubic incision. We placed the 10x20 mm size meshes intraperitoneally, according to the group of the corresponding animal, and fixed them with 5.0 polypropylene. The skin was sutured using 4.0 nylon. Analgesia was done with a 10mg/kg intramuscular injection of dipyrone. After 28 days of the procedure, we carried the euthanasia, according to the CONCEA Guidelines for the Practice of Euthanasia, 2013, and the Brazilian Guide for Good Practice in Animal Euthanasia from the Federal Council of Veterinary Medicine, 2013. We performed it with the intravenous administration of a 10% Potassium Chloride solution, 5mg/kg, under anesthesia with intravenous Thiopental, 10mg/kg, and inhalatory isoflurane.

We them opened the abdominal cavity with a U-shaped incision that, when lifted, allowed the evaluation of adhesions. We analyzed their presence or absence, including only adhesions on the meshes and excluding those on the midline suture and on the transfixing stitches, since regardless of the prosthesis used, there is a predisposition of the tissue to form adhesions on suture locations[16].

For the evaluation, the area affected by the adhesions was projected in graph paper, on a sketch of the same size of the mesh (10x20 mm). For more precision, visceral adhesions were sectioned and put out to analyze the previously hidden portion of the mesh. From these projections over the graph paper, we obtained the percentage of mesh covered by adhesions. The mesh attached to the peritoneum was considered incorporated, and when held only by the fixation points, was treated as not incorporated.

The results were then submitted to statistical analysis through the Mann Whitney test for evaluation of the mean and the Fisher's test for the frequency, adopting $p \leq 0.05$, or 5%, as the level of significance.

RESULTS

There were no post-operative complications or deaths. One polypropylene mesh and seven polypropylene with poliglecaprone meshes did not show incorporation to the parietal peritoneum (Table 1). In addition, all the meshes presented with adhesions.

In Group I, the percentage of the meshes' surface covered by adhesions on the right side (polypropylene) varied from 12% to 49%, with a mean of 25.69±13.61%, while on the left side (polypropylene with poliglecaprone), the covered surface percentage

Table 1. *Number of incorporated meshes.*

Incorporation	Polypropylene	Polypropylene with Polyglecaprone	Total
Yes	19	13	32
No	1	7	8
Total	20	20	40

Fisher's exact test à 0.0201

ranged from 13% to 100%, with an average of 49.45%±25.57 ($p<0.05$) (Table 2, Figure 1).

In Group II, the percentage of the meshes' surface covered by adhesions on the right side (polypropylene with poliglecaprone) varied from 8.5% to 100%, with an average of 39.95±36.77%, while on the left side (polypropylene), the percentage ranged from 15% to 100%, with a mean of 42.45±28.07% ($p>0.05$) (Table 3, Figure 2).

Regardless of the groups, we found that the polypropylene mesh had the percentage of the surface covered by adhesions ranging from 10.5% to 100%, with a mean value of 34.07±24.21%, while on the polypropylene with poliglecaprone mesh, the covered percentage varied from 9% to 100%, with an average of 44.7±32.85% ($p=0.12$) (Table 4, Figure 3). In both meshes, adhesions were to the omentum (98.5%) and the spermatic cord (80%). The liver was present in 20% of cases (5% in the polypropylene and 15% of the polypropylene with poliglecaprone) and the small bowel in 2.5 % of cases (Figure 4).

Table 2. *Percentage of mesh surface covered by adhesions in Group 1.*

	Area with adherences	
Animal	Right Side	Left Side
1	18.5	100
2	37.5	53.5
3	49	80
4	17.4	44
5	10.5	68.5
6	25	13
7	12	43
8	19	30
9	49	42
10	19	20.5
Mean	25.69	49.45
SD*	13.62	25.57
%SD*	53.02	51.71

** SD= Standard derivation Mann-Whitney's test $p<0.05$*

DISCUSSION

The intraperitoneal use of surgical meshes in the repair of incisional hernias can induce the formation of adhesions, intestinal obstruction and fistulae[5,6]. The direct contact of the prosthesis with the viscera contributes significantly to the process[11]. In a study by Halm *et al*.[17], 76% of patients in which the mesh was placed intraperitoneally developed adhesions, of whom 20% needed bowel resection. In addition, complications were present in 77% of patients who required reoperation, increasing the incidence of postoperative complications. The most feared complication, intestinal obstruction, is associated with higher rates of morbidity and mortality[9,10], what drives the search for a composition of meshes that present fewer complications, while maintaining resistance and strength to traction.

When inserted intraperitoneally, in general a mesh induces a foreign body reaction and the

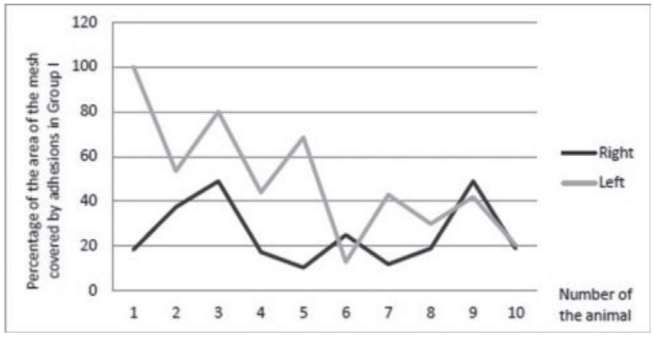

Figure 1. *Percentage of mesh area covered by adhesions in group I. Note: right Side – polypropylene; left side – polypropylene with poliglecaprone.*

Table 3. *Percentage of mesh surface covered by adhesions in Group 2.*

	Area with adherences	
Animal	Right Side	Left Side
11	100	20
12	44	56.5
13	8.5	18
14	10	17
15	9	76
16	80	62.5
17	10	26.5
18	100	100
19	13	33
20	25	15
Mean	39.95	42.45
SD*	36.77	28.08
%SD*	92.04	66.15

** SD= Standard derivation Mann-Whitney's test p<0.05*

formation of adhesions, which represent a pathological process of the peritoneal healing[18]. Among the main causes of adhesions are the presence of foreign bodies, peritoneal inflammation, ischemia, trauma and abrasion[19]. Surgical trauma triggers an inflammatory process that comprises both vascular and cellular changes, as well as the formation of a fibrin matrix, which gradually results in the development of a tissue composed of fibroblasts, macrophages, and other inflammatory cells. This process of peritoneal repair is involved with the incorporation of the prosthesis, and may progress to the formation of adhesions[20].

With the advent of the laparoscopic approach and the consequent increase in the incidence of adhesions[5,6,10], the demand for meshes with lower complications has gained strength. An ideal mesh it should: not induce the formation of adhesions; not trigger allergic or foreign body reactions; not be carcinogenic, adhesive or erosive; resist infection; be adjustable to the abdominal wall; and have good resistance and tensile strength[11]. However, for Minossi *et al.*, no material would present all of them[21]. The material, its weight and porosity exert influence on the formation of adhesions, on the intensity of inflammatory reaction and on

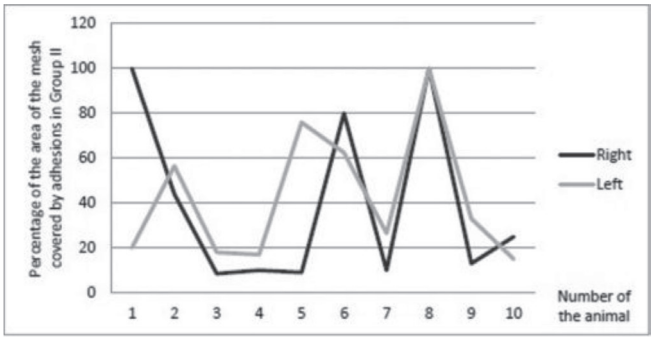

Figure 2. *Percentage of mesh area covered by adhesions in Group II. Note: right side – polypropylene with poliglecaprone; left side – polypropylene.*

the consistency and tissue organization of the peritoneum in recovery[22].

Experimental studies with surgical meshes for evaluation of biocompatibility and adhesion formation use animal models, such as rabbits[23-25], sheep[26], pigs[15], and, especially, rats[11,27]. The variables analyzed include incidence, extent, quality and, in some studies, resistance to rupture and tenacity.

The polypropylene mesh with heavy weight (80-100 g/m²) and average pore size (0.8mm) is currently the most used[5]. Consecrated by its excellent biocompatibility, incorporation, maintenance of abdominal wall traction and low cost, it is associated with a high incidence of adhesions[14,22]. In experimental studies, the formation of adhesions is observed in 100% of meshes, covering from 50% to 100% of their surface[11,12,27]. The authors described the omentum as the most often involved structure, followed by the liver and the bowel.

In this study, we observed adhesions in 100% of animals in which we implanted the polypropylene mesh. The percentage of mesh covered by adhesions varied from 10.5% to 100%, with an average of 34.07±24.21%. We could observe a higher formation of adhesions on the left side, where the percentage of mesh covered ranged from 15% to 100%, with a mean of 42.45±28.07%, versus 12-49% of surface covered and average of 25.69±13.61% on the right side. Moreover, only one of the 20 implanted meshes did not show incorporation to the parietal peritoneum.

Adhesions involving the small intestine represent greater risk for development of bowel obstruction[19]. However, in some cases the omentum

Table 4. *Percentage of area covered by adhesions in both meshes, regardless of insertion side.*

Animal	Area with adherences	
	Polypropylene	Polypropylene with Polyglecaprone
1	18.5	100
2	37.5	53.5
3	49	80
4	17.4	44
5	10.5	68.5
6	25	13
7	12	43
8	19	30
9	49	42
10	19	20.5
11	20	100
12	56.5	44
13	18	8.5
14	17	10
15	76	9
16	62.5	80
17	26.5	10
18	100	100
19	33	13
20	15	25
Mean	34.07	44.7
SD*	24.21	32.85
%SD*	71.09	73.51

** SD= Standard derivation Mann-Whitney's test p<0.05*

might as well be involved. In addition, the heavy weight polypropylene meshes, weighting more than 40mg/m², are related to complications such as abdominal discomfort, infection and fistulae. In turn, the porosity of the material influences cell colonization and inflammatory reaction. Meshes with small pores induce a subtle cell colonization, but intense inflammatory reaction and adhesion formation. In contrast, large pore meshes, in addition to being more flexible, ensure lower foreign body reaction, allowing their integration to the tissues without the formation of a fibrous capsule[14,22].

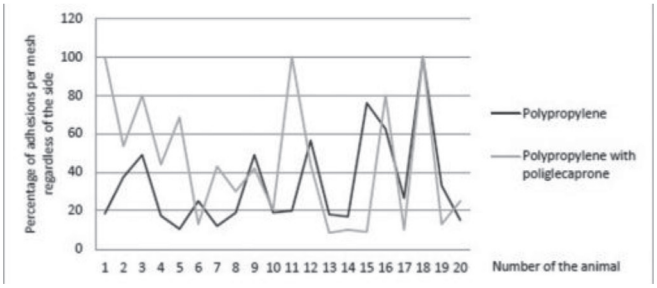

Figure 3. *Percentage of adhesions per mesh regardless of insertion side.*

In this context, the association of polypropylene mesh with poliglecaprone filaments would allow fewer complications compared with the classic polypropylene mesh. The absorbable component of the prosthesis, poliglecaprone, would facilitate the intraoperative handling of the mesh, on both endoscopic and open repair[15]. The mesh used in this study consisted of equal parts of low weight (28g/m²) polypropylene with large pores (3-4mm) and poliglecaprone, characterized by its good biocompatibility, both histological and immunochemical, in addition to its extensive development and high tensile strength[11,15].

In an experimental model using Wistar rats, Burger *et al*.[11] compared the polypropylene and poliglecaprone mesh to other prostheses, evaluating adhesion formation, incorporation and tensile strength. The analysis was carried out seven and 30 days after the insertion procedure. The polypropylene with poliglecaprone mesh was not superior to the polypropylene one.

Schreinemacher *et al*.[16] also did not found significant differences between the polypropylene and the polypropylene with poliglecaprone meshes when they studied adhesion formation and incorporation after seven and 30 days postoperatively in rats in a study with six prostheses. The authors reported a smaller area covered by adhesions in the group evaluated at 30 days, but this difference was not significant. In that group, also, all the animals that received the polypropylene with poliglecaprone mesh developed visceral adhesions, versus 35% in those with polypropylene mesh. As of incorporation, there were no significant differences between the meshes.

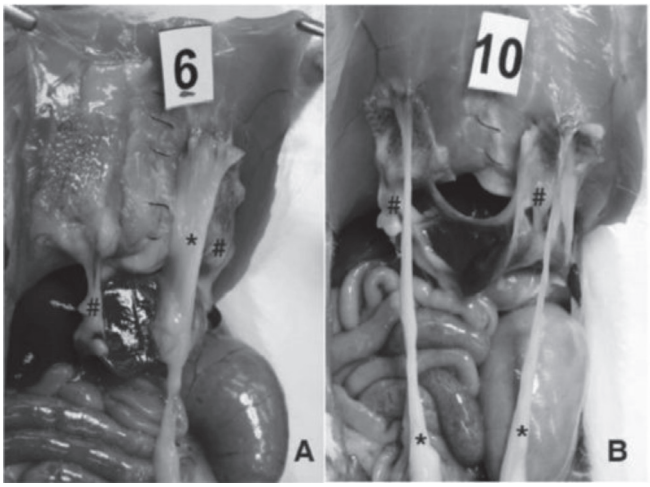

Figure 4. *Adhesions in animals 6 and 10 from Group I (polypropylene mesh on the right and polypropylene with poliglecaprone mesh on the left). Note: * = spermatic cord; # = omentum.*

Bellón *et al*.[25] analyzed the polypropylene with poliglecaprone mesh and other prostheses in the correction of defects of the abdominal wall in rabbits. With respect to adhesions, there was no significant difference when compared to the polypropylene mesh. Still, the adhesions were observed through laparoscopy after 72 hours of the procedure, showing no difference when analyzed seven and 14 days postoperatively.

Aramayo *et al*.[23] produced an incisional hernia in 40 rabbits and evaluated three prostheses used for repair. The area of adhesion induced by the polypropylene mesh was significantly larger when compared with the mesh made of polypropylene with poliglecaprone.

Bellón *et al*.[24], in an experimental model using rabbits, compared the lightweight polypropylene mesh with the polypropylene with poliglecaprone one. After analysis at 14 and 90 days after the procedure, they concluded that the formation of adhesions in the peritoneal face of the prosthesis was significantly less extensive on the mesh with absorbable component at 90 days. The adhered structures were the omentum and the bowel.

The results of the current work agree with those presented by different studies regarding adhesion formation. All meshes induced the formation of adhesions and there was no significant difference between them. For the mesh made of polypropylene with poliglecaprone, the percentage covered by adhesions ranged between 8.5 and 100%, averaging 44.7±32.85% (p=0.12). After evaluating each animal within a group, we noticed a significant difference on adhesion formation between them, which hinders the establishment of a pattern. This variation may be related to the individual response of each of the animals. This prosthesis also presented a higher incidence of adhesions involving the liver, 15% versus 5% with the polypropylene mesh.

When inserted on the left side, the percentage of mesh covered by adhesions was significantly higher when compared with the polypropylene mesh. However, when analyzed regardless of the insertion site, none of the meshes proved to be significantly superior to the other. The different intra-abdominal organ disposition between the sides and the increased mobility of the omentum, which was present in 98.5% of the sample adhesions, may justify this disparity. In turn, as of incorporation, the difference was significant. Out of 20 implemented meshes, seven did not show incorporation, as opposed to only one of the polypropylene meshes.

Among the modifications applied to prostheses used in laparotomy closure, the addition of absorbable material to the mesh composition aims to reduce the induction of foreign body reaction, while enhancing the complacency of the abdominal wall[28]. In theory, these changes would ensure lower adhesion formation. However, according to the exposed, the composite mesh was not superior to the standard one. For some authors, also, the foreign body reaction induced by the partially absorbable meshes was higher in the early stages after the procedure, and normalized in a later analysis by Bellón *et al*.[24].

It is important to observe that it is difficult to extrapolate the results of experimental studies to the practice in humans, considering that these models use mostly rodents. The biological response of the animals used in experiments can be different from that presented by humans. Furthermore, the different analysis periods used by different studies,

as well as their different methodologies, contribute to limit the application of experimental studies in medical practice.

Despite increasing research, there are no available meshes that do not induce adhesion formation, and their use remains a challenge, especially when left in contact with abdominal viscera.

The analysis of the results shows that, in rats, both studied meshes have the same ability to form adhesions.

ABSTRACT

Objective: *to compare intraperitoneal adhesion formation in rats when using polypropylene and polypropylene with poliglecaprone meshes.* **Methods:** *we used twenty male, Wistar rats, divided in two groups. In group 1, the rats received the polypropylene mesh on their right side and the polypropylene with poliglecaprone mesh on their left side. In group 2 the position of the meshes was inverted. After 30 days, we analyzed the presence or not of adhesion formation, including only those over the meshes. The findings undergone an analysis through the Mann-Whitney test, at a level of significance of p≤0.05.* **Results:** *all meshes presented adhesions. We verified that, for the polypropylene meshes, the percentage of their surface covered by adhesions varied from 10.5 to 100%, with an average of 34.07±24.21%, while for the polypropylene with poliglecaprone mesh, the percentage covered by adhesions varied between 8.5% and 100%, with an average of 44.7±32.85% (p=0.12).* **Conclusion:** *both meshes lead to adhesion formation, none being superior to the other.*

Keywords: *Hernia. Tissue Adhesions. Surgical Mesh. Comparative Study.*

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Parapneumonic pleural effusion: reality and strategies in an Amazon university hospital

Derrame pleural parapneumônico: realidade e estratégias em um hospital universitário na Amazônia

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A B S T R A C T

Objective*: to define the profile and analyze the postoperative evolution of children with parapneumonic pleural effusion (PPE), and to evaluate strategies used in the presence of diagnostic and therapeutic limitations, emphasizing the open thoracic drainage (OTD).* **Methods***: we conducted a cross-sectional, prospective, analytical study in which we followed children admitted in an Amazon university hospital with surgically addressed PPE, from October 2010 to October 2011.* **Results***: we studied 46 patients, most children under three years of age (74%), with no gender predominance. A significant portion of the sample (28%) had inappropriate body mass index. We found short stature in five patients (11%), which tended, in general, to a worst postoperative outcome when compared with children of normal height (p=0.039). The average duration of symptoms till admission was 16.9 days. Empyema was a common diagnosis in the first surgery (47.8%), and its bearers had longer duration of chest tube drainage (p=0.015). Most children (80.4%) were operated only once. The mean length of hospital stay was 25.9 days. Thoracic drainage (water-sealed) was the most common procedure (85%), with conversion to OTD in 24% of the sample, thoracotomy being rare (4%). There were no deaths.* **Conclusion***: the studied individuals often had advanced disease and nutritional disorders, affecting outcome. OTD remains a valid option for specific situations, and further studies are needed for confirmation.*

Keywords: *Pneumonia. Pleural Effusion. Empyema, Pleural. Child. Thoracic Surgery.*

INTRODUCTION

Pneumonia, a common and potentially severe disease in children, accounts for about 1.9 million deaths a year worldwide. Most fatal cases occur in poor countries, where underreporting is an additional negative factor[1]. In Brazil, despite the overall reduction in pneumonia deaths in young children, a high mortality rate persists, with discrepancies between different regions. The rate found in the North corresponds to that found in the South eight years ago[2,3]. There has been an overall increase in the incidence of pneumonic complications, particularly the parapneumonic pleural effusion (PPE)[4].

PPE is classified as complicated and non-complicated. The non-complicated is an exudative reaction to the adjacent pulmonary infection and, in general, is reabsorbed with antibiotic treatment and cure of pulmonary infection. It is a non-purulent effusion, with no germs on direct examination (Gram) or culture. The complicated PPE is purulent, somewhat opaque, or presents germs on culture or Gram. The empyema, defined as the accumulation of intrapleural pus, is the typical complicated PPE[5].

PPE has been the source of several studies in recent decades. Not without much discussion, the evidence established a relative standardization for its diagnosis and treatment. In this context, useful are the ultrasound, the use of fibrinolytic agents and early debridement of the pleural cavity by Video-Assisted Thoracoscopic Surgery (VATS)[5].

The João de Barros Barreto University Hospital (HUJBB/UFPA), an Amazon reference in infectious diseases, has a large number of pediatric admissions due to pneumonia complications. A local preliminary study in 2010 revealed, in addition to a high children prevalence of PPE, the lack of permanent availability of ultrasound, of fibrinolytic agents or VATS for the population. It also observed the use of water-sealed Closed Thoracic Drainage (CTD) in most cases, and the

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conversion into open thoracic drainage (OTD) for the refractories. It also found that classic thoracotomy was hardly performed, and yet the discharge of patients in good general condition was the rule.

Thus, it has become imperative to study this pediatric population treated in lack of what is ideally established by the recent literature. It is necessary to define the role of OTD in the discharge of these children and their subsequent return to school and family life, concomitantly with their characterization, whose regional peculiarities are little known by the small number of related publications.

METHODS

We prospectively followed all pediatric patients admitted to HUJBB/UFPA diagnosed with PPE, who suffered any surgical intervention, in the period between October 2010 and October 2011. The sample was of children coming from other smaller hospitals of the Unified Health System (SUS, where they await availability of bed in the institution where the research took place. We continued follow-up until April 2012, through periodic access to outpatient medical records after discharge. The minimum admission follow-up until outpatient discharge was 1.6 months, and maximum, 6.2 months, with an average of 3.3. We excluded children whose effusion had non-pneumonic causes and cases with conservatively treated PPE.

Local Protocol

After the PPE diagnosis, when in moderate size according to the judgment of the thoracic surgery team, puncture is immediately indicated under local anesthesia and sedation. At that time, purulent liquid or any turbidity indicates immediate CTD, which is also held in relapses of previously evacuated effusions. The drain is maintained while the output remains liquid or air, and is removed when the flow ceases, with underlying pulmonary expansion.

In refractory cases, when there is no postoperative lung expansion after fifteen days due to the organization of empyema and pleural thickening, CTD is converted to OTD. We use the OTD term instead of the classic term "pleurostomy" or "open thoracostomy" because, unlike the latter, there is no rib resection, or even a muscular approach. Simply, the drain is cut about three centimeters above the skin, at the bedside. This drain segment is usually removed after hospital discharge, during the consultation at the clinic, when there is confirmation of adequate pulmonary re-expansion.

Because there is no availability of VATS for pediatric patients, pulmonary decortication is performed by classical thoracotomy, and therefore is reserved for use only in extreme cases that do not respond to the described protocol, or have dramatically unfavorable evolution. The patients admitted already with CTD, held in the source hospitals, are conducted similarly.

Variables studied

We studied age, gender, origin, nutritional status, previous surgery, duration of symptoms until admission, fever, hospital stay, time of thoracic drainage, macroscopic appearance of effusion, performed surgeries and postoperative outcome.

Data analysis

We organized a database using Epi Info version 3.5.1. All analyzes were conducted in R (R Core Team, Vienna, Austria). We performed statistical analyzes using Student's t test for quantitative variables and G test, and the X^2, to compare categorical variables. We defined statistical significance as $p \leq 0.05$.

Ethical aspects

All stages of the study were assessed and approved by the Ethics in Research Committee of the João de Barros Barreto University Hospital, Federal University of Pará, Brazil (Protocol nº 2161/2010-CEP/HUJBB).

RESULTS

We followed 46 patients. There was no gender predominance, and more than half, 25 (54.3%) was from the interior of the state.

The mean age was 2.7 years (±2.4), the youngest child was two months-old and the oldest, 12.4 years-old. The majority had less than five years

of age (87%) and 74%, less than three. Infants (up to two years) composed 46% of the sample (Figure 1).

Regarding nutritional status, five patients (11%) had low stature, and was found inadequacy of body mass index (BMI) in 13 subjects (28%), thinness being slightly more present than overweight (7 vs. 5 patients).

The average duration of symptoms until admission was 16.9 days (5-45 days range). Eleven (24%) children had already been operated (CTD) in the local hospital. In 22 individuals pleural effusion was grossly purulent at the first procedure in HUJJ/UFPA, having been characterized as "empyema".

The study group had 56 surgical performed procedures, which corresponds to 1.2 surgeries per child in the sample. Only nine of the 46 children were subjected to more than one operation, which means that 80% of the sample had only one operation, showing success of the initial procedure in these patients (Figure 2).

The first surgery was CTD in 39 patients, alone or preceded by chest puncture on the same occasion. Isolated puncture or thoracentesis occurred as the initial procedure in five (11%) patients, and classical thoracotomy with decortication in two (4%). These two serious patients had been admitted already with CTD (Figure 3). In the nine cases in which a single surgery was not enough, CTD was also the most common surgical procedure, being performed on five of these children.

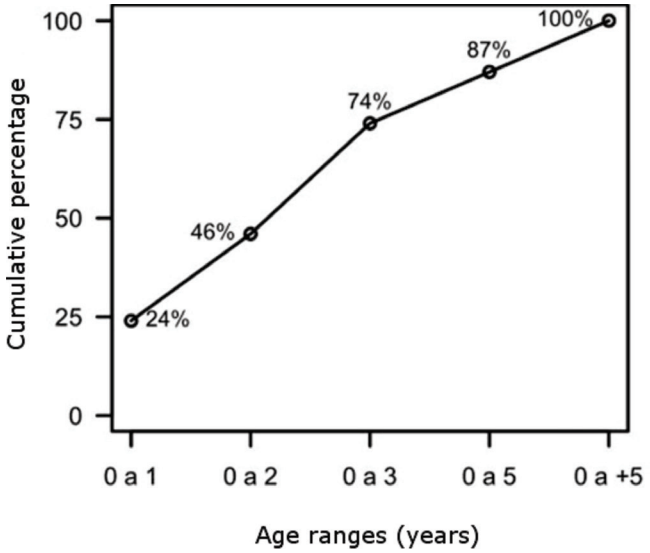

Figure 1. *Cumulative percentage of patients' ages (years).*

Considering the whole sample, 11 patients required OTD at some time during hospital stay. Only one had the drain removed during hospitalization and the remaining ten were discharged bearing the device segment, subsequently withdrawn in the clinic.

The postoperative course was classified into four levels: (i) discharge without OTD, (ii) OTD / discharge without drain, (iii) OTD / discharge with drain; and (iv) multiple surgeries. The first three groups were subjected to only one surgical-anesthetic procedure, progressing in descending order of therapeutic success, all being better, however, than the latter group, in which individuals were operated more than once. We observed that, in general, children with normal height for the age progressed more satisfactorily (Test G = 8.36; p=0.039) (Figure 2).

The average number of days that patients were in CTD was 12 (2-38). The average time with draining devices (CTD or OTD) in the pleural space was 14 days. After conversion from CTD to OTD, patients stayed in hospital for more 4.8 days on average.

There was a significant difference regarding thoracic drainage time and purulent effusion (t test = 2.54, p=0.015), showing that patients with empyema at the first procedure had longer drainage time (Figure 3).

The average hospitalization time was 25.9 days (7-86). We found no correlation between the length of stay and the other variables.

DISCUSSION

As opposed to the male predominance among children with PPE demonstrated in most populations studied, in this study there was no gender

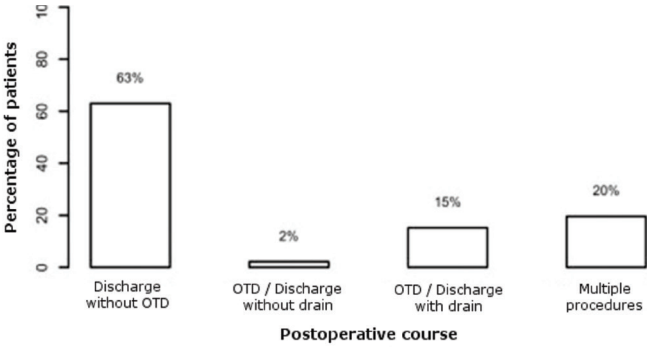

Figure 2. *Percentage of patients according to postoperative evolution.*

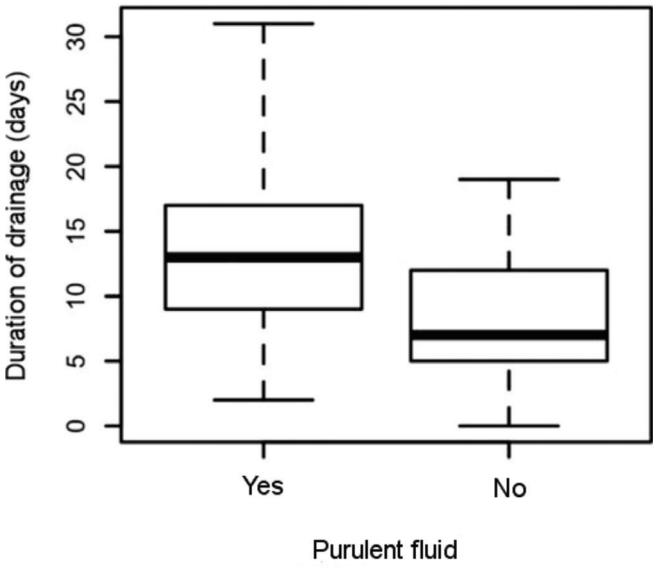

Figure 3. *Characterization of drainage duration (days) in relation to the occurrence of purulent effusion, in which a difference was found between the groups (Student's t test = 2.54, p=0.015).*

predominance[6-8]. Most international studies, although stating that pneumonic complications significantly affect young children, found higher mean age (4-7.6 years), and lower proportion of infants and preschool children than in our study, in which 87% had less than five years. This trend, however, is in agreement with that reported by Brazilian literature, with an average age between two and 2.9 years[4-11].

The prevalence of short stature is higher than the national average (11% vs. 7.2%). Considering the strong tendency of reduction of the the prevalence of height deficit with increasing income, we can conclude that, at least in part, socioeconomic factors are major determinants of high malnutrition rate in the initial physical examination of children admitted to HUJBB, a known reference hospital of the Unified Health System (SUS), where the disadvantaged population economically is the rule[12]. Children of normal height showed better postoperative outcome. One could also expected them to present a shorter hospital stay and fever time, though this did not happen. One would probably observe this with a longer study period and therefore with a larger sample[13].

The disease duration until hospital admission was 16.9 days, this delay being greater than the one reported in the literature (6.4 to 15 days). Unfortunately, the evolution of PPE bearers is worse when this time is greater than four days, which may explain the high prevalence of complicated PPE and empyema[13].

The delay in the transfer of patients to the tertiary hospital is remarkable. In Pará, the difficulties begin well before admission. The State is more than twice the size of France, with extreme difficulty of transportation in the region dominated by the Amazon forest and its rivers, where more than half the population (52.4%) live below the poverty line, and has just over two hospital beds per thousand inhabitants and[13-15].

The duration of fever after hospital admission was 9.8 days on average, agreeing with the reported in the literature (4.2 to 12.8 days)[7,9,16].

A considerable amount of children gets to HUJBB after going through some kind of operation to approach the pleural effusion. Thus, 24% of patients had undergone a surgical procedure in origin hospital. In fact, the children take so long awaiting transfer to the reference hospital that it is no longer rare that they have been operated in those institutions. Although after hospitalization they are all conducted in a similar manner, this is an important limitation of this study.

In almost half of the children, we observed grossly purulent pleural fluid in the initial procedure, a proportion higher than the one found in the literature (15.5 to 33%). The considerable waiting for definitive treatment justifies this finding so unfavorable to early cure[7].

Ultrasonography has high sensitivity in the staging of effusion. One study demonstrated that although only 12% of children with PPE had empyema, 65.6% already had septa in the thoracic sonography before the procedure. Unfortunately, this diagnostic feature is not part of the routine in HUJBB due to its limited availability. It is worrisome to think that the proportion of patients admitted with effusion in organizational stage is unknown, though probably enormous, as evidenced by the high frequency of frankly purulent liquid in the first procedure[14].

A large portion of the sample (80.4%) undergone only one operation, featuring success of the initial procedure. Today, there are few studies using only CTD, without VATS, fibrinolytic agents or topical saline, at least. A study published by Soares *et*

al.[7] is one of them, and therefore allows comparisons as for the success of the first operation. In it, 52% of children with PPE were subjected to CTD, and 18% of the sample went through another procedure, mostly classical thoracotomy. In our study, however, this most dramatic feature was used only twice (4.3%) and also in two cases operated the first time at other institutions.

The striking prevalence of empyema, just to mention one of the evidence of disease severity, denies any assumption that the followed cases were in the early stage of complication, which would justify the low indication of thoracotomy. We assume that this can be attributed to the appropriate conversion of CTD to OTD described in patients the prolonged evolution, which prevents patients from undergoing more aggressive interventions and their possible consequences (postoperative in Intensive Care Units, transfusions of blood products, vigorous analgesia, insertion of deep venous catheters, etc.)[7,17].

In another national study, Freitas *et al*.[8] achieved an even higher rate of cure with only one procedure (88%). In this multi-institutional study, they analyzed cases of PPE in the fibrinopurulent stage, using VATS as the initial approach. It is one of the few investigations that uses pleurostomy, although limited to cases refractory to VATS, with good results.

We did not use pleurostomy in this study, as it is not part of HUJBB protocol for pediatric PPE. The transformation of CTD in OTD, described above, does not involve going to the operating room or anesthesia, since it comprises the simple section of the device next to the chest wall. Moreover, we did not use any kind of open thoracic window prosthesis, although there have been good results with this feature in adults, and the reasonably wide drain seems to guarantee the viability and persistence of the stoma[17,18].

Certainly, the OTD described may not contribute as much as early VATS would to the reduction of hospital stay and costs. However, it allowed several children to return to their homes, as all had clinical and radiological recovery within four months after discharge, with no deaths.

In conclusion, the HUJBB faces enormous difficulties in managing the considerable number of pediatric patients with severe pneumonic complications, pleural effusion. This population is mostly of young children, with long time until admission, usually approached with advanced disease, and high prevalence of nutritional disorders, which seems to contribute to prolonged hospital stay and duration of chest drainage. However, they usually undergo only one surgical-anesthetic procedure, and hospital discharge is commonly obtained by converting closed chest drainage to an open one. This strategy seems to be valid for these patients in the absence of the most modern and resources that the evidence recommends. They rehabilitate and return to their usual activities, though further studies are needed to confirm this assumption. Thus, this study may be useful in guiding alternative conducts to the equally disadvantaged hospitals in the North, or even in other regions of the country, while there is no availability of instruments that allow the application of the guidelines proposed by the current literature, with real benefit to the pediatric population.

R E S U M O

Objetivo: definir o perfil e analisar a evolução pós-operatória de crianças com derrame pleural parapneumônico (DPP), bem como, avaliar estratégias utilizadas na vigência de limitações diagnóstico-terapêuticas, enfatizando a drenagem torácica aberta (DTA). **Métodos:** estudo transversal, prospectivo, analítico, no qual foram acompanhadas as crianças admitidas em um hospital universitário da Amazônia com o diagnóstico de DPP abordado cirurgicamente, no período entre outubro de 2010 a outubro de 2011. **Resultados:** foram estudados 46 pacientes, a maioria menor de três anos de idade (74%), sem predominância de sexo. Significativa parcela da amostra (28%) possuía índice de massa corpórea inadequado. Baixa estatura foi encontrada em cinco pacientes (11%), que tenderam, em geral, à pior evolução pós-operatória, quando comparados com as crianças de estatura normal (p=0,039). A duração média dos sintomas à admissão foi 16,9 dias. O empiema foi diagnóstico comum na primeira intervenção cirúrgica (47,8%), e seus portadores apresentaram maior duração da drenagem torácica (p=0,015). A maioria das crianças (80,4%) foi operada apenas uma vez. A média de dias de internação hospitalar foi 25,9 dias. A drenagem torácica fechada em selo d'água foi a cirurgia mais realizada (85%), precisando ser convertida em DTA em 24% da amostra e toracotomias foram raras (4%). Não houve óbitos. **Conclusão:** os indivíduos estudados possuíam frequentemente doença avançada e distúrbios nutricionais, repercutindo na evolução clínica. A DTA permanece como uma opção válida para situações específicas, e novos estudos ainda são necessários para confirmação.

Descritores: Pneumonia. Derrame Pleural. Empiema Pleural. Criança. Cirurgia Torácica.

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Integrated predictive model for prostatic cancer using clinical, laboratory and ultrasound data

Modelo preditivo integrado para a presença de câncer de próstata utilizando dados clínicos, laboratoriais e ultrassonográficos

Gustavo David Ludwig, AcCBC-SC[1]; Henrique Peres Rocha[1]; Lúcio José Botelho[2]; Maiara Brusco Freitas[2].

ABSTRACT

Objective*: to develop a predictive model to estimate the probability of prostate cancer prior to biopsy.* **Methods***: from September 2009 to January 2014, 445 men underwent prostate biopsy in a radiology service. We excluded from the study patients with diseases that could compromise the data analysis, who had undergone prostatic resection or used 5-alpha-reductase inhibitors. Thus, we selected 412 patients. Variables included in the model were age, prostate specific antigen (PSA), digital rectal examination, prostate volume and abnormal sonographic findings. We constructed Receiver Operating Characteristic (ROC) curves and calculated the areas under the curve, as well as the model's Positive Predictive Value (PPV).* **Results***: of the 412 men, 155 (37.62%) had prostate cancer (PC). The mean age was 63.8 years and the median PSA was 7.22ng/ml. In addition, 21.6% and 20.6% of patients had abnormalities on digital rectal examination and image suggestive of cancer by ultrasound, respectively. The median prostate volume and PSA density were 45.15cm^3 and 0.15ng/ml/cm^3, respectively. Univariate and multivariate analyses showed that only five studied risk factors are predictors of PC in the study (p<0.05). The PSA density was excluded from the model (p=0.314). The area under the ROC curve for PC prediction was 0.86. The PPV was 48.08% for 95%sensitivity and 52.37% for 90% sensitivity.* **Conclusion***: the results indicate that clinical, laboratory and ultrasound data, besides easily obtained, can better stratify the risk of patients undergoing prostate biopsy.*

Keywords: *Prostatic Neoplasms. Biopsy. Prostate-Specific Antigen.*

INTRODUCTION

Prostate cancer (PC) is a major cause of morbidity and mortality worldwide[1,2]. In the United States, PC is the most commonly diagnosed visceral cancer; in 2015, it is estimated that there were over 221,000 new cases and about 27,500 deaths[3], a mortality of 12.4%. In Brazil, it is the second most common cancer in the male population, after nonmelanoma skin cancer, and the second leading cause of cancer death in men[4]. According to the National Cancer Institute (INCA) 61,200 new cases are estimated in 2016[5].

The prostate specific antigen (PSA) was first used for detection in the 90s. This method revolutionized the disease panorama, causing a considerable increase in the number of men diagnosed with PC, by indicating prostate biopsy. This allowed an early diagnosis of the disease and theoretically increased curability[6,7]. However, PC is detected in only 30% and 45% of men undergoing initial biopsy, with even lower rates for subgroups with PSA of 4-10 ng/ml, for example[8,9], showing a low specificity. For some of these men, the tumor could be very small and the biopsy sensitivity was not enough, but most of the time the patient did not even had PC. This is due to the inability to adequately predict PC positivity likelihood using only PSA and digital rectal examination (DRE). Thus, it is necessary to accurately assess the pretest probability of a positive biopsy, since this procedure is not without risk.

Many risk factors have been correlated with the detection of PC, but their combined contribution can be difficult to quantify. Different predictive models were created in order to work around this problem. Garzotto *et al*.[10] used data of age, PSA density, DRE and ultrasound data to build their model, but the population was in its majority white and all Americans. Zhao *et*

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al.[11] developed a model with the Chinese population, restricting PSA values in the 4-10 ng/ml range. These predictive models may have reduced accuracy when used in other target populations, such as the Brazilian. It is known that afrodescendants have a high risk of PC and this population amounts to only 4.2% of the population present in the work by Garzotto, for example[10,11].

The aim of this study was to develop a predictive model for detection of prostate carcinoma by incorporating clinical, laboratory and ultrasonographic data. This would therefore reduce the need for prostate biopsies in patients at low risk, and consequently, the morbidity associated with this procedure.

METHODS

We analyzed the records of 445 patients treated between September 2009 and January 2014 in a reference radiology service in Florianopolis – Santa Catarina State, Brazil. We included patients older than 40 years, with seven variables into account (age, DRE, PSA, prostate volume, PSA density, transrretal prostate ultrasound and ultrasound-guided prostate biopsy with at least 12 fragments). We excluded patients with associated diseases that could compromise the data analysis, those previously submitted to prostatic resection and those in use of 5-alpha-reductase inhibitors. We then selected 412 patients for the analysis.

All patients underwent DRE performed by a member of the urology team, classified as normal or abnormal, the latter including prostate hardening, presence of nodulation or irregularities. After DRE, we performed the ultrasound-guided transrectal biopsy. The device used was the Samsung UGEO H60 model USS-H60NF40/US. We measured the prostate in three dimensions and estimated the prostate volume using the modified formula for elongated ellipsoid (0.52 x [length(cm) x depth(cm) x height(cm)]). We checked suspicious areas for the presence of PC. We considered as highly suspicious the hypoechoic nodules and diffusely heterogeneous prostates. We calculated the PSA density by dividing the serum PSA the calculated prostate volume. All patients underwent transrectal prostate biopsy using an 18 gauge, 20cm biopsy needle. We obtained a minimum of 12 fragments from each patient, with harvesting of additional fragments should there be highly suspicious areas. The same pathology laboratory was in charge of examining the biopsy specimens for the presence of adenocarcinoma.

We organized and registered data in a Microsoft Office Excel 2007® database, with double entry. We performed statistical analysis using the Statistical Package for Social Sciences (SPSS), version 16.0 for Windows.

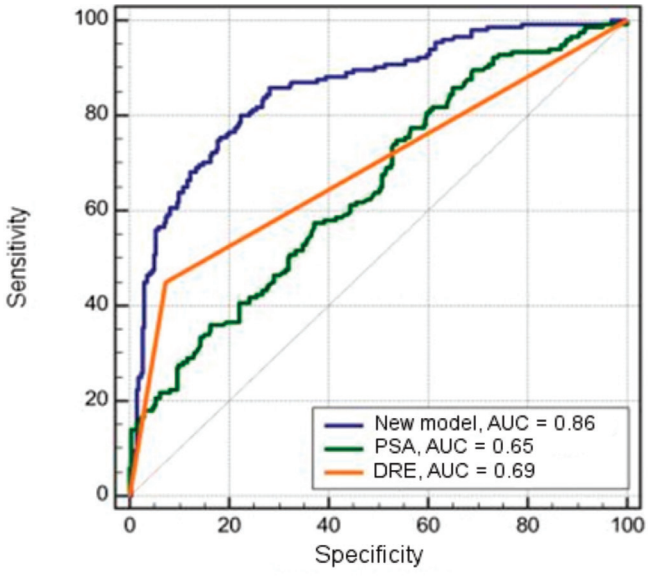
We describe and present the quantitative variables age, prostate volume, PSA density and PSA as mean, standard deviation, median, minimum and maximum, and the qualitative variables, in frequency ranges according to the appearance in the groups. For comparison between groups, we used the Student's t test when parametric, the Mann-Whitney test when nonparametric, and the chi-square test when the variables were categorical.

We carried out a logistic regression analysis, having as the outcome variable the presence or absence of PC. In the crude analysis, the variables studied were age, DRE, PSA, prostate volume, PSA density and ultrasound abnormalities suggestive of cancer. In the final model, we included the variables with $p<0.20$ (age, DRE, PSA, prostate volume, sonographic abnormalities suggestive of cancer). We considered as variables associated with the outcome the ones with $p<0.05$. We evaluated the goodness of fit by means of sensitivity and specificity metrics and by the construction of the Receiver Operating Characteristic (ROC) curve. We constructed the ROC curve using the MedCalc Statistical Software, version 14.8.1 (Software bvba, Ostend, Belgium). Areas under the curve greater than 0.9 have high accuracy, while 0.7-0.9 indicates moderate precision, 0.5-0.7, low precision, and 0.5, test due to chance[12].

RESULTS

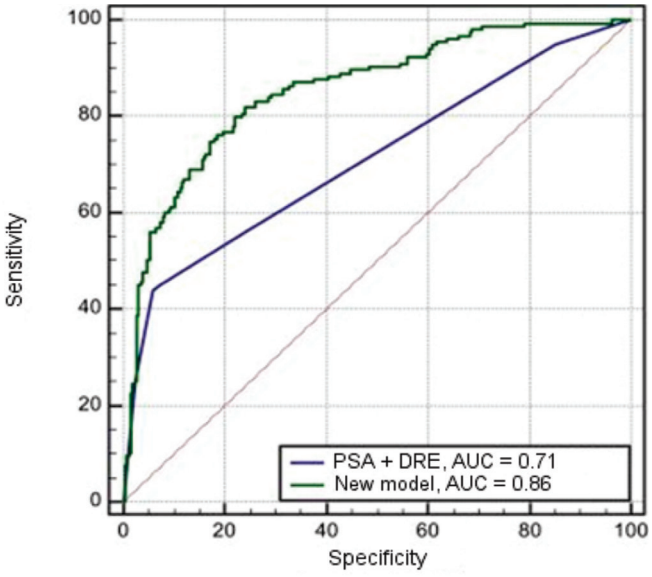
Table 1 shows the characteristics of the study population. The patients' age ranged from 40 to 85

Figure 1. *ROC curve of the new model (age, prostate volume, DRE, ultrasound and PSA), PSA and DRE.*



PSA: prostate specific antigen; DRE: digital rectal examination.

Figure 2. *ROC curve of the new model (age, prostate volume, DRE, ultrasound and PSA) and PSA and DRE.*



PSA: prostate specific antigen; DRE: digital rectal examination.

years (mean 63.85±8.51). The median PSA level was 7.22ng/ml. DRE was classified as altered in 21.6% of patients (Table 1).

When dividing the age groups, level of PSA and DRE according to biopsy result (positive and negative), was found statistical significance for all: p=0.005 for age; p<0.001 for PSA levels; and p<0.001 for DRE. We divided the study population into PSA lower than 4.0ng/ml, between 4.0 and 10 ng/ml, and greater than 10.0ng/ml, and classified them as for the presence or absence of PC (Table 2).

Sonographic Findings

We observed lesions suggestive of prostate cancer in 20.6% of patients. The median prostate volume was 45.15cm^3. The median PSA density was 0.15ng/ml/cm^3 (Table 1). When dividing these variables into positive and negative biopsy groups, we found statistical significance for all, with p<0.001.

Biopsy Results

We obtained a minimum of 12 specimens from all patients during the procedure. Prostate adenocarcinoma was identified in 37.62% (155 of 412 patients – Table 1).

Development of Predictive Model

For the univariate logistic regression, the significant predictors for a positive biopsy were: age, with *odds ratio* (OR) of 1.04 (p=0.005); prostate volume, OR 0.96 (p<0.001); altered DRE, OR 1.51 (p<0.001); ultrasound suggestive of cancer, OR 6.2 (p<0.001); PSA levels between 4-10 ng/ml, OR 2.25 (p=0.007); and PSA value ≥10.0ng/ml, with OR 4.80 (p=0.007). We did not observe statistical significance for the variable PSA density: OR 1.53 (p=0.314 – Table 3).

The multivariate logistic regression appointed as significant predictors for the presence of prostate carcinoma: age (p=0.017); prostate volume (p<0.001); altered DRE (p<0.001); ultrasound suggestive of cancer (p<0.001); and PSA (p=0.012) (Table 3).

With the data obtained, we built a ROC curve with all model variables to evaluate the accuracy compared with PSA and DRE alone (Figure 1). We also constructed a ROC curve for the comparison of the model with PSA and DRE combined (Figure 2). The area under the curve was 0.86 for the model, in contrast to isolated PSA 0.65, 0.69 for isolated DRE and 0.71 for combined PSA and DRE.

Table 1. *Clinical characteristics and comparison between patients with positive and negative biopsy.*

		Prostate cancer		
Variable	Total	Positive biopsy	Negative biopsy	p value
Total (n)	412	155	257	N/A
Age				
Mean ± Sd	63.85 ± 8.51	63.85 ± 8.44	62.93 ± 8.43	0.005*
Median	63	65	62	
Range	40-85	40-85	43-84	
Prostate volume				
Mean ± Sd	51.30 ± 26.94	41.66 ± 19.42	57.11 ± 29.12	< 0.001**
Median	45.15	36.80	49.70	
Variation	6.80-219.10	17.10-136.70	6.80-219.10	
Dre, n (%)				< 0.001***
Normal	323 (78.4)	85 (26.3)	238 (73.7)	
Altered	89 (21.86)	70 (78.6)	19 (21.4)	
Ultrasound, n (%)				< 0.001***
Normal	327 (79.4)	88 (27.0)	239 (73.0)	
Altered	85 (20.6)	67 (78.6)	18 (21.2)	
PSA				< 0.001**
Mean ± Sd	17.50 ± 53.00	32.87 ± 83.74	8.24 ± 7.94	
Median	7.22	8.35	6.86	
Range	0.59-654.00	0.59-654.00	0.62-93.40	
PSA Density				< 0.001**
Mean ± Sd	0.39 ± 1.15	1.81 ± 0.75	0.17 ± 0.20	
Median	0.15	0.24	0.12	
Range	0.02-12.80	0.20-12.80	0.20-1.96	

*PSA: prostate specific antigen; SD: standard deviation; n: number; N/a: not applicable; * Student T Test; ** Mann-Whitney Test; *** Pearson's Chi--square test; p<0.005.*

Setting the sensitivity to 95% for the proposed model and isolated PSA, we found a specificity of 38.15% and 16.34%, respectively. From these values, we calculated the Positive Predictive Value (PPV) using the prevalence of PC in the study patients, and found 48.08% for the model and 40.64% for isolated PSA. This would imply a reduction of 15.46% in the number of biopsies. By setting the sensitivity to 90%, specificity increases to 51.36% for the model and to 20.33% for PSA. We found a PPV of 52.37% for the model and 40.52% for isolated PSA, resulting in a reduction of 22.62% in biopsies.

DISCUSSION

The screening for prostate cancer based on PSA and DRE still has important limitations, since the PSA is highly sensitive, but it is not cancer-specific and

Table 2. *PSA values and presence of PC.*

		Prostate cancer	
PSA	Total	Yes	No
< 4.00	52	10	42
4.00-10.00	255	89	166
> 10.00	105	56	49
Total	412	155	257

PSA: prostate specific antigen; n: number.

most men with elevated PSA do not have PC[13]. The difficulty of screening for this disease is to establish protocols that have high positive predictive values, to stratify high-risk individuals for PC.

A branch of the Prostate Cancer Prevention Trial (PCPT) investigated the prevalence of PC in 2950 men who used placebo and had PSA levels below 4.0ng/ml and DRE considered normal, i.e. patients considered of low risk for PC[14]. The results showed that the disease could be diagnosed in all PSA levels, including high-risk tumors. This indicates that the PSA should not be considered as the only factor in choosing patients for prostate biopsy[15]. The findings of this study corroborate this, since approximately 20% of patients with PSA less than 4.0ng/ml had PC diagnosis (Table 2).

Because of these limitations, statistical models began to be developed to more accurately predict the risk of PC in the biopsy. Eastham *et al*.[16] published, in 1999, the first study demonstrating a model that included age, ethnicity and PSA. Only PSA was an independent predictor of positive biopsy in their analysis, with an area under the curve of 0.75. However, the study was conducted during the period in which the default was the harvesting of six prostate fragments. This may limit the analysis results, as this pattern has less sensitivity to the currently used twelve fragments[17]. In the previously mentioned Prostate Cancer Prevention Trial, Thompson *et al*.[18] used the placebo arm results to assess the risk of PC considering age, ethnicity and family history. Although this study has been innovative and had wide acceptance, there are certain limitations. In PCPT, 89% of the 5519 patients had a level of PSA in the range considered "normal", i.e., <4.0ng/ml, and only 150 patients had PSA levels greater than 6ng/ml, unlike what we find in many clinical settings. Furthermore, the PCPT was limited to men over 55 years, excluding its use a large number of patients.

Karakiewicz *et al*.[1] developed two predictive models with three independent cohort data, where men were referred for prostate biopsy based on PSA values, percentage of free PSA and alterations in DRE. They collected the data from the first and second cohorts in Montreal, Canada, where 4193 men underwent biopsy guided by ultrasound and had six fragments removed, after digital rectal examination and measurement of PSA values. Of these, 514 also underwent measurement of free PSA. The third cohort consisted of 1762 patients from the University Hospital Hamburg - Eppendorf, Germany. These men had criteria for sextant biopsy and had collected PSA, percentage of free PSA and DRE. The predictive model based on age, DRE, PSA and percentage of free PSA showed better accuracy than the model that used only age, DRE and PSA, with areas under the ROC curve of 0.77 and 0.69, respectively[1]. One limitation of this study was the failure to assess the impact of ethnicity, all patients being Caucasian. Another limitation was the use of only six biopsy fragments[19].

This study evaluated, within the same population, the best combination of variables to be used for PC prediction and then created models that meet these characteristics. We saw that the most commonly used criteria for screening of patients with prostate cancer, PSA and DRE, have low accuracy, with values of area under the ROC curve of 0.71 when used together. The model developed and demonstrated in this work presented the best accuracy among the tested combinations, with values of the area under the

Table 3. *Gross and adjusted analysis of factors associated with prostate cancer.*

Variable	Gross			Adjusted		
	Regression coefficient	*Odds ratio* (95% CI)	*p* value	Regression coefficient	*Odds ratio* (95% CI)	*p* value
Age	0.04	1.04 (1.005:1.071)	0.005	0.39	1.04 (1.006:1.072)	0.017
Prostate volume	-0.04	0.96 (0.946:0.973)	< 0.001	-0.04	0.96 (0.945:0.973)	< 0.001
DRE			< 0.001			< 0.001
Normal	1	1		1	1	
Altered	1.51	4.53 (2.308:8.800)		1.62	5.05 (2.609:9.776)	
Ultrasound			< 0.001			< 0.001
Normal	1	1		1	1	
Altered	1.83	6.2 (3.015:12.807)		1.99	7.32 (3.562:15.012)	
PSA Density	0.43	1.54 (0.668:3.516)	0.314	-	-	-
PSA			0.007			0.012
< 4.00	1	1		1	1	
4.00-10.00	0.81	2.25 (1.079:4.701)		1.27	3.54 (1.535:8.177)	
> 10.00	1.60	4.80 (2.181:10.566)		1.15	3.15 (1.201:8.267)	

PSA: prostate specific antigen; 95% CI: 95% confidence interval.

ROC curve of 0.86 for predicting the risk of PC. The results obtained are consistent with those obtained in other studies[1,10,16,20]. Most of the published studies have been limited to PSA values less than 10.0ng/ml, with the justification that any patient with values above that would be subjected to a prostate biopsy[10,11,16]. In this study, we chose not to limit the PSA, as there was a rate of nearly 50% negative biopsies in this population subgroup, which would open room for a better patient's selection for biopsy including these PSA values. It would be a new paradigm that needs further study and deepening, but would have the main benefit of avoiding repeated biopsies in such patients.

Some limitations are present in the model presented in this study. First, it we did not take into account the possible outcome of a repeated biopsy for those with negative findings on an initial biopsy, taking into consideration that false negatives may occur[21]. Second, we collected secondary character data retrospectively, and thus, their records were not designed and completed to meet the research objectives. Finally, the proposed model has not been validated externally. This can cause it to present different results in other populations. This raises the need for other research centers to confirm and validate the results of any predictive model in use[22-24].

The results indicate that the clinical, laboratory and ultrasound information, besides easily obtained in clinical practice, can better stratify the risk of patients undergoing prostate biopsy.

R E S U M O

Objetivo: desenvolver um modelo preditivo para estimar a probabilidade de câncer prostático previamente à biópsia. **Métodos:** de setembro de 2009 até janeiro de 2014, 445 homens foram submetidos à biópsia prostática em um serviço de radiologia. Pacientes com doenças que pudessem comprometer a análise de dados, submetidos à ressecção prostática ou usando inibidores de 5-alfa-redutase foram excluídos do estudo. Dessa forma, 412 pacientes foram selecionados. Variáveis incluídas no modelo foram idade, antígeno prostático específico (PSA), toque retal, volume prostático e achados ultrassonográficos anormais. Curvas de Características Operacionais (ROC) foram construídas e áreas sob a curva foram calculadas, assim como os Valores Preditivos Positivos (VPP) do modelo. **Resultados:** dos 412 homens, 155 (37,62%) tinham câncer de próstata (CAP). A média da idade foi 63,8 anos, a mediana do PSA foi 7,22ng/ml. Além disso, 21,6% e 20,6% dos pacientes apresentou anormalidades no toque retal e imagem sugestiva de câncer pela ultrassonografia, respectivamente. A mediana do volume prostático e da densidade do PSA foram 45,15cm^3 e 0,15ng/ml/cm^3, respectivamente. Análises univariada e multivariada demonstraram que apenas cinco fatores de risco estudados são preditores de CAP no estudo (p<0,05). A densidade de PSA foi excluída do modelo (p=0,314). A área sob a curva ROC para predição de CAP foi 0,86. O VPP foi 48,08% para sensibilidade de 95% e 52,37% para sensibilidade de 90%. **Conclusão:** Os resultados indicam que informações clínicas, laboratoriais e ultrassonográficas, além de serem facilmente obtidas, podem estratificar melhor o risco de pacientes que serão submetidos à biópsia prostática.

Descritores: Neoplasias da Próstata. Biópsia. Antígeno Prostático Específico.

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Sleep deprivation and drowsiness of medical residents and medical students

Privação do sono e sonolência excessiva em médicos residentes e estudantes de medicina

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ABSTRACT

Objective: *to evaluate sleep quality and daytime sleepiness of residents and medical students.* **Methods**: *we applied a socio-demographic questionnaire, the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS) to a population of residents and medical students.* **Results**: *hundred five residents and 101 undergraduate medical students participated. Residents presented higher mean PSQI (6.76±2.81) with poorer sleep quality when compared with undergraduates (5.90±2.39); Both had similar measures of sleepiness by ESS (p=0.280), but residents showed lower duration and lower subjective sleep quality.* **Conclusion**: *medical students and residents presented sleep deprivation, indicating the need for preventive actions in the medical area.*

Keywords: *Sleep Wake Disorders. Disorders of Excessive Somnolence. Education, Medical.*

INTRODUCTION

Sleep disturbances are common among night shift workers and may reduce performance, cause increased morbidity, fluctuation in mood, decreased efficacy, increased risk of accidents, and reduced life expectancy[1-5]. Sleep deprivation and the disturbance of its rhythmicity affect the sleep-wake cycle differently from the circadian cycle[1,6-8], causing impacts on work capacity[9,10], such as tiredness, fatigue, irritability, stress, lack of enthusiasm in daily activities , performance decline, cognitive deficit and demotivation[1,7]. Although there is intra-individual and temporal variation in sleep, its disorders are associated, less or more intensely, with behavioral and social relations disorders, decreased attention and concentration, delayed response to stimuli, daytime drowsiness and Burnout Syndrome[8,10,11].

Research shows that residents have an average of six hours of sleep per night, which is lower than the average adult population, who sleeps from seven to nine hours / night[1]. In addition, there is a reduction in the quality of life indices and elevation of scores on depression and anxiety scales when compared with other doctors and medical students[1,9-13]. A recent study with young physicians on the acute effects of sleep deprivation due to night work demonstrated, through psychomotor tests, a greater latency in the response to simple stimuli, more errors and worse index of perfection, whereas in the Toulouse-Piéron test they found a larger number of omissions and a low concentration index. These conditions may compromise patient care, especially in emergency and trauma surgery services, as well as the own physician'shealth. In view of this, this study aimed to investigate sleep quality and daytime sleepiness of residents comparing with medical students in the final stage of graduation.

METHODS

We conducted a descriptive research between August and November 2013 with resident physicians and medical students from Curitiba – Paraná, through a project approved by an ethics committee (CEP 307.644).

Inclusion criteria were: adult over 18 years of age, enrolled in a medical residency program or in the

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medical school internship period, in the internal medicine and surgical clinical sectors, without hierarchical link with the researchers and who agreed to participate in the research through a Signed the Informed Consent Form. We excluded incomplete questionnaires and individuals under treatment for sleep disturbance.

The approach occurred intentionally and through accessibility during the intervals of activities in teaching hospital settings. After adequate orientation of the participants, we handed the self-application, anonymity-preserving measurement instruments, comprising the following: a) questionnaire for socio-demographic characterization and internet use; b) Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS), both versions translated into Brazilian Portuguese, tested and validated[1].

The Pittsburgh Sleep Quality Index (PSQI) has seven components: 1) subjective quality of sleep; 2) sleep latency; 3) duration of sleep; 4) habitual sleep efficiency; 5) sleep disorders; 6) use of sleeping pills; 7) daytime sleepiness and daytime disturbances. Each part has specific scores, with 21 points being the maximum score. Scores greater than five indicate poor sleep quality[1].

The Epworth Sleepiness Scale (ESS) has eight statements about the tendency to daytime sleepiness in everyday situations, taking into account the individual's way of life in recent weeks. Responses are attributed to a 4-point Likert scale, and the sum of these points results in the final score. Normal scores are up to 10, pathological scores between 11 and 15, and very pathological, between 16 and 24[1].

We analyzed the qualitative variables related to the participant's formation (intern or resident) by means of absolute and relative frequencies, and the quantitative variables by mean and standard deviation. We compared the qualitative variables of personal data and history between the groups using the Chi-Square test for Independence, and in cases of statistical significance, we analyzed pairs of data by means of the Adjusted Residues test. We evaluated the variables 'internet use during the day', 'internet use at night', 'number of subjects doing shifts' and 'number of working subjects' by means of the Chi-square test for K Proportions, followed by the Marascuilo test.

We analyzed the variable 'Pittsburgh Sleep Quality Index' (PSQI) and its respective domains, and the variable 'Epworth Sleepiness Scale' (ESS) as for the data distribution pattern using the Lilliefors test, and the homogeneity of the variances between the interns and residents groups, through the Levene test. We found that the PSQI variable was in congruence with the assumptions of normality and homoscedasticity, so we compared the means of the two groups with the t-test for independent samples. The other variables were not in agreement with those assumptions, so we analyzed themusing the nonparametric Mann-Whitney-U test. In all tests, we used a significance level of 5%, and performed the analyzes with the software XLStat2013 (Addinsoft, 2013).

RESULTS

The sample consisted of 206 participants, with 105 resident physicians and 101 undergraduate students working in the specified areas during the study period. We excluded two residents and six interns due to incomplete completion of the questionnaires. Regarding sex, there was a greater amount of female residents (53%) compared with medical students, who had male prevalence (51%). The age group of the residents was concentrated between 25 and 29 years (73%), and of the interns, between 20 and 24 (67% – x^2=127.5, p<0.05). Most residents (84%) and interns were single (98%). Only four residents mentioned having children (4%), and this was not observed among the undergraduates (x^2=105.0, p<0.05).

Most of the medical students came from private institutions (82%), while among residents the distribution of frequencies was homogeneous between public (46%) and private (54%) institutions (x^2=9.287, p<0.05). As for internet use for work or study, we found that residents use it both during the day (98%, x^2=165.048, p<0.05) and at night (97%, x^2=151.423; p<0.05), with frequencies significantly higher than the interns (9% and 12%, respectively – Table 1). However,

Table 1. *Absolute and relative Frequencies (in parentheses) of history related variables. p-value Chi-square test for Independence*.*

		Academics	Residents	p
Undergraduates institution	Public	7[b] (18%)	48[a] (46%)	0.002
	Private	32[a] (82%)	57[b] (54%)	
	Not informed	62	0	
Residents institution	Public	0 (0%)	58 (55%)	Does not apply
	Private	0 (0%)	40 (38%)	
	Both	0 (0%)	1 (1%)	
	Not informed	0 (0%)	6 (6%)	
	Does not apply	101 (100%)	0 (0%)	
Use of internet	Day	9[b] (9%)	103[a] (98%)	< 0.0001
	Night	12[b] (12%)	102[a] (97%)	< 0.0001
Shifts per week		1[b] (1%) (1 shift)	93[a] (89% – 2 ± 1)	< 0.0001
Weekly hours of work		1[b] (1%) (12 hours)	104[a] (99% – 77 ± 21)	< 0.0001

[a,b] *Indicate statistical difference (p < 0.05) between groups of students and residents within each variable category.*

on average, residents reported staying on the internet 1.32±1.21 hours during the day and 1.60±1.05 hours at night, and the academics, 2.11±1.27 hours during the day and 1.27±0.87 hours at night.

About 89% of the residents performed weekly shifts (x^2=159.168; p<0.05) with an average of 2±1 shifts per week; 99% worked in other places (x^2=198.075, p<0.05), totaling on average 77±21 hours of work per week. In this sample, only one intern mentioned paid work (Table 1), although they all carried out student-teaching shifts.

When assessing the total score of the Pittsburgh Sleep Quality Index (PSQI), we found a significant difference between the means of the interns and residents groups (t= -2.36, p=0.019). Residents had a higher mean PSQI index (6.76±2.81), showing poor sleep quality when compared with the group of medical students (5.90±2.39 – Table 2).

Among the domains of the PSQI instrument, we observed higher values regarding sleep duration and subjective sleep quality among residents (p<0.05). Residents had lower sleep duration and worse subjective sleep quality when compared with interns, with no differences among the other domains (Table 2).

When evaluating the total score of the Epworth Sleepiness Scale (ESS), there was no significant difference between the values of the interns and residents groups (U= -4744.5, p=0.280). Such a result indicates that interns and residents showed similar measures of drowsiness (Figure 1).

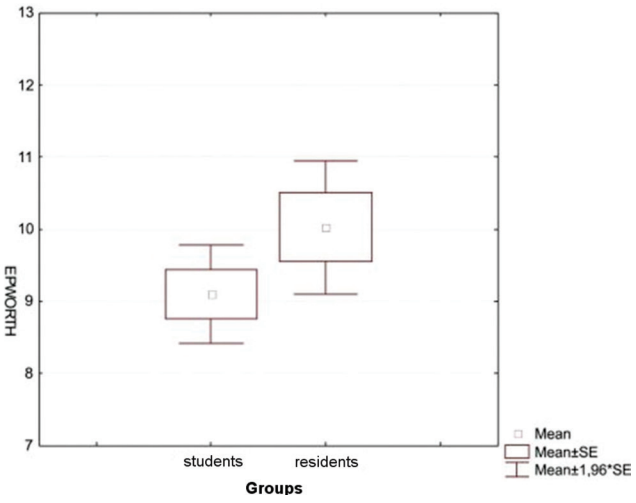

Figure 1. *Mean, standard error, and confidence intervals of the Epworth Sleepiness Scale between students and residents.*

Table 2. *Averages and standard deviations of the Pittsburgh Sleep Quality Index and its respective domains, and Epworth sleepiness Scale.*

	Students	Residents	p
PSQI *	5.90±2.39	6.76±2.81	0.019
Latency to sleep **	1.10 ± 0.85	1.09 ± 0.95	0.74
Habitual sleep efficiency **	0.31 ± 0.11	0.45 ± 0.20	0.37
Sleep duration **	0.73 ± 0.68	1.10 ± 0.83	0.00
Disorders **	1.16 ± 0.49	1.15 ± 0.62	0.88
Subjective sleep quality **	1.15 ± 0.66	1.49 ± 0.84	0.01
Need for sleeping medication **	0.21 ± 0.61	0.70 ± 0.27	0.83
Daytime dysfunction **	1.44 ± 0.76	1.48 ± 0.80	0.67
Epworth Sleepiness Scale **	9.10 ± 3.47	10.03 ± 4.80	0.280

P-value of t-test for independent samples and Mann-Whitney-U test**.*

DISCUSSION

Sleep disorders affect a considerable number of individuals around the world and are of extreme scientific interest because of their direct and indirect consequences to personal and collective health[10,14-16]. The peculiarities of the requirements of medical training can cause sleep restriction and fragmentation[17,18], together with individual and socio-organizational factors of work and study. The present sample was composed of young adults, residents and medical students, with an age similar to that of the national literature[1,17]. However, students are younger than residents, are single and without children, and these variables can influence sleep pattern. The lower age range of Brazilian physicians when compared to Portuguese ones[6] may be justified by methodological and educational differences between the two countries.

Sleep disturbances are frequent in the face of important changes in style and rhythm of life[11,19]. Globalization, access to technology, and a growing tendency to connect in social networks are likely to interfere with sleep hygiene, and in the present sample, it is possible that the time spent on the internet is greater than reported. Doctors and medical students use the internet on a daily basis, and modern hospitals have access to internal protocols via internet platforms, besides the growing popularization of digital mobile technology. In this study, data related to internet use were self-reported and may contain memory bias.

On the other hand, work under on-call shifts, worsened by stress and sleepingdifficulties, causes shorter and non-restingsleep episodes[1,5,10,19]. In the present sample, the average weekly working hours of the residents (77 hours) exceeded the recommended one (60 hours), probably due to other external professional ties. These findings concern the potential detrimental effect on training, physical, mental and psychological well-being and the availability of time for leisure, physical activities, social interaction and rest[10,13].

As for the PSQI, the mean index for residents was 6.76, similar to the results of Cardoso *et al*.[1], who found an index of 6.2 for both genders. The recommended limits for the PSQI are values below 5, that is, both studies indicate poor sleep quality among residents.

Moraes *et al*.[20] found that medical students in São Paulo took 21.83 minutes to sleep and that they slept, on average, 6.80 hours. Cardoso *et al*.[1], using the PSQI instrument, demonstrated that medical students from Goiás took an average of 15.31 minutes to sleep and had an average sleep duration of 6.13 hours. This same study demonstrated statistical significance when comparing the sleep pattern of the residents with the sleep pattern of the first year students. In the present investigation, there was a significant difference between

averages of interns and residents, showing that residents had worse sleep quality.

A research with 602 Emergency Medicine Residents demonstrated excessive sleepiness in 38% (ESS 11-16) and severe sleepiness in 7% (ESS>16) according to the Epworth scale[21]. In Curitiba-PR, an evaluation of 136 residents of various specialties showed pathological sleepiness indexes in 76% (mean ESS 12.6±4.0), being higher in women and in the first year of residence, without significant difference between specialties, but with a decrease in the daytime sleepiness score during the residence training[10,13]. Standards of professional and extraprofessional activities of men and women tend to be different and may interfere with sleep patterns.

Studies on the prevalence of excessive daytime sleepiness in Brazilian medical students also showed inadequate habits and sleep deprivation, with oscillations during the semester and weekends[4,22]. The following ESS scores averages were found among students: 10.72 at the University of Brasília and 10 at the University of São Paul[20]. In the present study, the levels of sleepiness detected were similar between residents and medical students, differing from other studies national studies[1,20], and point to the need to adopt educational strategies aimed at health promotion, including daily and regular physical activity, which can be a resource to improve tolerance to night work.

Among the limitations of this study, it is worth noting that we did analyze variables potentially capable of influencing the occurrence of sleep disorders (such as psychological profile, financial difficulties, preparation for selective processes, family conflicts, food, physical activity and leisure). There was also no stratification according to the variables gender, age, modality and year of medical residency or shifts' characteristics. In addition, we not use Polysomnography, Multiple Sleep Latency Test (MSLT), sleep diary and other resources. Despite these limitations, this research showed important aspects of sleep deprivation in medical training and provokes debate on the relevance of sleep in a society that operates 24 hours, and an increasingly accelerated and connected way, mediated by machines and technologies.

The increase in Burnout syndrome in the medical field[5,11] may impact sleep quality. Possibly its occurrence, causes and manifestations differ between residents and students. The application of instruments to measure occupational stress could reveal other aspects and topics for further investigation.

Research evaluating anesthesiologists has revealed that sleep and fatigue from night shifts can affect agility, attention, cognitive function, reflexes, and motivation for work[23]. Moreover, surgical environments are generally confined, noisy, busy and stressful places[23]. We should also point out that constant exposure to bright spaces and to the violet blue light emitted by digital devices such as smartphones, computers and tablets can influence the circadian rhythm by affecting the natural release of melatonin, the hormone involved with the sleep-wake cycle[24].

Thus, it is important to encourage medical students, physicians and residents to learn to healthily manage their living habits and occupational challenges, especially in the surgical areas, to minimize repercussions on the quantity and quality of sleep, as well as on patient care. Practical measures for good sleep hygiene are essential: a) Controlling situations that induce increased arousal – avoid consumption of stimulant medications, caffeine, cigarettes, alcohol, light, temperature and noise in the room, stress, mental work or vigorous exercise close to bedtime; b) Planning the length of sleep and wakefulness – observe regularity at bedtime and waking up time, controlling access and excessive use of digital networks; c) Resting, relaxing and practicing physical activities in the period free of work or shifts, minimizing risks and damages to health and social life; and d) Applying measures that facilitate adaptation to the shift to reduce internal dyssynchronization and sleep disorders related to the circadian rhythm.

In conclusion, in this sample, residents had a higher PSQI mean when compared with medical students, and although ESS sleepiness scores were similar between groups, residents showed lower sleep duration and lower subjective sleep quality. Sleep deprivation requires health promotion actions among residents and medical students.

R E S U M O

Objetivo: avaliar a qualidade de sono e a sonolência diurna de residentes comparando com estudantes de medicina. **Métodos:** foram aplicados questionário sociodemográfico, Índice de Qualidade do Sono de Pittsburg (PSQI) e Escala de Sonolência de Epworth (ESE) numa população de residentes e estudantes de medicina. **Resultados:** participaram 105 residentes e 101 estudantes da graduação médica. Os residentes apresentaram maior média do PSQI (6,76+2,81) com pior qualidade de sono quando comparados aos acadêmicos (5,90+2,39); ambos tiveram medidas semelhantes de sonolência pela ESE (p=0,280), porém os residentes mostraram menor duração e pior qualidade subjetiva de sono**. Conclusão:** estudantes e residentes apresentaram privação de sono indicando necessidade de ações preventivas na área médica.

Descritores: Transtornos do Sono-Vigília. Distúrbios do Sono por Sonolência Excessiva. Educação Médica.

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Comparative analysis of the effects of *Copaifera multijuga* oil-resin and nitrofurazona in the cutaneous wound healing process

Análise comparativa dos efeitos do óleo-resina de Copaifera multijuga e da nitrofurazona na cicatrização de ferida cutânea

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A B S T R A C T

Objectives: *to evaluate, histologically and macroscopically, the influence of Copaifera multijuga (Copaíba) oil-resin on the healing process of cutaneous wounds, comparing it with nitrofurazone.* **Methods**: *we divided 36 rats into three groups of 12 animals, according to the treatment to be administered. Group SL (control) received saline on the lesion; the Group OIL received topical treatment with Copaíba oil; and the Group NITRO was treated with Nitrofurazone. We inflicted a circular wound of 8mm in diameter on the back of each animal. We subdivided each of the three groups of 12 animals into three subgroups, according to treatment time and euthanasia (7, 14 and 21 days). All animals received the proposed treatment daily. We photographed the lesions for area measurement, as well as for evaluation of macroscopic aspects. We resected and stained the scars to quantify and qualify elastic fibers, collagen, degree of epithelization, neovascularization and inflammation.* **Results**: *although the saline solution provided a faster wound closure in its initial phase, after 14 days the wound size of the three groups tested was the same. Levels of inflammation and neovascularization were similar in all three groups. The amount of collagen and elastic fibers was higher in the Nitrofurazone and Copaíba oil groups.* **Conclusion**: *in male Wistar rats, Copaifera multijuga oil-resin positively influences the healing process, but it is less effective than nitrofurazone in healing by secondary intention.*

Keywords: *Wound Healing. Plants, Medicinal. Collagen. Collagen Type I. Collagen Type III.*

INTRODUCTION

In recent years, there has been a growing interest in folk medicine, with the use of natural products for the control of diseases[1]. Consequently, there was an increase in the number of herbal medicine, to obtain cheaper compounds with effects similar to traditional drugs[2].

Although widely marketed and used by the population for the most varied purposes, Copaíba oil still leaves doubts as to its efficacy and safety. There are problems in its use, such as contamination, authenticity and the mixing with other oils of vegetable origin, which in addition to altering the possible desired therapeutic effect, can be detrimental to consumers' health[3].

Found mainly in the biomes of the Amazon basin and the cerrado, the "copaibeira", as it is popularly known, is a tree belonging to the *Copaifera* genus, family of legumes, the main ones being *C. officinaliis*, *C. reticulata*, *C. langsdorffii*, *C. guyanensis* and *C. multijuga*, from whose trunks an oil-resin or balm can be extracted[2,4,5]. Used since the 16th century for medicinal purposes[2,6], Copaíba oil is described in the literature as anti-edematous[5], anti-inflammatory[3,7,8], antibacterial[8,9], insecticide[5,6,8], antifungal[10] and wound healing[8,11]. It is popularly adopted in the treatment of several diseases, such as cystitis, bronchitis, chronic diarrhea, rheumatism, psoriasis, tumors[9] and gonorrhea[4].

These therapeutic effects are due to the presence of diterpenes and sesquiterpenes[12], such as copalic acid and β-caryophyllene sesquiterpenes and α-copaene[11]. Paiva[13] studied the formation of colitis induced by the application of acetic acid In rats and found Copaíba oil to be a potent anti-inflammatory agent, which was attributed to the fact that diterpene inhibited the transcription activity of the Nuclear-Kb Factor (FN-kB)[11],

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an important molecule involved in the cellular activation process of the innate immune response[13].

Nitrofurazone is an antibactericidal agent of the furans family, whose mechanism of action is the inactivation of ribosomal proteins and other macromolecules, with consequent inhibition of proteins, DNA, RNA and cell wall synthesis, blocking the aerobic metabolism of bacterial cells. It can be used as adjuvant in the healing process of cutaneous wounds, since in addition to the antimicrobial activity, it interferes in the formation of granulation tissue. Its topical use is adequate, since it does not suffer significant absorption through whole or burned skin, nor through the mucosa[14,15]. It is found commercially as an ointment (30mg), at a concentration of 2mg/g.

The objective of this research was to histologically and macroscopically evaluate the influence of *Copaifera multijuga* oil-resin on wound healing of rats, comparing it with nitrofurazone.

METHODS

We used 36 adult, male rats of the same age, *Rattus norvegicus albinus rodentia mammalia*, from the Wistar line, from the TECPAR vivarium. All animals were acclimated and kept in the laboratory of the Paraná Evangelical Faculty (FEPAR), receiving water and chow for the species ad libitum, and respecting the ethical principles of animal handling and experimentation defined by the Animal Experiment Ethics Committee and the Brazilian Legislation on Animal Experimentation, Federal Law Nº 6638, of 1979. The research project was submitted and approved by the Ethics Committee on the Use of Animals of FEPAR (protocol number 004988/2012).

We divided the sample into three groups of 12 animals each, according to the proposed treatment: the Control group (Group SL), received only 0.9% saline solution on the lesion; the Test Group (Group OIL) received topical treatment with pure Copaíba oil, at the dose of 0.3ml/day; the Comparison group (Group NITRO) was treated with topical Nitrofurazone (2mg/ml) 0.3ml daily.

We weighed and identified all animals. We subdivided each of these groups into three cages, each with four animals, according to the time they would be submitted to euthanasia, seven, 14 and 21 days[16].

With the animal duly anesthetized with inhalational isofluorane in anesthetic bell until the deep plane, tricotomy was done on the back of the animal attached to a plank in the ventral decubitus position, with scissors and disposable razor[2]. Then, we performed the site antisepsis with 70% alcohol[3] and made a circular wound using a dermatological punch, measuring 8mm in diameter, removing skin and subcutaneous, without damaging the underlying aponeurosis. Hemostasis was achieved by digital compression and gauze[16].

All animals received the proposed topical treatment for each group daily, respecting the 24-hour interval between the applications. In each of these applications, a gauze dressing was made around the animal with micropore tape, so that the animals were not subject to limitation of respiratory incursions and did not have direct contact with their wounds and the wounds of the other animals of the cage. We managed postoperative pain with tramadol 50mg/ml at a dose of 5mg/day, intramuscularly for three days.

At the end of each pre-established period (7, 14 and 21 days), we again weighed four animals from each group and killed them by anesthetic overdose with inhaled isofluorane. The animals were then attached to the surgical board, where the lesions were analyzed macroscopically by high-resolution photographs (8mp) obtained from a fixed camera on a pedestal, with an auxiliary light focus and a millimeter scale present in the field. We submitted the obtained images to software analysis (AutoCad 2013), and accurately measured the area of each wound[16].

We resected the dead animals' cutaneous scars respecting a margin of at least 3mm from the edge of the lesion, and immediately put them in previously identified flasks with buffered formalin.

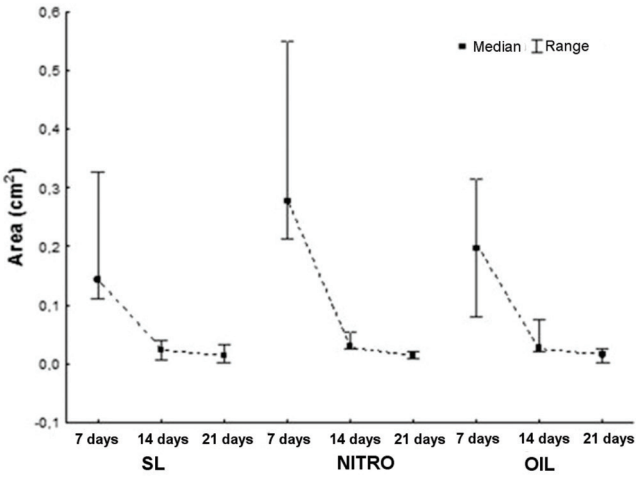

Figure 1. *Wound area as a function of experiment time.*

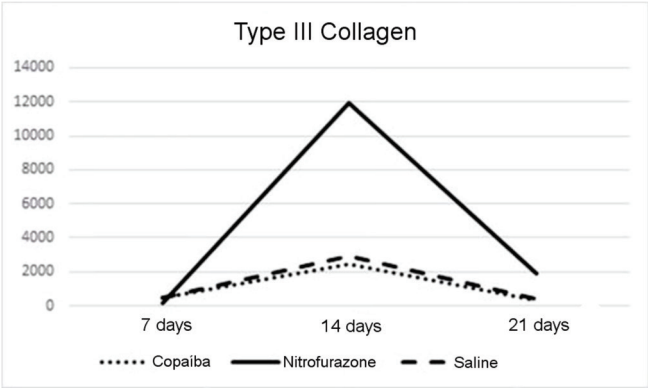

Figure 2. *Type III collagen fibers.*

The FEPAR Histotechnical laboratory provided the preparation of the slides with Hematoxylin and Eosin (HE) staining for morphometric analysis (epithelization, classification and degree of inflammatory process, and vascularization), Sirius-red staining (quantified and qualified collagen, types I or III) and Weigert staining for analysis of elastic fibers. The same pathologist evaluated all HE slides with a optical microscopy, without being aware of the group they belonged to. For the evaluation of the amount and type of collagen fibers, as well as the amount of elastic fibers, we captured five images from each wound, with the aid of a microscope with coupled camera and polarized light lens. We then submitted the images to the ImagePro 2013 software, which counted the amount of type I and type III collagen fibers in each slide, as well as counting the elastic fibers[17].

For the description of quantitative variables, we considered the mean, median, minimum value, maximum value and standard deviation. For the description of qualitative variables, we used frequencies and percentages. We used the non-parametric Kruskal-Wallis test to compare independent groups (groups at each moment and moments within each group), with p-values lower than 0.05 indicating statistical significance. We analyzed the data with the statistical software Statistica, v.8.0. All the results received statistical treatment, adopting $p<0.05$ as the level of significance.

RESULTS

We compared the groups at each moment by testing the null hypothesis of equal results in the three groups versus the alternative hypothesis of different results. When comparing the areas of the wounds to each other within the same moment of the experiment, we observed no statistical significance ($p>0.05$). Although the groups SL and OIL had better results in the first seven days, on the 14th day of the experiment

Table 1 - *Wound epithelialization by group according to the day of analysis*

	SL Group		NITRO Group		OIL Group	
Days of evolution	Present	Absent	Present	Absent	Present	Absent
7	1	3	4	0	4	0
14	4	0	4	0	4	0
21	4	0	4	0	4	0
Total	9	3	12	0	12	0

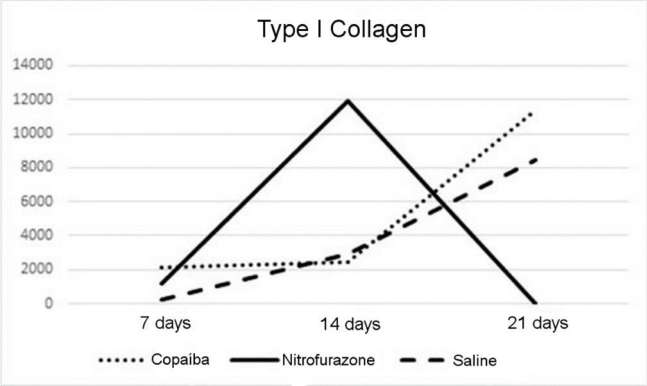

Figure 3. *Type I Collagen fibers.*

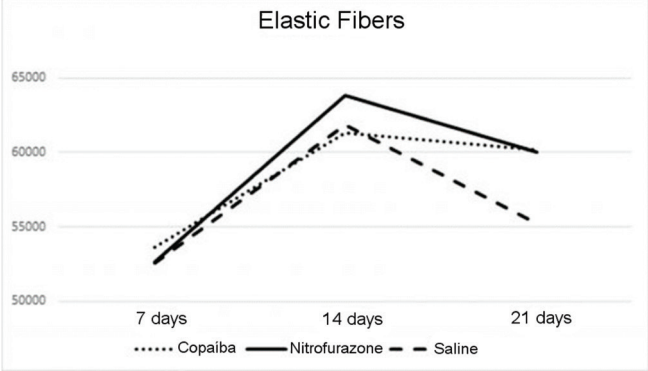

Figure 4. *Elastic fibers.*

all the animals had wounds of very similar area, remaining in this tendency until complete healing. Figure 1 shows the statistics of the area variable as a function of time within each group.

We analyzed inflammation, epithelization and neovascularization based on histopathological analysis of the HE-stained slides (Tables 1, 2 and 3).

By analyzing and quantifying types III and I collagen fibers in each group and comparing with the time of analysis, we obtained the data shown in Figures 2 and 3.

We observed that saline had the worst performance, not stimulating the production of collagen in the same proportion as the other tested compounds. Copaíba oil was more capable of converting type III (young) collagen to type I (mature) collagen, a fact that has a positive effect, since the higher the amount of mature collagen, the greater the wound's mechanical resistance.

Applting the same method used to measure the collagen fibers (except for the staing used, the Weigert's), we obtained an estimate of the amount of elastic fibers in each wound (Figure 4). Elastic fibers are essential in that they give elasticity to the tissue, but as the latter gets more mature, the tendency is for some of them to join the collagen fibers, thus making the tissue more resistant.

DISCUSSION

Brazil has a rich flora in plants and compounds for medicinal use, a fact that has aroused more and more the interest of researchers, institutions and universities interested in herbal treatments or in search of new substances. Since not only the Copaíba oil but also other compounds have innumerable varieties of species within nature, standardizing research methods, as well as finding studies that can be directly compared, is a challenge.

Cutaneous healing is a complex process, influenced by a number of factors, such as nutritional status, systemic diseases, concomitant local or systemic infection and wound extension among others. In the present study, we chose Wistar rats due to the richness

Table 2- *Presence of inflammation in the wound by group according to the day of analysis*

	SL Group		NITRO Group		OIL Group	
Days of evolution	Present	Absent	Present	Absent	Present	Absent
7	4	0	4	0	4	0
14	2	2	1	3	4	0
21	2	2	0	4	0	4
Total	8	4	5	7	8	4

Table 3 - *Wound neovascularization by group according to the day of analysis*

	SL Group		NITRO Group		OIL Group	
Days of evolution	Present	Absent	Present	Absent	Present	Absent
7	4	0	4	0	4	0
14	4	0	4	0	4	0
21	4	0	2	2	4	0
Total	12	0	10	2	12	0

of data available in the literature on the characteristics of the skin and the cicatricial process of these animals, as well as the great resistance they display to infectious processes and surgical aggressions, besides being easy to obtain and to handle. The animals selected for the study were necessarily male, so that there was no interference of the hormonal variation due to females' estrous cycle, which could interfere in the tissue repair process[16].

We observed no significant difference between the mean areas of the wounds, except that the wounds of the nitrofurazone group had a smaller tendency to reduce size on the 7th day when compared with the two other groups, a difference that we did not observe at 14 and 21 days, a fact corroborated by other studies[18].

The findings of inflammation, epithelialization and neovascularization were similar to those observed by Teixeira[18], and we could observe a greater presence of inflammatory component in the Copaíba group, with evolution to the disappearance of the inflammatory process at day 21 in all groups. All the wounds showed an excellent capacity of neoangiogenesis and, in light microscopy, a rich capillary network with endothelial and red blood cells, which is in agreement with Estevão's findings[19].

In the quantification of collagen fibers, we found that at day seven, Copaíba oil was more effective than the other two compounds in the induction of collagen formation, predominantly of type I. This differs from the work of Vieira *et al*.[3], who found that the animals of the Copaíba oil group presented less collagen fibers when compared with the animals of the saline group. This divergence of data may be because they used *Copaifera reticulata* instead of *Copaifera multijuga*, used in this study.

At 14 days, there was an expressive increase in the amount of collagen of both types I and III in the wounds of the nitrofurazone group, reaching levels close to those of healthy skin (4:1 ratio). There was not a significant increase in the number of such fibers in the Copaíba group, the same happening in the saline group.

With 21 days of experiment, we could observe that both the OIL and NITRO groups reached good levels of collagen fibers, enough to maintain tissue resistance and retraction force. Saline did not prove to be a good agent inducing the formation of collagen fibers, with approximately 20% less collagen fibers than the other groups.

By the Weigert coloration, we could measure the amount of elastic fibers in each wound. These give greater elasticity to the tissue, besides interspersing with the collagen, conferring greater resistance. Nitrofurazone proved to be the best inducer of elastic fiber formation, but was closely monitored by the other two groups until the 14th day. On day 21, there was a large drop in elastic fiber levels in the SL group, and the NITRO and OIL groups finished the experiment with very similar levels.

In Wistar male rats, Copaíba oil contributed positively to the healing of cutaneous wound by secondary intention, but due to the difficulty of obtaining an oil-resin with good origin, its use is limited. The authors suggest works on the systemic effects of the use of the Copaíba oil, to gather more scientific data and to obtain a basis for the use of this compound by the population.

R E S U M O

Objetivo: avaliar histologicamente e macroscopicamente a influência do óleo-resina de *Copaifera multijuga* no processo de cicatrização de feridas cutâneas, comparando com o grupo submetido ao uso da nitrofurazona. **Métodos:** foram utilizados 36 ratos, divididos em três grupos de 12 animais, conforme o tratamento a ser administrado. Grupo SF (controle, recebeu soro fisiológico sobre a lesão), Grupo ÓLEO (tratamento tópico com óleo de Copaíba), Grupo NITRO (tratamento tópico com Nitrofurazona). Foi confeccionada uma ferida circular de 8mm de diâmetro no dorso de cada animal. Cada um dos três grupos de 12 animais foi subdividido em três subgrupos, de acordo com o tempo de tratamento e de eutanásia (7, 14 e 21 dias). Todos os animais receberam o tratamento proposto diariamente. As lesões foram fotografadas para mensuração de sua área, bem como, avaliados aspectos macroscópicos. As cicatrizes foram ressecadas e coradas, para quantificar e qualificar as fibras elásticas, colágenas, grau de epitelização, neovascularização e inflamação. **Resultados:** embora o soro fisiológico tenha proporcionado um fechamento mais rápido da ferida em sua fase inicial, a partir de 14 dias o tamanho das feridas dos três grupos testados se equivaleu. Níveis de inflamação e neovascularização foram semelhantes nos três grupos. A quantidade de fibras colágenas e elásticas foi maior nos grupos Nitrofurazona e Óleo de Copaíba. **Conclusão:** em ratos machos da linhagem *Wistar,* o óleo-resina de *Copaifera multijuga* influencia positivamente no processo de cicatrização, porém é menos eficaz que a nitrofurazona na cicatrização por segunda intenção.

Descritores: Cicatrização. Plantas Medicinais. Colágeno. Colágeno Tipo I. Colágeno Tipo III.

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Reconstruction of face and scalp after dog bites in children

Reconstrução de face e couro cabeludo após mordeduras caninas em crianças

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ABSTRACT

Objective*: to evaluate the immediate reconstruction of face and scalp after canine bites in children.* **Methods***: we conducted a prospective series of cases treated at the Emergency Unit of the Asa Norte Regional Hospital, Brasília - DF, from January 1999 to December 2014. At the time of patient admission to the emergency, the primary wound closure of the face and scalp bite was performed, regardless of the time or day of the event. The primary treatment of the bites was by means of direct suture, flaps rotation or grafting, depending on the type of wound and surgeon's decision.* **Results***: the study comprised 146 children, with the zygomatic region and scalp being the main sites of head bites. All patients received surgical treatment within the first 24 hours after admission. There were no infectious complications in the cases studied.* **Conclusion***: the findings suggest that the immediate closure of canine bites on the face and scalp in children is safe, even when carried out several hours after injury.*

Keywords: *Face. Scalp. Bites and Stings. Dogs. Child. Reconstructive Surgical Procedures.*

INTRODUCTION

Bites are common injuries, usually seen in hospital emergencies, accounting for 0.3% to 1.1% of visits[1]. They represent a public health problem because, in addition to the threat to the physical integrity of people, canine bites can transmit rabies and cause serious infections. This fact has mobilized public opinion, politicians and health professionals to make changes in Brazilian legislation and campaigns to prevent and treat those injuries[1,2].

It is estimated that 36.5% of American households own at least one dog and 30.4% have at least one cat[3]. In addition, an estimated 4.5 million bite victims occur annually in the United States[3]. Of these, 6000 to 13,000 patients per year require specialized treatment and hospitalization due to canine bites, with an annual average of 19 deaths, ranging from 11 to 33 deaths per year from 1979 to 2005[4].

Children are the main victims of canine attacks, both in morbidity and lethality[5]. It is believed that half of the children were bitten by dogs at some stage of their lives, and one of the main injury sites in this age group is the head, which increases morbidity[1]. The usual recommended conduct is that wounds caused by bites should not be closed, and reconstruction delayed until after the period of greatest risk of infection has passed. However, in recent years, several authors have advocated the primary surgical treatment of canine bites that occur on the face and scalp[6,7].

The objective of this study was to evaluate the immediate reconstruction of face and scalp after canine bite in children.

METHODS

The study was a prospective series of cases and comprised 146 patients who were initially treated at the Emergency Unit of the Plastic Surgery Service of the Asa Norte Regional Hospital (Brasília-DF) from January 1999 to December 2014. Patients were admitted to the study consecutively. Exclusion criteria were: patients who already had signs of infection at the bite site on admission; Patients with an outpatient follow-up of less than 30 days; and patients aged 13 or over.

1 - Asa Norte Regional Hospital (HRAN), Plastic Surgery Service, Brasília, Distrito Federal, Brazil. 2 - Superior School of Health Sciences, Medicine School, Brasilia, Distrito Federal, Brazil.

Table 1. *Distribution of children victims of dog bites in the face and scalp, attended at the HRAN, Brasília, DF, according to the time elapsed from the event, to the site of injury and to the type of treatment.*

	Number of patients	%
Time from event		
< 6 hours	91	62.3
6 to 24 hours	40	27.4
> 24 hours	15	10.3
Site of injury		
Zygomatic	44	30.1
Scalp	39	26.7
Front	21	14.4
Nose	15	10.3
Lip	13	8.9
Ears	9	6.2
Eyelids	5	3.4
Treatment		
Suture	102	69.8
Grafting	38	26.1
Local flap rotation	6	4.1

Data were collected through a questionnaire with the patient or legal guardian. The variables analyzed were: age, gender, origin, time interval of the event to hospital care, aggressor agent, place of injury, characteristics of the lesions and treatment. The postoperative follow-up was done through weekly consultations for at least 30 days. The sutures were removed between the seventh and tenth postoperative days.

The conduct in cases of bite on the face and scalp was copious irrigation of the wound and cleaning with 1% polyvinylpyrrolidone degermant solution (PVPI) or 2% chlorhexidine and saline solution. The primary closure on the arrival day was done by means of direct suture, local flap rotation or grafting. There was no limit of hours or days between the time of the event and the surgical procedure, that is, when the patient arrived at the hospital emergency room, the procedure was performed regardless of the time or day of the event. The devitalized tissues were debrided and there was no sign of wound infection at the time of closure. In cases of lesions near the main parotid duct or the tear duct, the integrity of these structures was evaluated and repair was performed, when necessary.

Tetanus and rabies prophylaxis were performed as appropriate. All study patients received antimicrobials during seven days. The antibiotic of choice was a 1st generation cephalosporin (cephalexin).

The work was approved by the Ethics in Research Committee of the State Health Department of the Federal District, under CAAE number 52737216.2.0000.5553.

RESULTS

The study comprised 146 children, with a mean age of seven years (ranging from 1 to 12). The majority of the patients were male (60.3%) and 105 (70.9%) were from the Federal District. Children who were nine years of age or less were the main victims, representing 79.4% of the sample. Regarding the time of care, 91 (62.3%) patients were seen in the first six hours after the accident (Table 1).

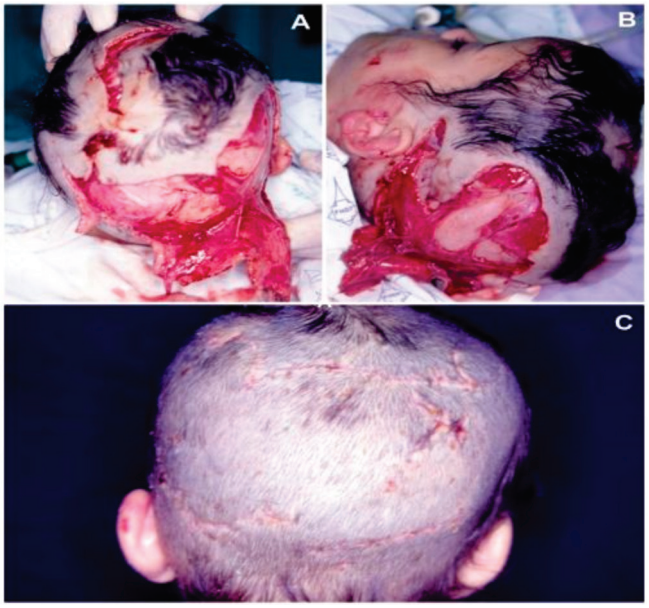

Figure 1. *A and B) Child with extensive scalp lesion due to canine bite, without loss of substance, subjected to the immediate closure; C) Postoperative 2-month evolution.*

The zygomatic region was the main site of bites on the face in children, followed by the scalp (Figures 1 and 2). No wound showed signs of infection on admission. All patients received surgical treatment within the first 24 hours after hospital admission.

Regarding the severity of the lesions, 44 (30.1%) patients presented loss of substance. There were two cases of bone fracture in the face and skull. One of the patients had extensive scalp lesions associated with fractures of the occipital, temporal and zygomatic bones, and underwent neurosurgical and soft tissue treatment (Figure 2).

The most common type of treatment was direct suture in 102 (69.8%) cases, followed by skin grafting (26.1%) or local flap rotation (4.1%). The type of anesthesia most used was general due to the fact that they were children with extensive lesions. There was no case of human or animal rabies, neither deaths nor infections in the study (Figure 3 and 4).

DISCUSSION

Canine attacks to children are an important cause of morbidity and, to a lesser extent, lethality, accounting for 80 to 90% of all bites seen in emergency units[1]. It is estimated that the rate of canine bite care in American emergencies is 1.3 per 1000 inhabitants, leading to 44,000 canine bite injuries annually[8]. However, this rate is less than realistic, with only 36% of canine bites being treated in the hospitals or informed to authorities[8,9].

Children are the most affected, as 26% of childhood bites require medical care, compared to 12% in adults. Children are the main fatal victims of canine attacks, since 80% of canine bites in children occur in the head and neck, whereas this region is affected in adults in less than 10% of cases[5]. The high prevalence of head bites in children is attributed to the short stature and increased face exposure associated with the spontaneity of bringing the face close to the dogs[9,10,11]. In most cases, attacks involve familiar or family dogs, usually away from the physical presence of an adult, and there is no specific breed of dog that is more involved in the attacks[2,4,12].

A complete clinical examination is essential, associated with a detailed examination of the wound under general anesthesia, as appropriate. Especially in children, there is a possibility of associated lesions

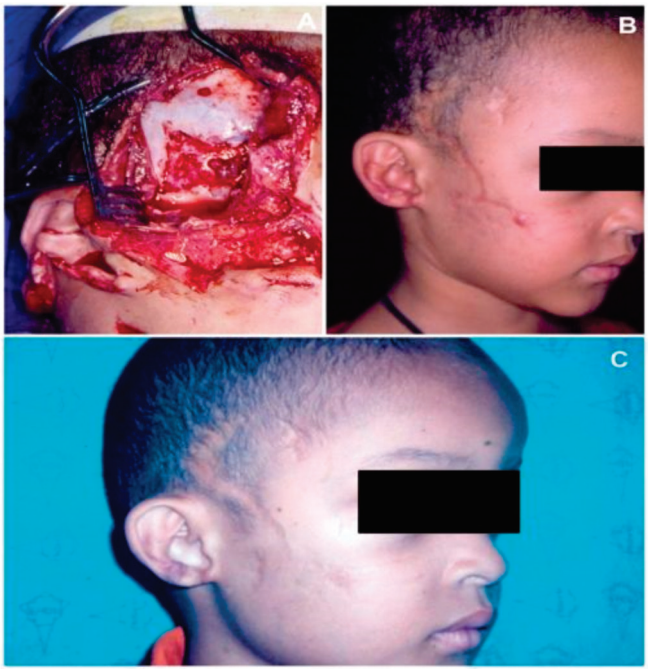

Figure 2. *A) A five years old child with temporal bone fracture due to canine bite, submitted to neurosurgical treatment and immediate closure of the lesions on the face; B) Postoperative 2-month evolution; C) Postoperative 1-year evolution.*

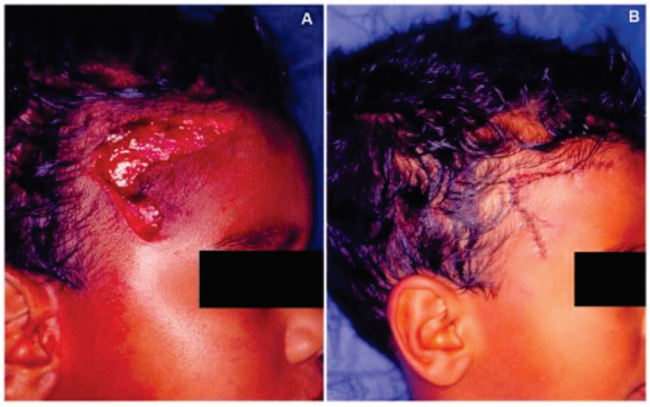

Figure 3. *A four years old child victim of canine bite on the face and scalp, submitted to immediate lesion suture; B) postoperative 7-day evolution.*

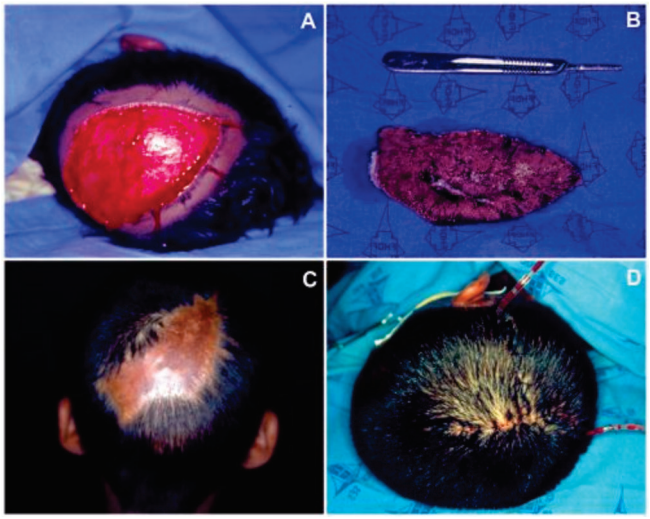

Figure 4. *A six years old child with partial avulsion of the scalp by canine bite, submitted to immediate grafting of the avulsed segment. After six months of grafting, she was submitted to resection of the grafted area with alopecia (A, B and C) and direct closure of the scalp (D).*

such as airways, cervical spine, vessels, nerves, eyeball, lacrimal apparatus, cranial and facial fractures, which should be remembered and investigated[13,14]. In our study, there was a child with multiple cranial and facial fractures, requiring neurosurgical intervention during the repair of facial and scalp lesions.

The most common site of canine head attacks in children was the zygomatic region. Other studies point to the lip or ear as the most frequent site but those are series that also involve adults[2,15].

The antibiotics of choice after bites on the face and scalp is amoxicillin with clavulanic acid or cephalexin (1st generation cephalosporin). The use of the culture to choose the antibiotic is only done in cases where the infection is already established, streptococci and staphylococci being the most frequent germs[7]. In canine attacks, prophylaxis of tetanus and rabies are mandatory[16].

The primary treatment of bites was by means of direct suture, grafting or local flaps, depending on the type of wound and the surgeon's decision, regardless of the time elapsed from the attack. It is important to properly debride the wound and minimize the use of deep or subdermal sutures. Whenever possible, sutured wounds are managed without closed dressing[13]. Direct suture was the treatment of choice in most patients, but in cases of avulsion of part of the scalp, the avulsed segment was grafted (Figure 4). Subsequently, after integration of the graft, the surgeon can initiate the expansion of the remaining scalp to cover the graft alopecia area.

Primary suture of lesions have advantages over delayed closure. Open lesions require daily dressings and high doses of analgesics during and after dressings changing. These disadvantages are avoided by immediate surgical repair, and the aesthetic damage is handled[13,17-19].

Post-bite recommendations, with or without surgical treatment, should include a description for patients and their caregivers of signs and symptoms of infection, indicating immediate reassessment in the event of such signs. Except for trivial cases, all victims of bites should be re-evaluated within 48 hours[3].

Wound infection is the most common complication after bites. The probability of infection is influenced by several factors, such as the aggressor animal, the location of the wound, factors inherent to the individual, the characteristics of the lesions and the time elapsed until medical care[2].

The etiological agents most frequently isolated from infected bite wounds are those of the oral flora of the offending animal or the victim's skin. In canine bites, the most isolated aerobic microorganisms are staphylococci, *Pasteurella spp*. (Mainly *P. canis* and *Pasteurella multocida*), streptococci, *Neisseria spp*. and *Corynebacterium spp*. Among the anaerobes, Fusobacterium, Porphyromonas, Prevotella, Propionibacterium, Bacteroides and Peptostreptococus stand out.

Punctate bites, hand bites, human bites, lesions longer than eight hours and wounds in immunocompromised patients (patients with diabetes mellitus or systemic lupus erythematosus, chronic renal failure, splenectomy, prolonged us e of corticosteroids) are at increased risk of infection. Considering that the study cases involved only canine bites in immunocompetent patients, these factors may have contributed to the non-existence of infection in the analyzed population. In addition, bites on the face and scalp have a lower chance of infection than elsewhere in the body due to the rich vascularization and postural drainage of this body segment[20].

In minor infected wounds, oral amoxicillin with clavulanate ensures excellent coverage for infected bites by dogs, cats or humans. In cases of allergy to penicillin, clindamycin may be used. In more sever infections, the treatment should be intravenous, with the use of ampicillin with sulbactan. In cases of infection with methicillin- or oxacillin-resistant S. aureus (MRSA or ORSA), the association with vancomycin is recommended[3].

There have been reports of disseminated infections, septic shock, meningitis and endocarditis after bites by dogs and cats. The etiological agents most involved in these types of infectious complications are *Capnocytophaga canimorsus* and *Pasterurella multocida*[21].

One should give special attention to sepsis by *Capnocytophaga canimorsus* in cases of febrile illness after canine bites, especially in patients with prior splenectomy or chronic alcoholism. Cases of severe systemic infections are more common after bites on the hands or fingers, and rarely after bites on the head[21-23].

Our work demonstrates that face and scalp lesions produced by canine bites can be repaired primarily. With this approach, a better aesthetic result is achieved with minimal or no risk of infection, reducing subsequent surgical procedures and improving morbidity. The primary closure of these lesions can be done through direct suture, local flap rotation or grafting, depending on the type of wound and the surgeon's decision.

R E S U M O

Objetivo: avaliar a conduta de reconstrução imediata de face e couro cabeludo após mordedura canina em crianças. **Métodos:** série prospectiva de casos atendidos na Unidade de Emergência do Hospital Regional da Asa Norte, Brasília/DF, no período de janeiro de 1999 até dezembro de 2014. No momento da admissão do paciente à emergência, foi realizado o fechamento primário da ferida proveniente de mordedura em face e couro cabeludo, independente da hora ou dia da agressão. O tratamento primário das mordeduras foi realizado por meio de sutura direta, retalhos ou enxerto, conforme o tipo da ferida e da decisão do cirurgião. **Resultados:** o estudo compreendeu 146 crianças, sendo que a região zigomática e o couro cabeludo foram os principais sítios das mordeduras na cabeça. Todos os pacientes receberam tratamento cirúrgico dentro das primeiras 24 horas após a admissão. Não houve complicações infecciosas nos casos estudados. **Conclusão:** os achados sugerem que o fechamento imediato das mordeduras caninas em face e couro cabeludo em crianças é seguro, mesmo quando realizado várias horas após a lesão.

Descritores: Face. Couro Cabeludo. Mordeduras e Picadas. Cães. Criança. Procedimentos Cirúrgicos Reconstrutivos.

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Evaluation of care for traffic accidents victims made by on duty emergency physicians and surgeons in the emergency room

Avaliação do atendimento às vítimas de acidentes de trânsito por plantonista clínico e cirurgião na sala de emergência hospitalar

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A B S T R A C T

Objective*: to evaluate the care for victims of traffic accidents by on call emergency physicians and/or surgeons in the emergency room.* **Methods***: we conducted a retrospective, descriptive and exploratory study on the care for traffic accidents victims in the urban area of Maringá-PR, between July 2013 and July 2014 in reference hospitals. We assessed demographics and vocational training through a questionnaire sent to the attending physicians.* **Results***: of the 688 records evaluated, 99% of patients had a prehospital Revised Trauma Score of 12. Statistical analysis showed that in the cases conducted by the emergency physicians (n=187), the recording of the Glasgow Coma Scale and the performance of surgical procedures were less common, whereas the recording of blood pressure values was performed in greater numbers when compared with cases led by surgeons (n=501). There was a statistically significant relationship (p<0.01) between the length of hospital stay and surgical specialty, with a greater chance (crude OR=28) in the period from one to six hours for the group treated by emergency doctors. Most physicians participating in the study were young, with emergency room time of up to one to two years, and with ATLS training. Among those who had attended the ATLS course, 60% did so in the last four years. Surgeons performed 73% of hospital treatments.* **Conclusion***: in the care of traffic victims with minor injuries, the Glasgow Coma Scale, the blood pressure levels, the type of treatment in the emergency room and hospital stay had different approaches between emergency physicians and surgeons.*

Keywords: *Accidents, Traffic. General Practitioners. Surgeons. Emergency Medical Services. Evaluation of Research Programs and Tools.*

INTRODUCTION

In recent years, Trauma has become one of the biggest public health problems[1]. In cases of traffic accidents (TA), thousands of lives are compromised each year, making constant the need for discussion, prevention planning and treatment of these victims[2,3].

In pre-hospital care provided by the Emergency Trauma Care Integrated Service (SIATE) of the Fire Department, triage and classification of victims are carried out according to the degree of severity, followed by primary care for stabilization of the urgency or emergency condition and later referral to a more complex service for the continuity of treatment[4].

In Brazil, not all hospital services have qualified professionals for the care of multiple trauma. Any doctor who has professional license can act as an emergency physician[5]. The Resolution 2077/14 of the Federal Medicine Council (CFM) deals with the regulation of the Emergency Hospital, as well as with the design of the medical team and the work system. Its Art. 3rd defines the obligation of care be performed by a doctor, though with no reference as to specialty[6]. In practice, it is observed that the "emergency room" doctor is specializes in internal medicine or general surgery, and should have appropriate skills and knowledge to work in the emergency room. However, the CFM Resolution nº 2149/2016 of July 22, 2016, approves the recognition of Emergency Medicine as a medical specialty, and Emergency Medicine as a Medical Practice Area[6]. These new well trained specialists may make a difference with appropriate and safe decisions when acting in emergency settings[7].

The difference of the specialized training and personality between the internal medicine physician and the surgeon is historical. Bellodi[8] noted that even today, the stereotypes of these doctors are equivalent,

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despite all the changes over time. To clinicians, formerly physicists, the appreciation of the mind, and to surgeons, the barbers, the risky procedures[8,9]. In another study with a group of Brazilian residents, the same author identified, amongst other variables, personality traits, the clinicians being quieter, detail-driven and more interested in interpersonal contact, while the surgeons are faster, more impulsive and more aggressive[10].

It is possible that this type of aggressive and impulsive personality is a decisive factor in choosing training courses that enable the surgeon to care for polytrauma patients. This formation goal tends to make this professional the most suitable and most qualified for this type of service, differentiating him/her from those with other interests.

Considering the studies showing different personality characteristics between clinicians and surgeon as a factor for specific training, it is fair to raise the following issue: "Is there a difference in trauma care provided by the emergency physician and the surgeon?". So far, there are no references in the literature comparing the polytrauma patient approach with the kind of specialty of the emergency room doctor.

The objectives of this study were to evaluate the care of victims of traffic accidents by emergency physicians and / or surgeons in the emergency room and to identify the emergency training of such doctors.

METHODS

We conducted an observational, documental, retrospective, descriptive and exploratory study, with traffic accident (TA) victims in urban areas, over 18 years of age, of both gender, attended by the prehospital rescue team – SIATE – in Maringa, PR, and sent to reference hospitals in the period from July 2013 to July 2014.

We obtained data from the site www.bombeiroscascavel.com.br, collecting the records made by Maringa Fire Department V Division, containing the name, day, time and type of event and the destination hospital. With this list, we then obtained the hospital records of patients and Rescue Attendance Reports (RAR).

The variables analyzed in this study were: type of medical specialty of the professional who attended the victim, recording of Glasgow Coma Scale (GCS) and of levels of Systemic Blood Pressure (SBP), procedures carried out by the professional and hospital stay.

As non-surgical procedures, we considered analgesia, clinical observation, neurological observation and sole evaluation; and as surgical procedures, analgesia + dressing, analgesia + immobilization, dressing, immobilization and suture.

We applied a questionnaire to doctors working at the emergency rooms to characterize the professionals as for demographic variables, professional training and difficulties in trauma patient care.

We ordered data in spreadsheets (Microsoft Excel for Mac 2011 Version 14.6.0) and analyzed them in a descriptive way through absolute numbers and percentages. We applied the chi-square test, uni and multivariate analysis with the software SAS 9.4, considering $p \leq 0.05$ as significant.

This study was approved by the Standing Committee on Human Research of the State University of Maringa (COPEP-UEM), opinion № 37686114.8.0000.0.

RESULTS

During the study period, 45 physicians (17 clinicians and 28 surgeons) were responsible for the care of 688 TA victims (177 attendances by emergency physicians and 501 by surgeons).

According to univariate analysis, there were statistically significant differences between variables related to medical specialty. The results are shown in Table 1.

GCS values were recorded in 345 evaluations made by surgeons and in 56 cases treated by clinicians. In 287 records, GCS recording was absent. The chance of a clinician not recording the GCS was 5.2 times higher than the surgeon's.

SBP values were recorded in 137 evaluations made by surgeons and in 129 by clinicians, lacking in 422 charts. The chance of a clinician recording SBP was six times higher than the surgeon's.

Hospital stay greater than six hours occurred in 10% (n=69) of treated cases; 99% of these visits were performed by surgeons. The chance of a clinician discharging a patient before six hours of observation was 28 times greater than the surgeon's.

Regarding the type of treatment provided in the emergency room, in 75% (n=515) of cases "nonsurgical" procedures were performed. The chance of a clinician performing a non-surgical procedure was 1.7 times greater than the surgeon's.

We also applied multivariate analysis and found a statistical correlation between variables, whose results are shown in Table 2.

As for the length of stay and type of treatment, we observed that these were not associated factors (Table 3).

Only 40% (n=18) of physicians responded to the questionnaire, identifying some features shown in Table 4. The profile found in this study were of young doctors, mostly male and Surgeons, 61% with ER time less than four years and with ATLS training. Of these, 60% had taken the course less than four years before.

DISCUSSION

There is no legal requirement in Brazil for the doctor attending the emergency room to be from a clinical or surgical specialty. In this sample, there was a contingent of surgeons greater than clinicians.

In the 688 patient records analyzed, we observed that surgeons have made 501 evaluations and proportionately more surgical procedures than clinicians have. This fact could be justified by the victim having lesions that justify the procedure or by the greater predisposition toward this conduct by the characteristics of the surgeon, such as impulsiveness, quick thinking and aggressiveness in conducts[11]. Surgeons tend to be more practical, objective and like manual activities, often with faster and more concrete results[10].

From a clinical point of view, the GCS score is an important neurological parameter and practically a synonym of gravity in head trauma (TBI). Scores between 3 and 8 are classified as severe trauma, between 9 and 12 as moderate and between 13 to 15 as mild[11].

In a study of patients rescued by emergency mobile care service, Souza[12] reported that despite its importance, GCS was neglected many times, reporting abstention to record this value in 3.2% of cases. Ribeiro[13] identified charts without its records in 897 cases (97% of total) when filled by nurses prehospital, though with no references to notes in hospital care.

In this study, surgeons recorded GCS values in patients' charts at hospital admission more frequently than clinicians did (69% versus 30%, respectively). The vast majority of victims assisted (400 – 58%) had scores between 13 and 15, and only one case presented score of 3. In 42% (n=287) this record was missing, and in some reviewed charts there was a description by the doctor that the victim was conscious, oriented and without motor deficits, inferring a high value for GCS; however, having not been registered, we did not consider it as recorded. This condition could explain the 42% of absence of GCS records in this sample.

In contrast, in cases reported in medical records (n=401), 86% were by surgeons, while only 14% by emergency physicians. The ATLS advocates the use of the GCS as an objective clinical measure of TBI severity, becoming routine to the doctor in polytrauma care, even in those

patients without TBI[10]. This finding is important for the proper evaluation of trauma patients in view of the possibility of unnoticed injuries evolving to a neurosurgical emergency[14].

Alavarce *et al*.[15] found that the SBP measure, besides being simple and easy to execute, should be carried out in all health care evaluations, independently of the attending physician specialty. In this study, we observed that surgeons recorded SBP values at hospital admission fewer times than clinicians did (27% versus 69%). A previous study found SBP recording in 85.3% of cases evaluated, differing from the latter because only 39% (n=266) of cases were recorded at admission, however, according to pre-hospital care data, SBP was recorded in 97% of case[16].

SBP levels are an important physiological parameter in the evaluation of polytrauma patients, depending on the types of injuries found, translating volume loss (bleeding). Although not reflecting the actual state of tissue perfusion, its systematic measurement is advocated[17]. The estimated blood loss based on the initial condition of patients with multisystem trauma can be classified into classes (I, II, III and IV). Each has signs and symptoms according to the degree of volume loss. Classes I and II comprise an approximate blood loss of up to 15% (volume = 750ml) and between 15 and 20% (volume = 750 to 1500ml), respectively. On physical examination, one does not observe a drop in SBP levels in these two classes. This fall will be identified in shock, i.e., classes III and IV[11,18].

In this study, most patients were victims of minor injuries and t-RTS 12 (corrected RTS 7.8408), with no evidence of hemorrhagic shock (mean systolic SBP 127mmHg), both in the prehospital assessment and at arrival at the emergency room. This could justify the lack of importance given by the surgeon to the measurement of blood pressure at that time and consequently to its recording.

Regarding the length of stay, we found that 621 patients (90.3%) remained for a time shorter or equal to six hours, and the majority (n=435) was attended by surgeons. We observed a greater chance of an emergency physician releasing the patient before six hours of observation. The relevance of this finding (OR=28) did not translate into better type of service or professional negligence. The result in question might be justified by the clinical picture and type of injury presented by the patient (t-RTS 12 and CODE 1 SIATE) opposing the medical specialty.

Vieira *et al*.[19], in a study conducted in Sergipe, showed that 76% of victims treated had length of stay of up to 12 hours. In another study conducted in Ribeirão Preto, Coelho *et al*.[20] reported that 39.8% of patients remained for less than six hours and 27.4%, between 24 and 30 hours, with no mention to the type of specialty.

Statistical analysis showed that there was an association between length of stay and surgical specialty (Tables 1 and 2). However, when related to the type of treatment, there was no statistical association, that is, the chance of an emergency

Table 1. *Univariate logistic regression model of variables related to medical specialty.*

Variable	Categories	Surgeons n=501 (73%)	Clinicians n=187 (37%)	Gross OR	95% CI	p-value
Glasgow Coma scale	Not recorded Recorded	156 345	131 056	5.2 1	[3.589; 7.452]	< 0.001
Systemic Blood Pressure	Not recorded Recorded	364 137	058 129	1 6	[4,098; 8.547]	< 0.001
Type of treatment	Non-surgical Surgical	362 139	153 34	1.7 1	[1.135; 2.630]	0.0107

OR: odds-ratio. CI: confidence interval. p-value: Chi-square test of Mantel-Haenszel.

Table 2. *Multivariate logistic regression model of the variables related to clinical specialty.*

Variable	Adjusted OR	95% CI	p-value
GCS recording	7.509	[4.818; 11.702]	< 0.001
SBP recording	8.33	[5.347; 12.987]	< 0.001
< 6-hour hospital stay	15.969	[2.102; 121.30]	0.0074
Type of treatment: non-surgical	1.696	[1.035; 2.781]	0.0107

Or: odds-ratio. CI: confidence interval. p value: Chi-square test of Mantel-Haenszel. GCS= Glasgow Coma scale. SBP= Systemic Blood Pressure.

physician performing a non-surgical procedure in hospital stays shorter than or equal to six hours was similar to a surgeon's (Table 3). Only 18% of care provided by clinicians needed surgical treatment in the emergency room, while for surgeons that number was 28%, which raised the suspicion of different complexity and time of stay, corroborating th significant finding (OR 28) mentioned above.

The results of the questionnaire applied to attending physicians (Table 3) showed that 89% of respondents were male, aged between 25 and 60 years and had surgical specialty. Most (50%) had time of ER over three years, and 39% of respondents had had ATLS training less than one year before.

Campos and Senger[21] reported that 31.7% of graduates worked in emergency services independently of being enrolled or not in some medical residency program. The easy insertion in these services pointed out the importance of proper training for care in this type of situation. Hamamoto[22] and Pego-Fernandes[23] reported the unpreparedness of recent graduates and the disorganization of the health care system, which hampers emergency care in public hospitals.

Still on ATLS, 81% of surgeons attended this training, while for the emergency physicians this percentage was 50%. This result suggests the initial hypothesis of this work, that surgeons are more interested in training for trauma care due to their training background and personality. Brito *et al*.[24] stated that training is of utmost importance for the improvement of professional performance, both individually and as a team, which corroborates the pressing need of the professional, regardless of specialty, to train in the respective field, besides making the professional feel more secure and able to provide adequate care[25].

For 13 (72%) physicians, technical training was considered sufficient, and 89% reported feeling safe in the diagnosis and treatment of multiple trauma victims. However, 89% of respondents said trauma care requires specialized training. This need of respondents goes against the principle of the impact of ATLS training for trauma care, which says that students may retain the course techniques and procedures for at least six years. According to the ATLS, this is the most significant impact of all[11]. All 18 respondents consider care protocols o be extremely important in the service.

Not all doctors who were part of the clinical staff of the emergency service in the hospitals

Table 3. *Correlation as to the type of treatment and length of stay.*

	Type of treatment			
Lenght of stay	Non-surgical	Surgical	Gross OR	95% CI
≤ 6h	467	154	1	
> 6h	48	19	1.2004	[0.6846; 2.1048]

Or: odds-ratio. CI: confidence interval. p-value: Chi-square test of Mantel-Haenszel.

Table 4 – *questionnaire variables applied to physicians (n = 18)*

Variables	Categories	Frequency	
		n	(%)
Gender	Male	16	89
	Female	02	11
Age	25-30	09	50
	31-40	05	28
	41-50	01	05
	51-60	03	17
Specialty	Surgical	16	89
	Clinical	02	11
Time in emergency room	< 1 year	0	0
	1 to 2 years	06	33
	2 to 3 years	03	17
	3 to 4 years	02	11
	> 4 years	07	39
Time since ATLS attendance	not held	04	22
	< 1 year	07	39
	1 to 2 years	02	11
	2 to 3 years	01	05
	3 to 4 years	01	05
	> 4 years	03	17
Technical training believed to be:	Enough	13	72
	Insufficient	04	22
	Didn't say	01	06
Security in the diagnosis of "imminent risk of life" in a trauma victim	No	0	0
	Yes	18	100
Security to perform necessary medical procedures to treat a trauma victim	No	02	11
	Yes	16	89
Believe one need specialized training for trauma care	No	02	11
	Yes	16	89
Believe protocols for trauma care are necessary	No	0	0
	Yes	18	100

ATLS: Advanced Trauma Life Support.

studied answered the questionnaire, only 51% (n=18) returning. This made it difficult the analysis of some variables. However, the results showed the need to implement care protocols at the hospital level for multiple trauma patients and to encourage the training of medical professionals involved in this type of care

Data from this study indicated a significant difference in care of trauma victims between clinical and surgical specialists. We did not assess the quality of care, but the focal differences in trauma care priorities. This result raises a reflection and discussion about a pressing need now, that is, the figure of the expert in emergency care in the Emergency Units. Differences in medical care provided to victims of trauma depending on the medical specialty are unacceptable. However, the training, even in renowned courses, does not prepare the professional the same way a medical

residency in the area does. This conclusion is explained in the speech of professionals when they say they feel secure as to their capacity to diagnose and treat multiple trauma victims, but at the same time, they claim to need specialized training in trauma care. It is essential that the competent bodies and associations establish policies that allow emergency healthcare institutions to hire medical experts in the field. This would ensure a safe care, for both the patients who are attended by skilled professionals, and for the professionals who, due to their training, perform the activities with confidence, dynamism and efficiency.

R E S U M O

Objetivo: avaliar o atendimento às vítimas de acidentes de trânsito por médicos plantonistas cirurgiões e/ou clínicos na sala de emergência hospitalar. **Métodos**: estudo retrospectivo, descritivo e exploratório do atendimento às vítimas de acidentes de trânsito da área urbana de Maringá-PR, entre julho de 2013 e julho de 2014, em hospitais referenciados. Questionário aplicado aos médicos plantonistas avaliou dados demográficos e a formação profissional. **Resultados**: dos 688 prontuários avaliados, 99% apresentavam *Revised Trauma Score* pré-hospitalar de 12. Análise estatística mostrou que nos atendimentos feitos por Clínicos (n=187), a anotação dos escores da Escala de Coma de Glasgow e a realização de procedimentos cirúrgicos foram feitas em menor número e, em contrapartida, a anotação dos valores de pressão arterial sistêmica foi realizada em maior número quando comparados com atendimentos feitos por Cirurgiões (n=501). Houve relação estatisticamente significativa (p<0,01) entre o tempo de permanência hospitalar e a especialidade cirúrgica, com maior chance (OR bruta=28) observada no período de uma a seis horas para o grupo atendido pelos Clínicos. A maioria dos plantonistas que participaram do estudo eram jovens, com tempo de atividade em sala de emergência hospitalar de um a dois anos e com capacitação no curso do ATLS. Entre os que participaram do curso do ATLS, 60% o fizeram nos últimos quatro anos. Cirurgiões realizaram 73% dos atendimentos hospitalares. **Conclusão**: nos atendimentos às vítimas de trânsito com lesões leves, a Escala de Coma de Glasgow, os níveis de pressão arterial sistêmica, o tipo de tratamento na sala de emergência e o tempo de internação hospitalar tiveram abordagens diferentes entre Clínicos e Cirurgiões.

Descritores: Acidentes de Trânsito. Clínicos Gerais. Cirurgiões. Serviços Médicos de Emergência. Avaliação de Programas e Instrumentos de Pesquisa.

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Keratocystic odontogenic tumor

Tumor odontogênico ceratocístico

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A B S T R A C T

Objective: *to evaluate the frequency of keratocystic odontogenic tumor (KOT) in the Oral Surgery Service (OSS) of the University Hospital Clementino Fraga Filho of the Federal University of Rio de Janeiro (HUCFF / UFRJ), with respect to recurrence rate, gender, age of recurrence and location of the injury.* **Methods**: *clinical records were reviewed and histopathological reports of KOT patients of the HUCFF/UFRJ between 2002 and 2012. Patients diagnosed with KOT were divided into two groups for the occurrence of relapse: positive (n=6) and negative (n=19).* **Results**: *regarding the location, there was a predilection for the mandible. In the average age of patients in the positive group was 40.5 and the negative group, 35.53. In the distribution by gender, positive group showed equal distribution, different from that observed in the negative group, which showed a predilection for males.* **Conclusion**: *KOT was the second most frequent injury in our patients, recurrence was lower among males and had the jaw as most affected location*

Keywords: *Odontogenic Tumors. Recurrence. Diagnosis, Differential.*

INTRODUCTION

Odontogenic tumors are neoplasias that develop exclusively in the gnatic bones, originating from odontogenic tissues by proliferation of epithelial tissue, mesenchymal one, or both. The term keratocyst odontogenic (KO) was introduced by Philipsen, in 1956, and referred to any maxillarycyst that presented keratin formation[1,2]. In 1962, the histological criteria and the specific clinical behavior were established for this lesion, which was different from the other jaw cysts[2,3]. The last World Health Organization (WHO) classification of odontogenic tumors called odontogenic keratocyst a keratocystic odontogenic tumor, based on the presence of genetic and molecular alterations, which would also be present in some neoplasias[4]. Despite this change in the KOclassification, Neville *et al*.[4] and Regezi *et al*.[5] continued to classify this lesion as an odontogenic cyst.

The keratocystic odontogenic tumor is an injury that requires special considerations because of its aggressive appearance and its potential for recurrence and malignization. It has slow and painless growth. There are twotheories for its development: the first from remnants of the dental lamina and the other from the proliferation of cells of the basal layer of the oral epithelium of the mandible and maxilla[3,6].

In the literature, there are few published studies that evaluate and correlate the presence or absence of recurrence among cases diagnosed as KOT with age, gender and location of the odontogenic lesion.

The objective of the present study was to evaluate the frequency of keratocystic odontogenic tumors in the Oral Surgery Service (SCO) of the Clementino Fraga Filho University Hospital, Federal University of Rio de Janeiro (HUCFF/UFRJ), regarding recurrence rate, gender, age of recurrence and lesion location.

METHODS

We conducted a retrospective study of data obtained from clinical records of the HUCFF/UFRJ Oral Surgery Service patients and histopathological reports issued by the HUCFF/UFRJ Pathological Anatomy Service from 2002 to 2012. The study included complete patient information on age, lesion location, gender, recurrence end treatmentemployed, besides the diagnosis of the lesions by histopathology according to the classification of the World Health Organization

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(WHO, 2005). The exclusion criterion was the absence of three or more relevant data in the medical record.

We tabulated the data in a database and analyzed them descriptively with the SPSS 20.0 program.

Surgeries were performed at the hospital and, depending on the extent and locality of the lesion, local or general anesthesia was chosen. The treatment of choice was curettage enucleation of the cyst. In cases of relapse, a second surgery was performed to remove the remaining lesion.

This work was approved by the Ethics in Research Committee (CEP) of HUCFF/UFRJ under opinion No. 993,649.

RESULTS

There were 96 cases of odontogenic lesions. Of these, 25 (26.04%) were diagnosed as KOT, these being more frequent in the age range of 10-20 years. Other observed odontogenic lesions thatare differential diagnosis with KOT were: ameloblastoma, dentigerous cyst, radicular cyst, central giant cell granuloma, traumatic bone cyst, Gorlin's cyst, residual cyst and odontogenic myxoma.

Of the total number of patients with KOT, 24% presented recurrence. Among those who relapsed, the predominant age group was from 41 to 50 years. Weassessed the relationship between age and relapse (Figure 1) with the Mann Whitney test, which did not reveal statistical significance (p>0.05). The age distribution of patients with odontogenic keratocysts can be seen in Table 1.

The patients'mean age in the positive group was 40.5, and in the negative, 35.53. In the positive group, the minimum age was 17 years and the maximum, 55. In the negative relapse group, the minimum age was 13 years and the maximum, 96 (Table 1).

The positive group had an equal gender distribution, differently from the negative group, which presented a male preference (Table 2). However, the assessment of relapse in relation to gender, which we performed through the Fisher's exact test, was not statistically significant (p>0.05).

As for location, there was predilection for the mandible, with 56% of the cases negative for relapse; Among the relapsingcases, the mandible was also the most frequent location (Table 3).

Table 1. *Average, median, standard deviation, minimum and maximum age between groups.*

Recurrence		Age	Gender	Location
Negative N	Valid	19	19	19
	Lost	0	0	0
	Average	35.53		
	Median	26.00		
	Standard deviation	22.267		
	Minimal	13		
	Maximum	96		
Positive N	Valid	6	6	6
	Lost	0	0	0
	Average	40.50		
	Median	46.00		
	Standard deviation	14.181		
	Minimal	17		
	Maximum	55		

Table 2. *Distribution of patients by gender between groups.*

			Recurrence		Total
			Negative	Positive	
Gender	Female		7	3	10
		% within gender	70.0%	30.0%	100.0%
		% within recurrence	36.8%	50.0%	40.0%
		% of total	28.0%	12.0%	40.0%
	Male		12	3	15
		% within gender	80.0%	20.0%	100.0%
		% within recurrence	63.2%	50.0%	60.0%
		% of total	48.0%	12.0%	60.0%
Total			19	6	25
		% within gender	76.0%	24.0%	100.0%
		% within recurrence	100.0%	100.0%	100.0%
		% of total	76.0%	24.0%	100.0%

DISCUSSION

The keratocystic odontogenic tumor is a maxillary odontogenic lesion of epithelial development, affecting mainly the maxilla and the mandible. Few published studies evaluated KOT regarding gender, age and location in a given region or country based on the 2005 WHO classification[7-12]. In our study, KOT was the second most common lesion, differing from the studies by Chrysomali *et al*.[13] and Johnson *et al*.[14], in which KOT was more prevalent.

In the present study of the 96 cases, KOT represented 26.04% of them, presenting a higher frequency when compared with the epidemiological data described by Meningaud *et al*.[12], who analyzed 695 cases diagnosed as odontogenic cysts and observed odontogenic keratocysts in 19,1%. Siriwardena *et al*.[15] investigated the frequency of odontogenic tumors in a given population in Sri Lanka, showing a KOT incidence of 25.7%. Tawfik *et al*.[16] reported an incidence of 19.5%.

In 2012, Servato *et al*.[17] reported the cases diagnosed at the Federal University of Uberlândia, Brazil, and described KOT as one of the most frequent odontogenic tumors, with a rate of 31.7%. Luo *et al*.[18] reported 1309 cases between 1985 and 2006, and Avelar *et al*.[19] observed a higher frequency of KOT than in the present study; the two rates were, respectively, 38.73% and 30%.

Chirapathomsakul *et al*.[8] analyzed KOT recurrence and observed seven recurrences (22.6%) in their study, which corroborates the data seen in the present study, in which six cases recurred (24%); Of these, 50% appeared in the age group of 41 to 50 years. Madras and Lapointe *et al*.[7] studied 21 KOT patients, and the proportion of recurrence of these lesions was 29%. Regezi *et al*.[5] reported a recurrence rate of 10 to 30%. This explains the importance of the patient's prolonged clinical and radiographic follow-up after removal of the odontogenic keratocystic tumor.

According to Katase *et al*.[20], KOT is a benign cystic neoplasm that may be associated with basal cell nevus carcinoma syndrome, characterized by multiple cystic lesions. Of the 25 cases of KOT considered in the present study, one case had the described syndrome. Ramaglia *et al*.[21] reported um case of an eight-year-old girl affected by basal cell nevus carcinoma syndrome and Habibi *et al*.[10] reported 8.1% of bearers of this syndrome.

Table 3. *Anatomical location of the KOT between groups.*

			Recurrence		Total
			Negative	Positive	
Location	Mandible		14	4	18
		% within gender	77.8%	22.2%	100.0%
		% within recurrence	73.7%	66.7%	72.0%
		% of total	56.0%	16.0%	72.0%
	Mandible and maxilla		0	1	1
		% within gender	0.0%	100.0%	100.0%
		% within recurrence	0.0%	16.7%	4.0%
		% of total	0.0%	4.0%	4.0%
	Maxilla		2	1	1
		% within gender	66.7%	33.3%	100.0%
		% within recurrence	10.5%	16.7%	12.0%
		% of total	8.0%	4.0%	12.0%
	Unspecified		2	0	2
		% within gender	100.0%	0.0%	100.0%
		% within recurrence	10.5%	0.0%	8.0%
		% of total	8.0%	0.0%	8.0%
	Maxillary Sinus		1	0	1
		% within gender	100.0%	0.0%	100.0%
		% within recurrence	5.3%	0.0%	4.0%
		% of total	4.0%	0.0%	4.0%
	Total		19	6	25
		% within gender	76.0%	24.0%	100.0%
		% within recurrence	100.0%	100.0%	100.0%
		% of total	76.0%	24.0%	100.0%

According to Lopes *et al*.[6], KOT is a differential diagnosis of odontogenic cysts or tumors, such as ameloblastoma, giant cell central granuloma, dentigerous cyst, adenomatoid odontogenic tumor, ameloblastic fibroma, traumatic bone cyst, central giant cell granuloma, lateral periodontal cyst and Gorlin's cyst. Regezi *et al*.[5] point out, as odontogenic lesions that are KOT's differential diagnosis, dentigerous cyst, ameloblastoma, odontogenic myxoma, adenomatoid odontogenic tumor and ameloblastic fibroma. Neville *et al*.[4] emphasize that the absence of KO bone expansion helps the differential diagnosis with root cyst and dentigerous cyst. In the present study, the differential diagnosis of KOT were: ameloblastoma, dentigerous cyst, radicular cyst, central giant cell granuloma, traumatic bone cyst, Gorlin's cyst, residual cyst and odontogenic myxoma, which corroborates the literature's findings.

The mandible is the most frequent site of odontogenic keratocyst[1,4,7,9,10,11,13,22-24]. According to Neville *et al*.[4], the mandible is affected in 60% or 80% of cases.

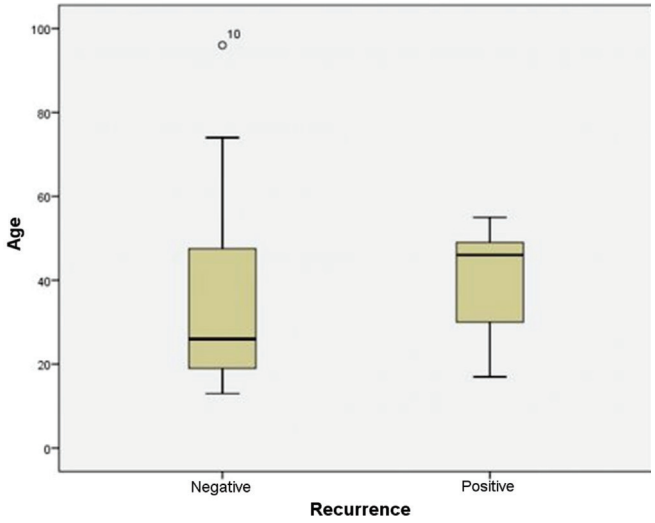

Figure 1. *Age of patients according recurring or non recurring KOT.*

The present study confirms the data from the literature. Among the cases studied, a simultaneous occurrence was found in the maxilla and mandible, as reported by Auluck *et al*.[25]. In the present study there was a case in which the KOT was present in the maxillary sinus.

Our study showed that KOT was more frequent in males. This is similar to that reported in other studies[1,4,11,13,15,16,22]. Avelar *et al*.[19] and Mallman *et al*.[11] contradict the literature data, presenting a higher frequency in the female gender.

The mean age was 36.72, higher than that observed in two previous studies, by Habibi *et al*.[10] and Avelar *et al*.[19]. Chirapathomsakul *et al*.[8] showed that the most frequent age group is 11-40 years. The current study found that the age group with the highest occurrence of KOT was 10-20 years, which is confirmed by other papers[11,13,17]. Sekerci *et al*.[2] observed a higher frequency of KOT in the age group between 20 and 29 years.

Madras and Lapointe[7] performed more aggressive treatment in 21 patients with KOT, with resection or enucleation complemented with Carnoy's solution, with or without peripheral ostectomy. Regezi *et al*.[5], on their turn, cited enucleation with peripheral bone curettage or ostectomy as a preferred management method. Habibi *et al*.[10] demonstrated that marsupialization followed by enucleation was more efficient, with no recurrences. The treatment performed in the cases of the present study was enucleation with cyst curettage.

Our results and the literature review expose the need for new scientific work on KOT and its characteristics, which we consider to be of utmost importance for the institution of the most adequate treatment to minimize recurrence of this odontogenic lesion.

R E S U M O

Objetivo: avaliar a frequência do tumor odontogênico ceratocístico (TOC) no Serviço de Cirurgia Oral (SCO) do Hospital Universitário Clementino Fraga Filho da Universidade Federal do Rio de Janeiro (HUCFF/UFRJ), no que diz respeito à taxa de recidiva, ao sexo, à idade de recorrência e à localização da lesão. **Métodos**: foram examinados os prontuários clínicos e laudos histopatológicos de pacientes do SCO do HUCFF/UFRJ no período de 2002 a 2012. Os pacientes diagnosticados com TOC foram divididos em dois grupos quanto à ocorrência de recidiva: positivo (n=6) e negativo (n=19). **Resultados:** com relação à localização, houve predileção pela mandíbula. Em relação à média de idade dos pacientes, no grupo positivo foi 40,5, e no grupo negativo, de 35,53. Na distribuição por sexo, o grupo positivo apresentou distribuição igualitária, diferentemente do observado no grupo negativo, em que predominou o sexo masculino. **Conclusões**: o TOC representou a segunda lesão mais frequente em nossos pacientes, tem menor recidiva no sexo masculino e tem a mandíbula como localização mais acometida.

Descritores: Tumores Odontogênicos. Recidiva. Diagnóstico Diferencial.

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Treatment of frontal bone fracture sequelae through inversion of the bone fragment

Inversão do segmento fraturado para tratamento das sequelas de fratura do seio frontal

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ABSTRACT

Treatment of frontal sinus fractures depends on the structures involved: the anterior wall, the posterior wall and the nasofrontal duct. It may vary from the correction of the defect in the anterior wall to the cranialization with obliteration of the nasofrontal duct. The inversion of the frontal sinus's anterior wall to correct the defect in the fractured region is a good treatment option for sequelae, since this technique eliminates or reduces the use of biomaterial in the area, and allows direct assessment of the permeability of the nasofrontal duct. This work describes the technique of fractured segment inversion for the treatment of frontal sinus fracture sequelae in a motorcycle accident victim.

Keywords: *Frontal Bone. Fracture Fixation. Craniocerebral Trauma.*

INTRODUCTION

The frontal sinus is a pneumatized cavity internally lined with epithelium of the ciliated respiratory tract, located between the internal and external tables of the frontal bone, maintaining close relation with other sinuses of the face, orbit ceiling, and anterior cranial fossa[1]. The anatomical characteristics of the frontal bone render it resistant to fractures, requiring trauma with high energy dissipation to occur, as in cases of auto accidents, which account for 52% of frontal bone fractures[1-4].

Frontal sinus fractures represent 2 to 15% of the maxillofacial trauma, and may be associated with other fractures of the middle third of the face, such as maxilla, zygomatic and naso-orbito-ethmoidal (NOE)[1,5-7]. Many classifications have been proposed in the literature to help manage such lesions, but most authors rely on the anatomical location of the fracture, involvement of the anterior wall, of the posterior wall and of the nasofrontal duct, either alone or in association[2,8].

The treatment of frontal sinus fractures may range from a simple fixation of the anterior wall to a cranialization and obliteration of the nasofrontal duct, depending on anatomical location, bone comminution, degree of displacement, and presence of brain injury[3,5,9,10]. In cases where only the anterior wall is affected, the treatment varies from reduction and bone fixation, and correction with titanium meshes or with the use of biomaterials[2,3,7,8,11]. In cases of sequelae of the anterior wall fractures, the inversion of the fractured segment becomes an interesting option to correct the local depression. The external face of the fractured anterior wall presents with a concavity, while its internal face becomes convex. Reversing this fractured segment through an osteotomy can correct the depression caused by the fracture, eliminating or reducing the use of biomaterials for aesthetic contour, and allowing the evaluation of the functionality of the nasofrontal duct by direct access after osteotomy.

The objective of this work is to demonstrate the technique of fractured segment inversion for the treatment of frontal sinus fractures sequelae.

TECHNICAL NOTE

A male patient, 20 years old, presented to the buccomaxillofacial surgery department of the Nova

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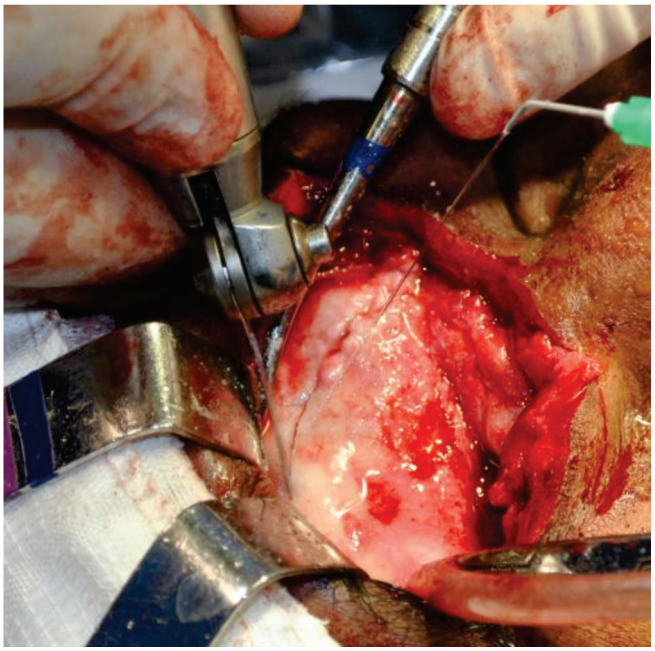

Figure 1 - *Exposure of the fractured bone segment in the frontal region.*

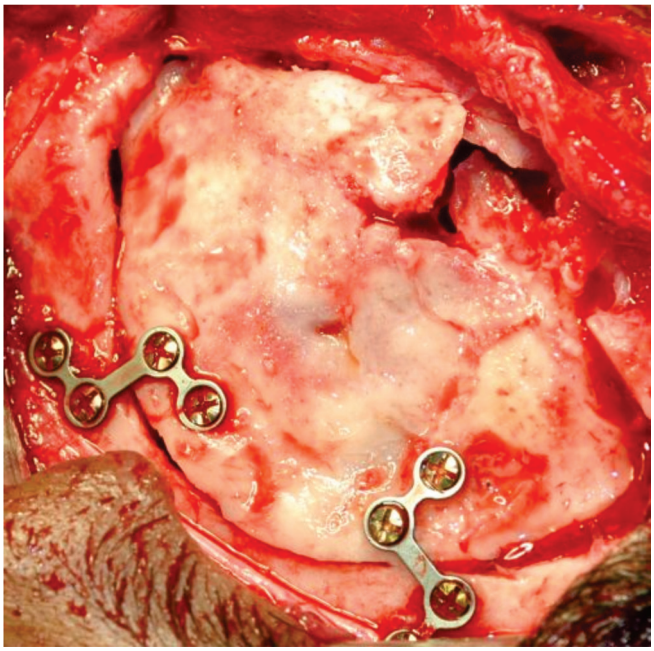

Figure 2 - *Bone segment repositioned after inversion and osteoplasty.*

Iguaçu General Hospital (Nova Iguaçu, Rio de Janeiro, Brazil), with a depression in the frontal bone region that occurred after a traffic accident 44 days before the consultation, while he drove a motorcycle without a helmet. The tomographic evaluation showed a displaced fracture of the frontal sinus anterior wall and a fracture of its posterior wall.

After 60 days of trauma, the patient underwent a surgical procedure under general anesthesia.

Surgical access in these cases can be performed by a pre-existing scar or by coronal access. After dissection of the anatomical planes, the bone segment is identified and evaluated as for the presence of areas of comminuted and not yet consolidated bone (Figure 1). The areas of comminution may fracture during osteotomy, which increases the need of biomaterial for correction of the defect.

We use an oscillatory saw under heavy irrigation with 0.9% saline for osteotomy of the fractured segment in a single piece. With the aid of periosteal detachers, the segment is carefully removed, providing direct access to the frontal sinus so that the nasofrontal duct permeability test can be performed if indicated.

We then invert the fractured segment, perform the osteoplasty and reposition the fragment with its internal face facing the external environment, providing the frontal sinus with its original anatomical shape and the availability to fix it with a system of 1.5-mm or 1.2-mm miniplates (Figure 2).

After fixation of the segment, we evaluate the shape of the frontal bone, and if necessary, use some kind of biomaterial to improve the anatomy, as in cases of small fractures of comminuted and not yet consolidated areas. We perform single sutures on the frontal musculature and subcutaneous tissue with 3.0 absorbable sutures and on the skin with 5.0 nylon intradermal stitches.

In the immediate postoperative period, the patient usually presents local edema and may complain of mild to moderate pain in the operated area. After three months, the edema regresses and it is possible to notice the correction of the pre-existing depression. After five years of postoperative follow-up, the patient showed no signs of infection or any other complication related to the procedure. The aesthetic result was maintained in this period.

DISCUSSION

The treatment protocols for frontal sinus fractures are reported in the literature through classifications and organograms, where the majority of authors assess the degree of displacement and /

or communication of the anterior and posterior walls, presence of intracranial lesions, and involvement or not of the nasofrontal duct[2,3,7-9].

When there is a dislocated and fragmented fracture of the posterior wall, the treatment of choice is cranialization, always associated with the obliteration of the nasofrontal duct, so that there is no communication of intracranial structures with the external environment[9,11]. Several techniques with different materials are described in the literature for this obliteration, such as abdominal fat, temporal fascia, pericranium, calcium phosphate, and hydroxyapatite[1].

Anterior wall displaced fractures are usually treated with open reduction and fixation with miniplates, but other methods of treatment, such as the endoscopically-assisted and the "camouflage" of the aesthetic defect, can also be used[2,3]. The main advantage of using the endoscope is the lower invasiveness, with conservative surgical access, resulting in better postoperative recovery, but with limited resolution of complex cases or sequelae[9-11].

In sequelae case, the technique of camouflage with biomaterials and titanium meshes is the most used, since it allows the correction of the esthetic defect without the need of an osteotomy, with overlaying of only one material. The disadvantages of this technique are the cost increase and the difficulty in performing the nasofrontal duct patency test[10]. The technique we describe, of inversion of the frontal sinus's anterior wall, allows correction of the esthetic defect in cases of sequelae, reducing or eliminating the need of grafts. This method simplifies the technique of fixation and does not present a high level of complexity, besides providing a direct access to the frontal sinus, allowing the evaluation of the duct permeability.

We conclude that inversion of the fractured segment is a good treatment option for cases of frontal sinus anterior wall fracture. Although requiring longer surgical time, this procedure presents some advantages when compared with the traditional techniques of "camouflage" of the depression.

RESUMO

O tratamento das fraturas do seio frontal depende das estruturas envolvidas: a parede anterior, a parede posterior e o ducto nasofrontal. Os tratamentos podem variar entre corrigir um defeito na parede anterior até a realização de uma cranialização com obliteração do ducto nasofrontal. O uso da inversão da parede anterior do seio frontal para corrigir o defeito na região fraturada representa uma boa opção de tratamento para os casos de sequelas, já que esta técnica elimina ou reduz a utilização de biomaterial nesta área, e permite avaliação da permeabilidade do ducto nasofrontal por acesso direto. Este trabalho descreve a técnica de inversão do segmento fraturado para tratamento de sequelas de fratura do seio frontal em paciente vítima de acidente motociclístico.

Descritores: Osso Frontal. Fixação de Fratura. Traumatismos Craniocerebrais.

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Exploring flow rate selection in *HIPEC* procedures

Explorando parâmetros de fluxo em procedimentos de HIPEC

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ABSTRACT

Cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC) has emerged as a main comprehensive treatment of peritoneal malignancies. However, current data on the literature are very heterogeneous in terms of its technical particularities, which require some efforts to standardization of practices. In these setting, we present some early data from a pioneering clinical trial in Brazil (ClinicalTrials.gov Identifier: NCT02249013) to explore the dynamic relationships between flow rates and temperature parameters in the first cases of our study, which may help in selecting better technical parameters during HIPEC procedures.

Keywords: *Injections, Intraperitoneal. Hyperthermia, Induced. Drug Therapy. Peritoneal Neoplasms.*

INTRODUCTION

Cytoreductive surgery (CRS) plus hypertermic intraperitoneal chemotherapy (HIPEC) has emerged as a main comprehensive treatment of peritoneal malignancies. The rationale of combining heat with intraperitoneal chemotherapy is the synergistic effect of heat with the cytotoxic drugs. Heat has a direct cytotoxic effect, potentiates the action of certain antimitotic agents, as well as increasing their penetration into tumor tissue. Similarly, hyperthermia can also reduce the mechanisms of tumoral resistance to chemotherapy and induce an efficient anticancer immune response[1]. In summary, these arguments have highlighted HIPEC as a promising oncological approach.

Many HIPEC techniques have been described and the current data are heterogeneous in terms of technical procedures, which require some standardization of practices that might permit systematic comparisons. The technical particularities of HIPEC include instillation circuit, timing of parietal closure, length of perfusion, target temperatures, and choice and dosage of antimitotic agents. Herein, flow rate is an important variable in achieving and maintaining goal temperatures during HIPEC, whereas a minimal temperature threshold is also critical to improve chemotherapy effects and survival outcomes[2,3]. In this setting, we aimed to explore the dynamic relationship between flow rates and temperature parameters during HIPEC procedures to help selecting a target flow rate set up.

TECHNICAL NOTE

This note involves a cross-sectional analysis of early data from our ongoing clinical trial (ClinicalTrials.gov Identifier: NCT02249013) regarding HIPEC procedures – the very first Brazilian clinical trial on this matter. This study is testing a short-term protocol of cisplatin-based HIPEC for treatment of peritoneal carcinomatosis of ovarian origin. Details of the study design are available at https://clinicaltrials.gov/ct2/show/NCT02249013?term=HIPEC+AND+ovarian+cancer&rank=4. Shortly, HIPEC was held immediately after cytorreduction according to the closed-abdomen technique. Our protocol involves the use of cisplatin (25mg/L of perfusate/m^2, total limit of 240mg) for 30 minutes with an intra-abdominal target temperature of 41-43°C. Perfusate (2L/m^2, ranging from 4L to 6L) circulated using an extracorporeal circulation device named *Performer HT* (RanD, Medolla, Italy – Figure 1), and the goal temperature was set up to 44°C. A flow rate of 300-500 ml/min was applied during the "patient filling phase" and increased to 700-1000 ml/min during

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Table 1. *Summary of relationship between flow rates and temperature parameters in HIPEC procedures.*

Parameters[1]	600ml/min	700ml/min	800ml/min	900ml/min	1000ml/min	p-value[2]
Inlet Temperature	43.6 (43.6-43.7)	43.3 (43.2-43.4)	42.8 (42.8-42.9)	42.8 (42.7-42.8)	41.8 (41.7-41.8)	< 0.001
Outlet Temperature	40.6 (40.5-40.7)	41.2 (41.1-41.3)	41.0 (40.9-41.0)	40.6 (40.5-40.6)	40.7 (40.6-40.7)	< 0.001
Mean Temperature[3]	42.1 (42.1-42.2)	42.2 (42.2-42.3)	41.9 (41.9-41.9)	41.7 (41.6-41.7)	41.2 (41.1-41.2)	< 0.001
Temperature Lost[4]	3.1 (2.9-3.2)	2.1 (2.0-2.3)	1.8 (1.8-2.0)	2.2 (2.2-2.3)	1.1 (1.0-1.2)	< 0.001

[1] Descriptive statistics summarized as median and IQR (interquartile range).
[2] According to Kruskal-Wallis test.
[3] Mean temperature: mean between inlet and outlet temperature probes.
[4] Temperature lost: difference between the inlet and outlet temperature probes.

the early "circulation phase". Thereafter, flow rate was adjusted between 600 to 1000 ml/min at intervals of 100ml/min, maintaining stable parameters into the peritoneal cavity just before the "drug circulation phase".

The device provided us with the main functional and patient parameters, and we recorded data from the "HIPEC phase" every minute. We permitted variations of ±10% in the flow rate values and rounded them accordingly. Flow rates were related to temperature parameters. We summarize descriptive statistics as median and interquartile range. We performed the statistical analysis and graph construction applying conventional methods in the STATISTICA Data Analysis Software System, Version 8.0 (Statsoft, Inc., Tulsa, OK, USA).

Data from the first five cases enrolled into our trial were analyzed involving 148 time-points of information, since two records were excluded because a variation higher than 10% in the flow rate. The mean of inlet temperature and losses from solution to peritoneal cavity was lower at 1000ml/min. Conversely, a lower rate resulted in higher inlet temperatures and temperature losses. Differences between inlet and outlet temperature probes were about 3°C at a flow rate of 600ml/min, and 1°C at 1000ml/min. The temperature lost to peritoneal cavity remained virtually stable by about 2°C at flow rates of 700, 800 and 900 ml/min. Table 1 summarizes these temperature parameters in regards to flow rates. Data on difference between inlet and outlet temperature probes is also presented in Figure 2.

DISCUSSION

HIPEC is now a preferred treatment of many peritoneal surface malignancies[1]. Unfortunately, no single technique has so far demonstrated its superiority, and several variations in techniques have produced heterogeneous and incomparable results. In this scenario, further efforts are needed to standardize the technical particularities of HIPEC, whereas temperature parameters and their dynamic relationship with other variables are important points to be scrutinized[2-5].

HIPEC involves the continuous heating and circulation of chemotherapy throughout the abdominal cavity in an attempt to enhance cytotoxicity[4]. Accordingly, flow rate is an important variable in achieving and maintaining goal temperatures during HIPEC, and a temperature threshold above 40°C is also critical to significantly enhance chemotherapy effects and improve survival outcomes[2-4]. By exploring the dynamic relationship between temperature parameters and flow rates in the first cases of our clinical trial, we noted that a higher flow rate may minimize the exchanging of heat from the system to the perfusate solution (i.e.: the mean inlet temperature was lower at 1000ml/min) and from the solution to the peritoneal cavity (i.e.: the mean of temperature losses was also lower at 1000ml/min). Conversely, a lower rate resulted in higher inlet temperatures and temperature losses. These findings confirm that heat exchanges are mitigated by higher flow rates, and that the peritoneal cavity may absorb

Figure 1. *Performer HT device in use during HIPEC procedure.*

more heat at lower flow rates. Herein, we found that the difference between inlet and outlet temperature probes were about 3°C at a flow rate of 600ml/min, and 1°C at 1000ml/min. Interestingly, the temperature lost to peritoneal cavity remained virtually stable at about 2°C at a flow rate of 700, 800 and 900 ml/min.

Despite increased flow rates are important to achieve and maintain uniform temperature distribution throughout the abdominal cavity during HIPEC, the assumption of added benefit for increased flow rates requires further considerations[2,4]. For example, even though there is a greater rise in overall esophageal temperature during perfusion at higher rates of flow, the average esophageal temperatures were lower as the flow rate was increased according to Furman *et al*.[2]. In their study, the average esophageal temperature rise during perfusion was 1.0°C at 2500ml/min, a similar temperature gradient that we found at a flow rate of 1000ml/min. Thus, we could suppose stable differences between inlet and outlet temperature (i.e.: heat lost to the peritoneal cavity and/or *viscera*) from 1000ml/min to 2500ml/min, as we found at a flow rate between 700ml/min and 900ml/min, and also, as these authors reported, at rates of 2000ml/min and 3000ml/min – about 0.8°C for both flow rates[2].

Another point of interest in this context is the dynamic relationship between hyperthermia and intra-abdominal pressures. Hyperthermia enhances diffusion in the visceral peritoneum, whereas increased pressure may enhance both visceral and parietal tissue concentrations of chemotherapy agents, without leading to increased systemic levels. The combination of the two achieves the highest tissue concentrations of chemotherapy, whereas a maximal distention of the abdomen by the perfusate is probably required to improve the synergism between such factors[4,5].

In conclusion, we present some dynamic relationships between flow rates and temperature parameters that may help in selecting better technical parameters during HIPEC procedures. These data resulted from our pioneering clinical trial in Brazil and also the very first to use the Performer HT device.

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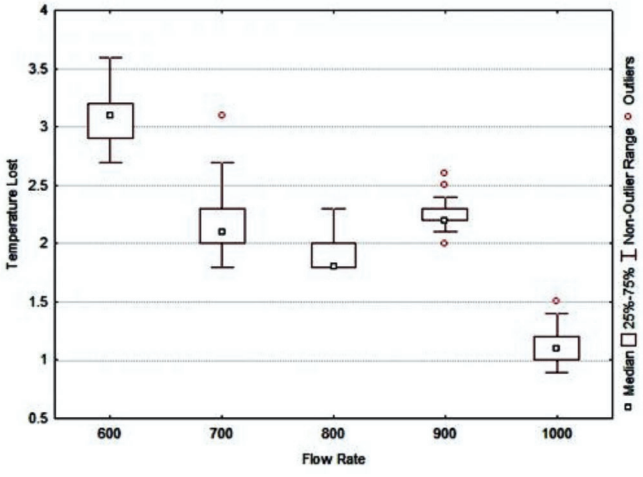

Figure 2. *Box Plot of temperature losses to peritoneal cavity (i.e.: differences between inlet and outlet temperature probes) according to flow rates.*

R E S U M O

Cirurgia citorredutora avançada e quimioterapia intraperitoneal hipertérmica (i.e.: *HIPEC*, sigla em inglês) têm se consagrado como promissora abordagem terapêutica multidisciplinar para neoplasias malignas peritoneais. Contudo, dados da literatura corrente são muito heterogêneos em torno de muitos de seus aspectos técnicos, o que demanda algum esforço na busca por padronizações do procedimento. Neste sentido, são apresentados dados de um ensaio clínico pioneiro no Brasil (*ClinicalTrials.gov Identifier*: NCT02249013), relacionando parâmetros dinâmicos de taxas de fluxo e temperaturas de perfusão nos primeiros casos do estudo, o que pode ajudar na seleção de melhores parâmetros técnicos para procedimentos de *HIPEC*.

Descritores: Injeções Intraperitoneais. Hipertermia Induzida. Quimioterapia. Neoplasias Peritoneais.

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Endovascular therapeutic options for the treatment of aortoiliac aneurysms

Opções terapêuticas endovasculares para o tratamento dos aneurismas aortoilíacos

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A B S T R A C T

About 20% of patients with abdominal aortic aneurysms have associated iliac aneurysms. Distal sealing during the endovascular treatment of aortic-iliac aneurysms is a challenge that has led to the emergence of several technical options to achieve this goal over the years. Internal iliac artery embolization is associated with the risk of ischemic complications, such as gluteal necrosis, lower limb neurological deficit, colonic ischemia, impotence and gluteal claudication. This article summarizes the technical options for endovascular treatment of aortoiliac aneurysms with different approaches to preserving the patency of internal iliac arteries.

Keywords: *Aortic Aneurysm. Iliac Artery. Endovascular Procedures.*

INTRODUCTION

The involvement of common iliac arteries occurs in 20% of patients with abdominal aortic aneurysms (AAA) and is a challenge to endovascular treatment because it compromises sealing and distal fixation of endoprostheses[1]. Several techniques have been developed to achieve the goal of sealing the aneurysmal sac. However, long-term treatment efficacy is dependent on careful selection[2]. The purpose of this review is to discuss the endovascular techniques for preserving internal iliac artery patency in the treatment of aortoiliac aneurysms (AIA).

Embolization of the internal iliac artery

Internal iliac artery (IIA) embolization prevents type-2 endoleak, resulting from the IIA retrograde flow into the aneurysm sac. Occlusion coils are implanted in the IIA prior to the implantation of an endoprosthesis to cover its origin and to extend to the external iliac artery (EIA)[3,4]. An occluder (nitinol plug) may also be used instead of the coils, with a better cost-effectiveness and a lower incidence of complications due to greater position control during release[5]. Complications of this procedure are due to the ischemic effects of IIA embolization. Gluteal claudication is the dominant symptom, and may manifest with different intensities and eventually regress over time. Its incidence varies from 13% to 50% and the risk is lower when the coils are positioned proximally to the IIA bifurcation[3,4,6].

In the literature, there are other complication reports of IIA embolization, such as sexual dysfunction, neurological deficit, urinary retention, gluteal necrosis and colonic ischemia[6,7].

Cerclage of the common iliac artery

Puech-Leo[8], in 2000, reported treatment of AIAs by adapting the previously described[9] technique of common iliac artery (CIA) cerclage for the treatment of endoleak in patients undergoing AAA endovascular treatment (Figure 1). Initially, extraperitoneal surgical access to CIA is performed. The artery is dissected cranially at its bifurcation, extending 2 to 3cm and two vascular tapes are passed around the vessel with a distance of 1cm between them. After completion of the retroperitoneal approach, inguinal incisions are made to expose the femoral arteries. The endoprosthesis is introduced and a forceps is placed at the level

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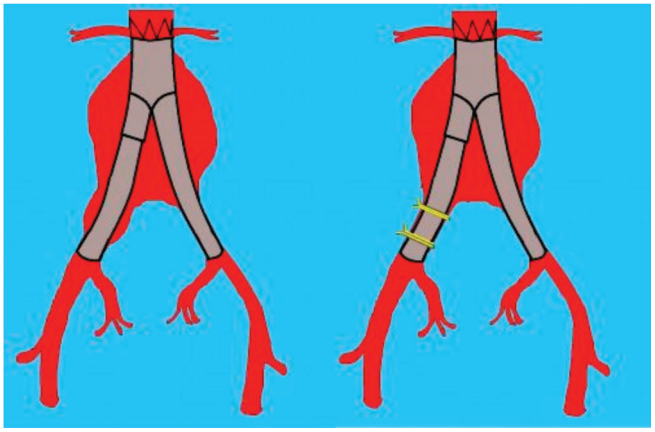

Figure 1. *Iliac cerclage technique. Representative scheme of the cerclage technique in the treatment of aortoiliac aneurysms.*

of the most caudal vascular tape, to be used as a radiopaque reference to fluoroscopy. After positioning and expanding the device, a balloon catheter of the same diameter as the endoprosthesis is introduced over fluoroscopy and inflated to the caudal end of the endoprosthesis. The two vascular tapes are tied until the resistance promoted by the balloon is perceived. The balloon is then deflated and removed for control angiography[8].

Iliac branches in bell-bottom

The bell-bottom technique was originally described with the use of a proximal aortic extension (cuff) selected based on the diameter of the iliac artery and positioned with at least 1cm overlap within the distal iliac branch and by at least 1cm in an area of the ectasized CIA (Figure 2A)[10]. The presence of a thrombus in the ectasia segment is a contraindication to this technique. The cuffs described in this configuration are expanded to adapt to the iliac branch, promoting adequate distal sealing in the ectasiated or aneurysmatic CIA. Thereafter, broad-diameter iliac branches specifically developed for this purpose have become available for use in the bell-bottom technique[11]. There is no consensus on the CIA limiting diameter recommended for the use of this technique. A study analyzing common iliac arteries up to 30mm in diameter submitted to the implantation of bell-bottom endoprostheses demonstrated a satisfactory long-term outcome (type-1B endoleak in 4% of cases)[11]. A comparative analysis showed no evolutionary difference between a group of patients with AICs submitted to the implantation of bell-bottom endoprostheses with a diameter between 20mm and 22mm and a group with a diameter between 24mm and 28mm[12]. The incidence of type-1B endoleak observed in the literature ranged from 0 to 11%[10-15]. However, the Mayo Clinic group reports late dilation of CIA affecting up to 86% of patients[10-12,14]. Nonetheless, some authors relate this late expansion to over-dimensioning greater than 15% of the endoprostheses implanted in the CIA[16], without correlation with adverse effects[14].

Sandwich

The sandwich technique for the treatment of aortoiliac aneurysms was initially described by Lobato[17]. This technique consists of the following steps: 1) femoral implantation of a bifurcated stent graft, with position of the contralateral iliac branch 1cm cranial to the CIA ostium; 2) IIA catheterization

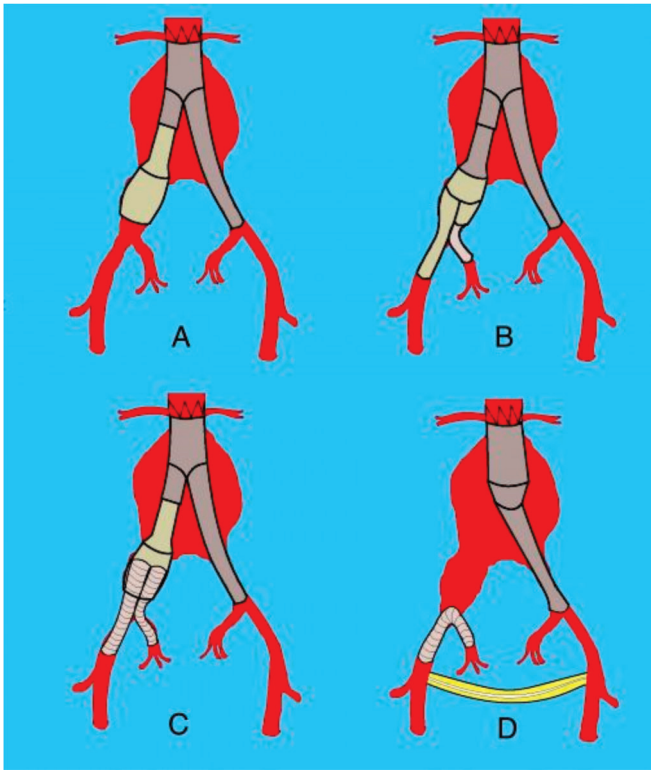

Figure 2. *Endovascular techniques for the treatment of aortoiliac aneurysms. A) bell-bottom; B) branched iliac endoprosthesis; C) sandwich; D) retrograde endovascular revascularization of the internal iliac artery.*

through left brachial access; 3) implantation of a coated, self-expanding stent in the IIA, with adequate overlap in the iliac branch, followed by implantation of the iliac branch of the endoprosthesis; 4) Modeling of the iliac branch and expanding the stent using balloon catheters; 5) implantation of the contralateral iliac branch (Figure 2C)[18]. Lobato[17] indicates overlapping of more than 6cm between endoprostheses to minimize the formation of gutters and the risk of leakage. Limitations of this technique include the need to use long iliac endoprostheses, the potential risk of compression of one of the parallel endoprostheses, and the absence of controlled data with a long follow-up period[2]. Despite these considerations, the technique is used in several centers with reports of low prostheses occlusion rates or leaks[19-22]. Lobato describes a series with 40 patients, with an average follow-up time of 12 months, observing 100% technical success rates, primary patency of 93.8%, and type-3 endoleak (associated with the technique) of 2.5%[23].

Branched internal iliac artery endoprosthesis

The IIA branching technique consists of the implantation of a bifurcated iliac stent combined with a coated stent connecting the latter with IIA. The ZBIS® endoprosthesis is available with external branches in the helical and straight configurations, the latter being the most used. This device is generally combined with an endoprosthesis implanted in the abdominal aorta (Figure 2B)[18,24]. In our country, Massière and von Ristow[24] developed a bifurcated branched device based on the Apollo platform, and used the Viabahn® connecting stent.

The following morphological criteria are described for the use of the ZBIS device technique: the presence of a non-aneurysmal segment of the EIA of at least 20mm in length and a diameter between 8mm and 11mm, with the length of the CIA greater than 50mm, luminal diameter of the CIA greater than 16mm and the presence of a non-aneurysmal segment of the IIA at least 10mm in length and with a diameter between 6mm and 9mm[2,18,25]. Using these criteria, a study of 51 patients undergoing AIAs treatment determined that only 38% of the patients analyzed fully met the requirements determined by the manufacturer[26].

Ferreira *et al*[27] published a study investigating 47 bifurcated devices implanted in 37 patients with an average follow-up time of 11.6 months. Technical success was obtained in 97.3% of the cases and a secondary patency rate in 22 months of 85.4%. They observed stent occlusion in five patients (10.6%), gluteal claudication in one case (2.7%) and no endoleaks. The incidence of complications associated with the device, evaluated by the combined incidence of type-1endoleak, type-3 endoleak and branch occlusion, varies from 7% to 13.8% in the literature. The incidence of gluteal claudication varies from 2.7 to 5.6%[26-31]. The main limitation to this technique is the anatomical prerequisites necessary for the device implanting[32].

A meta-analysis analyzing the performance of 236 connection, coated stents in five studies on branched endoprosthesis reported an incidence of occlusion in 6% of the cases and gluteal claudication in 3.4%, with the main causes being the IIA small diameter, IIA perioperative dissection due to excessive dilation, use of long stents, concomitance of IIA atherosclerotic disease, and compression associated with the use of the helical model branched device. A lower occlusion rate was observed in cases in which the expandable balloon stent was used as a connection stent. However, statistical methods could not be used due to the heterogeneity of the studies[31].

Until the moment of submission of this article, only initial results of the use of the Excluder® iliac branched endoprosthesis were published[32].

Retrograde endovascular revascularization of the internal iliac artery

The technique of retrograde endovascular revascularization of the internal iliac artery was initially described by Hoffer *et al*[33]. It consists of the implantation of a conical aorto-uni-iliac endoprosthesis, followed by the creation of a femoral-femoral cross-bridge and implantation of a contralateral coated stent, extending from the EIA to the IIA with the objective of preserving pelvic perfusion (Figure 2D).

Massière *et al*[34] described a series of 21 patients submitted to this technique for the treatment of complex aortoiliac aneurysms, unable of being submitted to another endovascular technique and with a high surgical risk. They used the Viabahn® connecting stent. The mean follow-up time was 52 months, with technical success in all cases, endoleak associated with the connection stent in one patient (4.7%), type-IB endoleak in one patient (4.7%) and occlusion of the coated stent in one case (4.7%) in 30 days[31].

The need for the extra-anatomical bridge constitutes a limitation to this technique due to the risk of infection and thrombosis, being reserved for selected cases. However, no complications associated with cross-bridge were observed and the technique allows the treatment of cases with complex anatomy, offering few anatomical restrictions to its use.

CONCLUSION

Each one of the various endovascular techniques available for the treatment of aortoiliac aneurysms presents its anatomical limitations. The complexity of these cases requires adequate selection of the technique that will allow the exclusion of the aneurysm, offering lower risk and better outcome in the long term.

R E S U M O

Cerca de 20% dos pacientes com aneurismas de aorta abdominal apresentam aneurismas ilíacos associados. A obtenção do selamento distal, durante o tratamento endovascular dos aneurismas aortoilíacos, constitui-se em um desafio que suscitou, ao longo dos anos, o surgimento de diversas opções técnicas para alcançar esse objetivo. A embolização da artéria ilíaca interna é associada ao risco de desenvolvimento de complicações isquêmicas, tais como: necrose glútea, déficit neurológico dos membros inferiores, isquemia colônica, impotência e claudicação glútea. Esse artigo resume as opções técnicas de tratamento endovascular dos aneurismas aortoilíacos com diferentes formas de abordagem de preservação da perviedade das artérias ilíacas internas.

Descritores: Aneurisma Aórtico. Artéria Ilíaca. Procedimentos Endovasculares.

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Comparison between high and low levels thoracic sympathectomy for the treatment of palmar and axillary primary hyperhidrosis: systematic review and meta-analysis

Comparação da simpatectomia torácica realizada em níveis altos e baixos para o tratamento da hiperidrose primária palmar e axilar: revisão sistemática e metanálise

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A B S T R A C T

Primary hyperhidrosis (PH) is a condition that has a great impact on affected individuals' quality of life, regardless of its location. Its surgical treatment is done through thoracic sympathectomy performed by videothoracoscopy. Standardization of the technique includes section of the sympathetic trunk at different levels, according to the site of symptoms. The aim of this review is to evaluate the efficacy of thoracic sympathectomy through a systematic literature review comparing sympathectomy at different levels of the sympathetic chain.

Keywords: *Hyperhidrosis. Sympathectomy. Thoracic Surgery, Video-Assisted. Meta-Analysis.*

INTRODUCTION

Hyperhidrosis is the excessive and uncontrollable sweating that goes beyond the thermoregulatory needs of the body. It occurs more often in the palm, axillary, plantar and face regions but can manifest in any region of the body. It is classified into primary, the most common, and secondary forms. The pathophysiology of primary hyperhidrosis (PH) is not yet well established, constituting an idiopathic, chronic, usually focal, bilateral and symmetric alteration. Secondary hyperhidrosis has several etiologies, among which we can highlight fever, antidepressant drug use, neurological disorders, hyperthyroidism, obesity, stress, among others[1,2].

PH affects men and women and manifests itself at various ages, being more common in adolescents and young adults. Approximately half of the patients have a positive family history[3,4]. The literature shows a highly variable prevalence for PH and its incidence varies according to cultural, climatic, and even conceptual, differences[4]. Strutton *et al*.[5] found a prevalence of 2.8% in the North American population. In Brazil, there is little data on PH prevalence. A study conducted in the city of Botucatu-SP showed a prevalence of 0.93%, predominantly in female patients[6].

Its pathophysiology is not well understood. Morphological studies in the sweat glands of PH patients did not show changes in their number and histology. A complex dysfunction of the sympathetic autonomic nervous system, responsible for its innervation, may be related to its etiology[2]. In an PH family history analysis, Yamashita *et al*.[7] found a pattern of non-dominant autosomal transmission.

Although PH is not a life-threatening condition, it has a major impact on quality of life, interfering in the social, professional, psychic and emotional domains[8]. This is the main factor that causes PH patients to seek medical help.

Treatment may be clinical or surgical. Conservative alternatives are topical agents, anticholinergic drugs and beta-blockers, iontophoresis and the use of botulinum toxin[9]. Surgical treatment can be done through resection of sweat glands, curettage of the subcutaneous tissue and liposuction. However, the most accepted and best-reported

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treatment is videothoracoscopic sympathectomy, performed at different costal levels according to the location of symptoms[4].

The purpose of this review was to compare the efficacy of videothoracoscopic sympathectomy performed at different levels of the sympathetic chain in patients with PH.

METHODS

We performed a search for the interest studies in the following databases: Pubmed, Embase, Cochrane, Lilacs and Clinical trials. The descriptors used to construct the search strategy were: primary hyperhidrosis, assisted video thoracic sympathectomy or videothoracoscopy. In order to increase the search sensitivity, we adapted the strategy to each base and, in addition, we used meSH terms for Pubmed, Cochrane and Clinical Trials databases, Emtree terms for Embase, and DEC terms for Lilacs. Two reviewers independently selected the studies. The eligibility criteria used were: prospective, randomized or quasi-randomized studies; Patients with PH; Presence of two groups comparing different thoracic levels for the sympathectomy, the highest or broadest level being considered the standard procedure. The primary outcome was symptom remission, and the secondary, the incidence of compensatory sweating.

We analyzed the titles and abstracts of the works found to identify the articles that obeyed the inclusion criteria. A third reviewer was available to resolve possible disagreements. We obtained the selected articles in their respective entireties and analyzed their bibliographic references in the search for other possibly eligible studies. Two reviewers independently extracted the data in a standard form. We evaluated the quality of the studies by verifying, for each one, the criteria of randomization, incomplete presence of outcome data, selective reporting of outcomes, presence of blindness for participants and investigators, and presence of other biases.

Since the primary goal of hyperhidrosis treatment is to improve patients' quality of life, for the primary outcome we included the data of patients who had complete remission of symptoms or who reported great satisfaction with surgery. We assessed compensatory sweating in a similar way, taking into account the data from all patients in whom the event significantly compromised quality of life.

For the meta-analysis, we considered the outcomes as dichotomous variables and the measure of effect was the relative risk, with fixed effect and confidence interval (CI) of 95%. We assessed the inconsistencies between studies through the heterogeneity test (I2), considering values above 70% as important. We summarized the results in the forest plot, with the combined estimate of the effect marked as a diamond at the bottom of the chart. Subgroup analyzes and sensitivity analyzes were planned to explain the possible causes of high

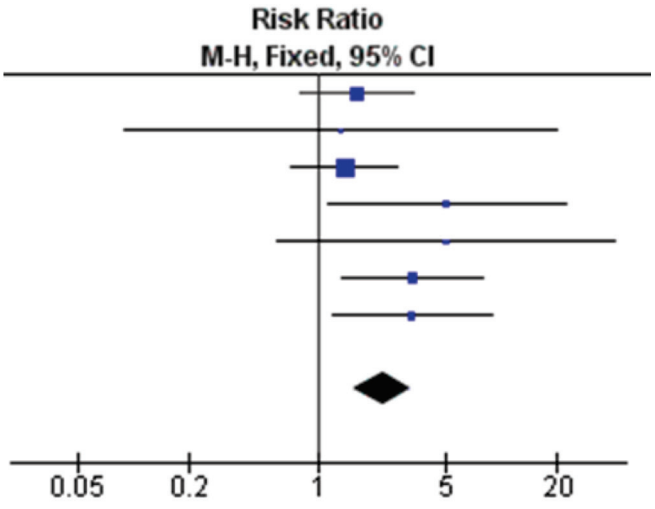

Figure 1. *Symptom control for palmar PH.*

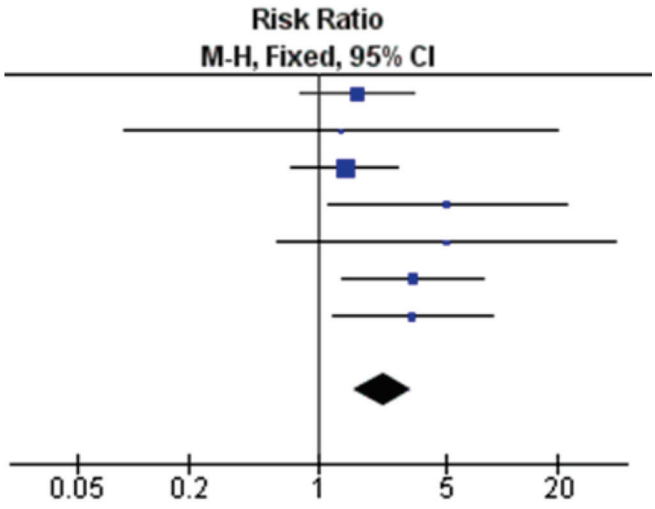

Figure 2. *Compensatory Sweating for palmar PH.*

Table 1. *Studies included in the review.*

Author/Year	High levels	Low levels	Levels compared	Location of symptoms
Baumgartner, 2007	61	60	T2/T3	Palmar
Ishy, 2010	20	20	T3/T4	Palmar
Li, 2008	115	117	T2-4/T3	Palmar
Liu, 2009	68	73	T3/T4	Palmar
Munia, 2007	32	30	T3-4/T4	Axillary
Munia, 2008	31	33	T3-4/T4	Axillary
Vicidomi, 2011	50	50	T2-4/T3	Palmar
Yang, 2009	78	85	T3/T4	Palmar
Yasbek, 2009	30	30	T2/T3	Palmar
Yuncu, 2013	17	43	T3-4/T4	Axillary

heterogeneity. We performed statistical analysis with the software Review Manager from Cochrane Collaboration, version 5.3.5, available free of charge for download.

RESULTS

The search conducted in April 2015 returned 1086 articles in Pubmed, 60 articles in Lilacs, 92 articles in Embase, two articles in Cochrane Central Station and five articles in Clinical Trials. After the removal of duplicate sources and analysis of titles and abstracts, we selected 33 articles for integral evaluation. From this amount, ten articles brought the inclusion criteria for this review. We performed a new search in August 2015, and included no more study in the review. The works analyzed data from 857 patients with palmar hyperhidrosis and 186 patients with axillary hyperhidrosis, totaling 1,043 individuals. There was a slight predominance of female patients and the mean age ranged from 21.2 to 29.7 years. Table 1 summarizes the main characteristics of each study.

As for the levels of surgery, for palmar hyperhidrosis, Yazbek *et al*.[10] and Baumgartner *et al*.[11] compared levels T2 and T3. Vicidomini *et al*.[12] and Li *et al*.[13] compared levels T2-4 and T3, and Liu *et al*.[14], Yang *et al*.[15] and Ishy *et al*.[16] compared levels T3 and T4. To perform the meta-analysis of the primary outcome, we considered the larger resections taking into account the first sectioned level. For palmar PH, was carried out the meta-analysis without two articles that were not included because they brought the results as averages.

The analysis performed with the four remaining articles included data from 413 patients. The relative risk (RR) found was 0.86 (95% CI 0.79-0.94) favoring the group submitted to the lowest resection. However, the heterogeneity (I2) found was 83% (p=0.0007). In order to explain this high heterogeneity, we performed a sensitivity analysis with the withdrawal of one study. Thus, we found an I2 of 0% (p=0.91) and RR of 0.95 (95% CI 0.88-1.03) without significant difference between the two types of resection (Table 2, Figure 1). For the secondary outcome (Table 2, Figure 2), compensatory sweating, the meta-analysis showed a greater risk of this event for the group submitted to the higher or larger resections, with RR of 2.26 (95% CI 1.57-3.25), and I2 of 0% (p=0.46).

As for the axillary symptoms, Munia *et al*.[17,18] compared levels T3-4 and T4 alone, and Yunku *et al*.[19] compared levels T3-4 with T3 alone. We made the meta-analysis for the primary outcome without including one study that reported the results as means. The results showed a RR of 0.83 (95% CI 0.70-0.99) and I2 41% (p=0.19), favoring the group submitted to the lower section (Table 2,

Figure 3). The chance of presenting compensatory sweating was higher in the group submitted to the higher section, with RR of 2.03 (95% CI 1.49-2.76), but with I2 of 94% (p<0.0001). We then performed a sensitivity analysis by excluding one study in which all patients in the higher resection group had compensatory sweating. Thus, the meta-analysis showed a RR of 7.25 (95% CI 2.30-22.84) and I2 of 0% (p=0.51), favoring the group submitted to the lowest resection (Table 2, Figure 4).

DISCUSSION

PH is a condition that, despite benignity, severely compromises the quality of life of affected individuals. Symptoms may begin in childhood and

Table 2. *Palma HP.*

	Higher level		Lower level			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed 95% CI
* Symptom control for palmar PH.						
Baumgartner, 2001	37	41	38	40	21.4%	0.95 [0.84, 1.07]
Li, 2008	89	115	96	117	53.0%	0.94 [0.83, 1.07]
Liu, 2009	15	62	40	69	0.0%	0.42 [0.26. 0.68]
Vicidomini, 2011	45	50	46	50	25.6%	0.98 [0.86, 1.11]
Total (95% CI)		206		207	100.0%	0.95 [0.88, 1.03]
Total events	171		180			
** Compensatory Sweating for palmar PH.						
Baumgartner, 2001	16	50	9	46	26.2%	1.64 [0.80, 3.33]
Ishi, 2010	1	15	1	20	2.4%	1.33 [0.09, 19.64]
Li, 2008	18	115	13	117	36.0%	1.41 [0.72, 2.74]
Liu, 2009	9	62	2	69	5.3%	5.01 [1.12, 22.29]
Vicidomini, 2011	5	50	1	50	2.8%	5.00 [0.61, 41.28]
Yang, 2009	18	78	6	85	16.1%	3.27 [1.37, 7.81]
Yasbek, 2009	13	30	4	30	11.2%	3.25 [1.20, 8,83]
Total (95% CI)		400			100.0%	2.26 [1.57, 3.25]
Total events	80		36	417		
*** Symptom Control for axillary PH.						
Munia, 2007	28	32	29	30	58.2%	0.91 [0.78, 1.05]
Yuncu, 2013	11	17	38	43	41.8%	0.73 [0.51, 1.06]
Total (95% CI)		49		73	100.0%	0.83 [0.70, 0.99]
Total events	39		67			
**** Compensatory sweating for axillary PH.						
Munia, 2007	11	32	2	30	68.1%	5.16 [1.24, 21.37]
Munia, 2008	11	31	1	33	31.9%	11.71 [1.60, 85.45]
Yuncu, 2013	17	17	34	43	0.0%	1.24 [1.04, 1.48]
Total (95% CI)		63		63	100.0%	7.25 [2.30, 22.84]
Total events	22		3			

** Heterogeneity: Chi^2=0.20, df=2 (P=0.91); I^2=0% - Test for overall effect: Z=1.16 (P=0.25)*
*** Heterogeneity: Chi^2=5.71, df=6 (P=0.46); I^2=0% - Test for overall effect: Z = 4.42 (P<0.0001).*
**** Heterogeneity: Chi^2=1.71, df=1 (P=0.19); I^2=41% - Test for overall effect: Z=2.12 (P=0.03).*
***** Heterogeneity: Chi^2=0.44, df=1 (P=0.51); I^2=0% - Test for overall effect: Z=3.38 (P=0.0007).*

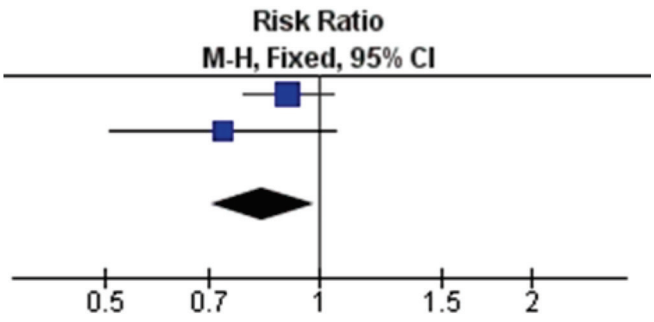

Figure 3. *Symptom Control for axillary PH.*

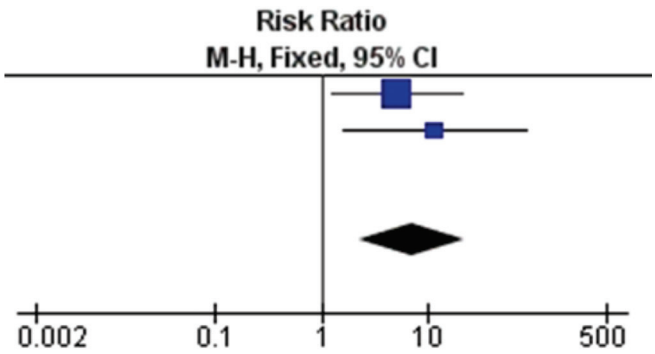

Figure 4. *Compensatory Sweating for axillary PH.*

tend to worsen during adolescence[4]. Responses with clinical treatments vary widely, but generally do not show satisfactory results. In this context, videothoracoscopic sympathectomy presents as an effective alternative, with low complications rates and satisfactory results[4,8].

The first sympathectomy reported was made in 1889. Kux, in 1940, performed the first thoracoscopic sympathectomy[20]. Since then, sympathectomy has gained strength in the treatment of PH and has become the standard procedure for these cases. Several techniques for the interruption of the sympathetic chain have been described and the literature does not yet indicate the superiority of any of them[4]. Despite the large number of published studies, a point of great interest and still a source of divergence is the costal level of sympathetic trunk section. In the literature there are retrospective series that did not show significant differences between the high and low surgical approaches[4]. This systematic review of prospective and randomized studies evaluated symptom control in 413 patients with palmar PH and the incidence of compensatory sweating in 817. For axillary PH, the number of patients was lower, 122 for the primary outcome and 126 for the secondary. Despite this, there was no significant heterogeneity in the analyzes.

The studies recorded no deaths and, although the rates of complications were poorly reported, they were low. This is due to the standardization of the surgical technique and the profile of the operated patients, who are usually young and without comorbidities.

For palmar hyperhidrosis, the meta-analysis did not show significant differences between the groups for the primary outcome. In the upper sections, 83% of the patients had remission of symptoms or significant improvement. For the intervention group, 86% of the patients presented the same results. For compensatory sweating, the difference between the groups was very clear, with a risk 2.07 times higher of the event occurring in the higher or broader resections. In the last consensus based on the literature organized by The Society of Thoracic Surgeons (STS)[4], the indication lower levels section for axillary hyperhidrosis showed low rates of compensatory sweating, but also lower rates of symptoms remission. This difference in outcome probably occurred because the STS review included prospective, randomized, non-randomized, and even retrospective studies.

For axillary, axillary-palmar, or axillary-palmar-plantar PH cases, the STS revision showed better results with surgery performed at lower costal levels. This review found similar results, and with statistical significance. For the primary outcome, rates in the high and low section groups were, respectively, 79% and 91%. The risk of developing compensatory sweating was 7.25 times higher in the control group. Data from the literature show important rates of compensatory sweating, varying from 14 to 90%. Obviously, there are many associated factors that must be considered, since a good part of these data derive from retrospective series with different indications and surgical techniques. In this review, in the control group, approximately 34% of the patients reported compensatory sweating, whereas this number was 5% for lower sections.

Despite the small number of studies available, the meta-analysis has shown that for palmar PH, lower

sections are as effective as high ones for symptoms control or remission, but display lower rates of compensatory sweating. As for axillary PH, procedures done at lower levels are more effective and have lower rates of compensatory sweating. Thus, low resections, based on data from the current literature, are the best options for the treatment of axillary and palmar PH, with good satisfaction rates and improvement of patients' quality of life. Further prospective and randomized studies are needed to elucidate which groups of patients benefit most from surgical treatment and which techniques may be most effective.

RESUMO

A hiperidrose primária (HP) é uma condição que, independentemente de sua localização, apresenta grande impacto na qualidade de vida dos indivíduos acometidos. Seu tratamento cirúrgico é feito através da simpatectomia torácica realizada por videotoracoscopia. A padronização da técnica inclui a secção do tronco simpático em diferentes níveis, de acordo com o local dos sintomas. O objetivo desta revisão é avaliar a eficácia da simpatectomia torácica por meio de uma revisão sistemática da literatura, comparando a simpatectomia em diferentes níveis da cadeia simpática.

Descritores: Hiperidrose. Simpatectomia. Cirurgia Torácica Videoassistida. Metanálise.

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Emergency cricothyrotomy: temporary measure or definitive airway? A systematic review.

Cricotireoidostomia de emergência: medida contemporizadora ou via aérea definitiva? Uma revisão sistemática.

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ABSTRACT

Being a fast and safe method in the hands of well trained professionals in both prehospital and intrahospital care, Cricothyrotomy has been broadly recommended as the initial surgical airway in the scenario "can't intubate, can't ventilate", and is particularly useful when the obstruction level is above or at the glottis. Its prolonged permanence, however, is an endless source of controversy. In this review we evaluate the complications of cricothyrotomy and the need of its routine conversion to tracheotomy through a search on PubMed, LILACS and SciELO electronic databases with no restriction to the year or language of the publication. In total, we identified 791 references, retrieved 20 full text articles, and included nine studies in our review. The incidence of short-term complications ranged from zero to 31.6%, and the long-term complications, from zero to 7.86%. Subglotic stenosis was the main long-term reported complication, even though it was quite infrequent, occurring only in 2.9 to 5%. The frequency of conversion to tracheostomy varied from zero to 100%. Although a small frequency of long-term complications was found for emergency cricothyrotomy, the studies' low level of evidence does not allow the recommendation of routine use of cricothyrotomy as a secure definitive airway.

Keywords: *Cricoid Cartilage. Airway Management. Advanced Trauma Life Support Care. Evidence-Based Emergency Medicine.*

INTRODUCTION

The early establishment of a safe airway is a basic principle of life support. Patient background, clinical scenario and professionals' abilities all play an important role on the achievement of a patent airway[1,2]. According to the American Society of Anesthesiologists, a difficult airway is "the clinical situation in which a conventionally trained anesthesiologist experiences difficulty with facemask ventilation of the upper airway, difficulty with tracheal intubation, or both" [3].

Endotracheal intubation (EI) is the preferable initial airway for trauma patients who present with apnea, reduced consciousness level, or imminent compromise of the airways. When EI cannot be achieved or is contraindicated, a surgical airway technique must be employed, especially for those patients in whom airway adjuncts, such as laryngeal mask and combitube, were tried and failed, or who suffered extensive maxillofacial or neck trauma[4-6].

Surgical airway procedures include surgical cricothyrotomy and tracheotomy. Cricothyrotomy, being a fast and safe method inthe hands of well trained professionals inboth prehospital and intrahospital care, has been broadly recommended as the initial surgical airway in view of the situation "can't intubate, can't ventilate". It is a particularly useful technique when the obstruction level is above or at the glottis. Its prolonged permanence, however, is an endless source of controversy. Some authors defend that it must be converted to a tracheotomy in 24-72 hours after the initial procedure,due to the associated risk of subglottic stenosis. Yet, conversion is not always possible on unstable and critically ill patients. Reports about patients with such a profile have demonstrated that, contrary to the classically established, cricothyrotomy may be well tolerated by long-term users, with acceptable complication rates[1,2,4].

Due to the inexistence of a systematic, in-depth and recent revision on such a relevant and pertinent theme, we aimed to assess the intraoperative

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and postoperative complications rates of emergency surgical cricothyrotomy, as well as to evaluate the need of its routine conversion to tracheotomy.

METHODS

Search strategy

We inserted the terms "cricothyrotomy", "cricothyroidotomy", and "coniotomy" on Pubmed's search tool. We also inserted the same terms, followed by their cognates in Portuguese, "cricotireoidotomia", "cricotireoidostomia", "cricotirostomia", "cricotireoidostomia", "cricostomia", and "cricotireoidostomia", and in Spanish, "cricotireoidotomía", "cricotireoidostomía", "cricotirostomía", "cricotomía", "cricostomía", and "cricotirotomía", on the search tool of Scielo and LILACS databases.

Inclusion criteria

We selected for further analysis all the abstracts retrieved by the search strategy up to January 8th, 2016, and whose full text were available on the electronic version of the journal in which they were published. We applied no restriction to the year or language of publication.

Exclusion criteria

We excluded the studies that focused on: 1) cricothyrotomy performed in a non-emergency setting; 2) cricothyrotomy executed on mannequins, cadavers, experimentation animals or virtual simulators; 3) the procedure's teaching methodology and learning curve; 4) techniques or equipments comparison; and 5) the procedure's time of execution or success rate , without mention to intra or postoperative complications,.

Data analysis

On the studies that met the inclusion criteria, we analyzed the following variables: study design; number of cricothyrotomies performed per study; patients' mean age; indication of the procedure, broadly categorized as "trauma" and "non-trauma"; setting in which the procedure was performed, whether "prehospital" or "hospital"; professional responsible for the execution of the procedure, categorized as "nurse", "paramedics", and "physician"; mean time of patient follow-up; cricothyrotomy complications, classified as "short-term complications", when manifested during or immediately after the procedure's execution, or "long-term complications", when manifested several hours to months after the procedure, and subclassified as "minor", when evolving to spontaneous remission and/or not requiring intervention and/or not persisting chronically, or "major", when requiring intervention and/or persisting chronically; number of conversions to tracheotomy; and period of time after which the conversion was done, when applicable.

Assessment of evidence quality

The selected studies were evaluated by their level of evidence, under the criteria of the Oxford Centre for Evidence-Based Medicine (2009).

RESULTS

Our search retrieved 23 references on LILACS, 66 references on Scielo and 702 references on Pubmed, totalizing 791. We selected 20 studies fortext reading, and from those, included nine in our review. The included studies were published between 1982 and 2012. Evidence level ranged from 3b[7,8] to 4[9-15]. All studies were retrospective (Table 1). The number of cricothyrotomies per study ranged from 10 to 95 (mean 35), totalizing 316 cricothyrotomies. Patients mean age varied from 32 to 50 years-old (mean 41). The indication for the procedure was a traumatic event in the majority of studies. In three studies[10,11,13], cricothyrotomy was performed only at a prehospital setting, while in other three[7,9,12], it was performed only at a hospital setting, and in the remaining three[8,14,15], in both prehospital and hospital settings. In all except two studies[11,13], physicians were the professional responsible for the procedure. Patients received long term follow-up in five studies[7-10,12], but only two[8,12] described the follow-up average time, which ranged between 23 and 51 months. Short-term complications varied from zero (in one third of studies) to 31.6%, and long-term complications varied from zero (in 40% of studies) to 7.86%. Conversion of cricothyrotomy to

Table 1. *Description of the studies included in our review.*

Author (year)	Evidence level*	Study design	Procedures per study	Mean age (y)	Event		Setting	Professional	Follow-up (mo)	Complications		Conversion to tracheo (%)	Time to tracheo (d)
					Tr	NTr				Short-term	Long-term		
McGill *et al.*, 1982	4	R	38	41	68.4%	31.6%	H	P	U	31.6% (Ma)	2.6% (Ma) 5.26% (Mi)	U	U
Miklus *et al.*, 1987	4	R	20	34.8	100%	0	PH	P	U	0	0	100%	1-5
Spaite *et al.*, 1990	4	R	16	37	100%	0	PH	PM	U	12.5% (Ma) 18.8% (Mi)	U	U	U
Gillespie *et al.* 1999	4	R	20	50	29%	71%	H	P	23	15% (Ma)	5% (Ma)	0	U
Wright *et al.*, 2003	3b	R	46	32	100%	0	H	P	U	0	0	53.3%	1-17
McIntosh *et al.*, 2008	4	R	17	U	82.4%	17.6%	PH	N, PM	U	5.9% (Ma) 23.5% (Mi)	U	U	U
Graham *et al.*, 2011	3b	R	95	36	100%	0	H, PH	U	51	5.9% (Ma)	2.9% (Ma)	67.7%	2
King *et al.*, 2012	4	R	54	50	100%	0	H, PH	P, PM	U	16.7% (Ma) 3.7% (Mi)	U	44.4%	U
Dillon *et al.*, 2012	3b	R	10	44.9	100%	0	H, PH	P, PM	U	0	U	100%	U

**According to the Oxford Centre for Evidence-Based Medicine (2009).*
Legend: d – days, H – hospital, Ma – major, Mi – minor, mo – months, N - nurse, NTr – non-trauma, P – physician, PH – pre hospital, PM – paramedic, R – retrospective, Tr – trauma, tracheo – tracheotomy, U – unavailable, y - years.

tracheotomy was mentioned in six studies[7,8,10,12,14,15], but was carried outin all patients in only two of them[10,15]. Time from cricothyrotomy to tracheotomy ranged from one to 17 days.

DISCUSSION

From the end of the 19th Century onwards, several attempts of systematization and standardization of airway management in critical patients were carried out to establish the safety of executed procedures, special attention being given to the study of their complications. In this context, Chevalier Jackson published a series of 200 cases of subglottic stenosis in 1921. All cases were secondary to the establishment of an airway, and 158 patients had undergone cricothyrotomy, referred as "high tracheotomy" by the author. He thus concluded that cricothyrotomy offered an alarming high risk of complications in comparison to conventional tracheotomy, as he stressed that those patients had no known previous inflammatory airway disease which could explain the high rates of subglottic stenosis[16].

Later, it was pointed out that some of the observed complications were due to the technique employed at the time, when airway was accessed through the thyroid cartilage, and not through the cricoid. Brantigan and Grow were the first to adopt a critical view of the results presented by Jackson and to introduce evidence contradicting his statements. In 1976, they published a study with 655 patients who underwent cricothyrotomy. Only 6.1% of those had complications, and none developed subglottic stenosis. They concluded that elective surgical cricothyrotomy complications were neither more severe nor more frequent than the complications after conventional tracheotomy[17]. After this, several subsequent studies continued on questioning the excessively high rate of subglottic stenosis described by Jackson.

In a prospective study performed by François *et* al, in 2003, 118 patients from an Intensive Care Unit who had their airway secured by means of either tracheotomy or surgical cricothyrotomy were followed up for six months, comparing and the incidence and severity of each technique's complications. Complications were classified as immediate (pneumothorax, bleeding, difficult cannulation), early (subglottic stenosis, acute respiratory failure, tracheoesophageal fistula, temporary or chronic dysfunction of vocal cords), or late (tracheal granuloma, non-healing wounds, and scars)[18].

Immediate complications, especially moderate bleedings, were more frequent on patients who underwent tracheotomy, which was justified by the presence of bleeding disorders in a greater number of such patients. However, all complications accounted for, they did not find a statistically significant difference between groups. Based on this, François *et al* stated that cricothyrotomy, being a more easily executed procedure, could be an invaluable alternative to conventional tracheotomy on the airway management of critically ill patients[18].

Cricothyrotomy has been accepted as the preferred surgical emergency airway on the scenario "can't intubate, can't ventilate" for its technical simplicity and fast accomplishment. The operative field of cricothyrotomy comprehends less noble structures of the neck than the one of tracheotomy. Tracheal cartilaginous rings are not complete, leaving the posterior wall of the trachea and the esophagus unprotected. Such anatomic structures are at greater risk of being inadvertently injured during the execution of tracheotomy. On the other hand, laryngeal and cricoid cartilages have the shape of a complete circumference, acting as a shield to the structures located posterior to them. Also, the incision of tracheotomy is placed more inferior than that of cricothyrotomy, so that the chance of pneumothorax, great vessels injury, or mediastinal perforation are greater[1,10].

Although it is generally accepted that cricothyrotomy is preferable to tracheotomy in an emergency situation, it is also routinely recommended that, once obtained, the airway must be secured with tracheotomy. For those who defend this position, conversion should be performed as soon as possible, as it would reduce the long-term complication rate associated with cricothyrotomy. Also alleged is that the conversion procedure itself carries minimal risks, comparable to those of elective tracheotomy[1].

Up to now, nevertheless, there are no published studies about complications derived from the conversion

itself. Two of the studies included in our review compared the permanence of cricothyrotomy with conversion to tracheotomy, and both concluded that conversion does not offer any benefit with regards to long-term complications[8,15,19].

In 2010, Talving *et al* reviewed 20 case series of emergency cricothyrotomy performed on trauma patients. They concluded that, despite being a safe initial airway, long term cricothyrotomy remained controversial. The review also underlined the absence of studies proving the benefits of routine conversion. The relevance of such statements, however, was impaired by the methodological deficiencies of the series included on their review[4].

In our review, we included nine case series, three of which reported a complication rate of zero. The most frequent major short-term complications were, first, the incorrect execution of the technique, resulting in injury of cartilaginous structures on the operative field, reported in five studies[10-14], and second,the failure of obtaining an airway, reported in two studies[9,11]. Taking into account that cricothyrotomy is indicated for patients in whom other procedures to secure the airway failed, or who present with some degree of anatomical distortion on the neck, it is not surprising that those are the main reported complications.

The broad variability on the complication rate, zero to 31.6%, might be influenced by the experience of the professional who executed the procedure, as well as by logistic issues of the setting in which it was performed. On the series published by King *et al* (2012), for example, all cricothyrotomies executed by paramedics evolved with immediate complications, while only 10% of those executed by surgeons had a similar outcome[14]. This finding is consistent with other studies, which reported higher rates of morbidity and mortality on prehospital procedures[20-23]. Because of this, there are authors who suggest cricothyrotomy should notbe performed on a prehospital setting, and patients should be ventilated with bag valve mask until arrival at the nearest trauma center.

However, this contradicts the results of the case series published by Spaite *et al* (1999), in which he demonstrated that only 12.5% of the prehospital cricothyrotomies performed by paramedic personnel evolved with major immediate complications. In his study, however, paramedics were submitted to yearly training and to strict supervision of physicians through mobile devices[11]. The nearness of the professional with the procedure, the anatomical points of reference and the different clinical scenarios that he/she could come across, are therefore essential to the reduction of short- and long-term complication rates.

The long-term complication most frequently reported, as expected, was subglottic stenosis, cited in two of the five studies that included patients' follow-up[8,12]. Yet, in general, long-term complications were rather infrequent, ranging from zero to 5.26%, notably lower than the short-term complication rates. One could thereby infer that post-cricothyrotomy adverse events are mainly self-limited or present a satisfactory outcome after a brief intervention, not leaving sequelae. This inference cannot, however, be validated by the present review, since the follow-up time of the majority of the series included might have been excessively short for the long-term complications to fully manifest themselves. It is known that subglottic stenosis has an insidious presentation, and in accordance to this, the two series that reported this complication were the ones that followed up the patients for longer time.

As an important limitation, our review presents the reduced number of included studies. Even though we have chosengeneric search terms, comprised simply by the name of the procedure and its synonyms, very few studies matched our selection criteria, pointing out to the scarcity of published studies about this theme.

The small number of procedures per study also hampered the achievement of consistent conclusions. Such caveat was foreseen and expected, as emergency cricothyrotomy is a procedure of exception, used as a last resource to obtain airway patency[3].

Also to be considered are the limitations inherent to the study design. None of the included studies was prospective, multicentric and randomized. Most were case series, so that the quality of evidence obtained prevents categorical recommendations. This was already anticipated, since ethic and legal issues involving the management of critically-ill patients

impose profound methodological restrictions on studies about emergency cricothyrotomy, as mentioned by another review[4].

The low level of evidence of the included studies does not permit deeming emergency cricothyrotomy a safe long-term airway. The assembled data suggests, though, that the procedure's long-term severe complications, notably subglottic stenosis, are not as frequent as surmised. Controlled, prospective studies with a larger sample are necessary to elucidate whether emergency cricothyrotomy can be considered a safe definitive airway.

R E S U M O

A cricotireoidostomia, por ser um método rápido e, em geral, realizado com sucesso em ambientes pré e intra-hospitalares por profissionais treinados, tem sido amplamente preconizada como a via aérea cirúrgica inicial diante da situação "impossível intubar, impossível ventilar" e é especificamente útil quando a obstrução das vias aéreas ocorre na glote ou em nível supraglótico. Seu uso prolongado é, contudo, controverso. Nesta revisão procuramos avaliar as complicações da cricotireoidostomia de emergência, bem como, a necessidade rotineira de sua posterior conversão para traqueostomia através de pesquisa de estudos publicados sobre cricotireoidostomia de emergência nas bases de dados *PubMed*, *LILACS* e SciELO, sem restrição quanto ao ano de publicação. Assim foram identificados 791 estudos, dos quais 20 foram selecionados para leitura do texto integral, e, destes, nove foram incluídos nesta revisão. A taxa de complicações em curto prazo variou de zero a 31,6%, e a de complicações em longo prazo variou de zero a 7,86%. A estenose subglótica foi a principal complicação em longo prazo, relatada em 2,9 a 5% dos procedimentos. A taxa de conversão para traqueostomia variou de zero a 100%. Apesar da incidência reduzida de complicações em longo prazo o baixo nível de evidência dos estudos revisados não permite recomendar a cricotireoidostomia como uma via aérea definitiva segura.

Descritores: Cartilagem Cricoide. Manuseio das Vias Aéreas. Cuidados de Suporte Avançado de Vida no Trauma. Medicina de Emergência Baseada em Evidências.

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INSTRUCTIONS FOR AUTHORS

SCOPE AND POLITICS

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Tables and figures should be numbered with Arabic numerals, with captions on the top containing one or two sentences, and explanations of symbols at the bottom. Cite the tables in the text in numerical order including only information necessary for understanding of important points of the text. The data presented should not be repeated in graphs. Tables should follow the above-mentioned Vancouver standards.

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ABOUT THE JOURNAL

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Objectives: To disseminate scientific works of the surgical area of medicine that contribute to its teaching and development.

History: The publication and dissemination of scientific activities of its members is one of the aims of medical societies. The Brazilian College of Surgeons (Colégio Brasileiro de Cirurgiões – CBC), founded in 1929, already in its first statute provided for the issuance of the "Bulletin of the Brazilian College of Surgeons" as its official division, whose starting number was published in January 1930.

In 1967, the National Directory of CBC changed its name to "Journal of the Brazilian College of surgeons", which, however, went on to be published without due regularity. From 1974 on, the journal began to be published bi-monthly, on a regular basis, to the present day.

In these more than 40 years of uninterrupted publication, the Journal of the CBC gained importance and scope. With standards and criteria for selection and publication of scientific articles in the area of General and specialist Surgery, including "peer review", the Journal of the CBC falls along the lines of the main international journals and has an Editorial Board that evaluates the merits for publication of submitted manuscripts.

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