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PATIENT PERCEPTION ON THE ACCOMMODATION SERVICES PROVIDED BY PUBLIC HEALTH FACILITIES IN TIMIS COUNTY



CIPRIAN BOGDAN, ADINA BUCUR

University of Medicine and Pharmacy Victor Babes Timisoara

ABSTRACT

Patients, as healthcare services consumers with limited knowledge on the medical process, consider quality as "getting better health and satisfaction", an entirely dissimilar vision to that of professionals and governments.

Studies assessing patient satisfaction revealed that quality is primarily for them a matter of accommodation services and technical endowment of healthcare facilities, followed by interpersonal relationships and, eventually, by professional competence. Since the patients, as all the other consumers, are not a homogenous group, their judgments on quality vary depending on personal characteristics and degree of consistency between provided and expected services.

The aim of this paper is to assess patients' addressability and accessibility to hospital units in Timis County, as well as their satisfaction regarding accommodation services and technical endowment of these facilities.

Method: In order to apply the questionnaires for patients, we have selected public hospitals in Timis County, except for children's and psychiatric ones. We have applied a non-probability sampling method, namely the fixed quota method, the monthly number of hospital admissions in each hospital being known. An average of 11.959 patients per month resulted from the total number of admissions in all the studied hospitals, from which we have calculated, by the means of SPSS 17.0 programme, a sample of 373 patients, with a +/-3% error. The questionnaires were distributed among hospitals based on their proportion from the total number of admissions in all the studied number of admissions in all the studied nospitals. The questionnaire comprised 22 preformed response questions, while four were open-ended questions. Questionnaires were applied during 2013 year.

Results: Female gender represented the greatest proportion of admitted patients (fig. 1), with people between 41-50 years being the best represented age group, while two aggregated age groups (51-60 years and 61-70 years) were approximately equal with the 31-40 years age group. Sixty-eight percent of patients considered the access to the hospital they have chosen was easy, and only 32% encountered problems. Ninety-one percent of patients were prior hospitalised in the same facility, as those hospitals are located in their town of residence, being thus the first choice in emergency situations, but also following recommendation of medical personnel in the outpatient setting. Patients' own choice for the same hospital was seen in only 42% of cases. Most patients consider the accommodation in the health facilities as good and very good. However, most of them are dissatisfied and very dissatisfied with hospital rooms and adjacent areas hygiene. Quality of meals provided by health facilities is low, which was negatively judged by the hospitalised patients. Regarding the general evaluation of the hospital, most patients proved to be dissatisfied and very dissatisfied. Provision of information by authorised personnel and ease of access to information is deemed by 86% of patients as unsatisfactory.

Conclusions: Most patients show their dissatisfaction in the general evaluation of the hospital they were admitted in, mainly because of the lack of information, the quality of meals and hygiene provided by the health facility where they were hospitalised.

The choice of the same healthcare facility is mostly due to the lack of alternatives and the need to solve their personal health issues.

Key words: quality management, healthcare services consumers, patient satisfaction

Correspondence to:

Adina Bucur University of Medicine and Pharmacy Victor Babes Timisoara Phone: +4 0723786442 E-mail address: adina.bucur@gmail.com Quality of healthcare is differently viewed by each of the players involved in health services: government, patients, professionals, and healthcare organisations management^[1,2].

Hence, from *the government's and third-party payers'* point of view, quality is associated with *effectiveness and appropriate use of resources*. This view seems to also be embraced, on the whole, by the managers of healthcare facilities, giving them an image of competence and excellence^[3].

Healthcare professionals (medical personnel) are a less homogenous group than funders. Physicians, as they are deeply involved in defining and assessing healthcare quality, are more concerned with *professional competence* and physical means adjusted to processes (technical endowment) and their consequences on patients' health^[4,6]. It is noticed that physicians tend to give greater importance to technical competence while neglecting the role of interpersonal relationships that we could call interpersonal competence^[5,7].

Some studies showed that these dimensions can be separately assessed as well, but experts have came to the conclusion that *the simplest and less expensive way to assess the quality of health services is to measure patients' satisfaction*^[8,9].

This assertion is consistent with the idea behind the most accepted definition of quality, regardless of type of services: *quality is satisfying the customer needs*.

Patients, as healthcare services consumers, having limited knowledge on the medical process, consider quality as *"getting better health and satisfaction"*, a completely dissimilar vision to that of professionals and governments^[10].

Studies assessing patient satisfaction revealed that quality is primarily for them a matter of accommodation services and technical endowment of healthcare facilities, followed by interpersonal relationships eventually, by professional and, competence. Since the patients, as all the other consumers, are not а homogenous group, their judgments on quality vary depending on personal characteristics and degree of consistency between provided and expected services^[11,12]. Eighty-eight percent of patients were admitted to hospital based on referral by family or specialist physician and only 12% through the emergency room^[12,4].

The aim of this paper is to assess patients' addressability and accessibility to hospital units in Timis County, as well as their satisfaction regarding accommodation services and technical endowment of these facilities.

METHOD

In order to apply the questionnaires for patients, we have selected public hospitals in Timis County, except for children's and psychiatric ones. We have applied a non-probability sampling method, namely the fixed quota method, the monthly number of hospital admissions in each hospital being known. An average of 11.959 patients per month resulted from the total number of admissions in all the studied hospitals, from which we have calculated, by the means of SPSS 17.0 programme, a sample of 373 patients, with a +/-3% error. The questionnaires were distributed among hospitals based on their proportion from the total number of admissions in all the studied hospitals. The questionnaire comprised 22 preformed response questions, while four were open-ended

during 2013 year.

Hospital	Patient percentage
County Clinical Emergency Hospital Timisoara	29.59%
City Clinical Emergency Hospital Timisoara	22.69%
Obstetrics-Gynaecology Clinical Hospital Timisoara	5.41%
Pneumo-phtisiology and Infectious Diseases Clinical Hospital	4.66%
Timisoara	
Cardiovascular Diseases Institute Timisoara	4.69%
Railway Hospital Timisoara	4.65%
Military Hospital Timisoara	5.55%
City Hospital Faget	3.81%
City Hospital Sannicolau Mare	5.41%
City Hospital Jimbolia	3.68%
City Hospital Deta	2.76%
City Hospital Lugoj	7.79%

Table I. Distribution of patients in the sample who received questionnaires

RESULTS

The questionnaires were randomly distributed to in-patients in the Timis County public hospitals.

We have analysed for this paper those questions highlighting patients' accessibility to the hospitals they have chosen and their opinions regarding the accommodation services they have benefited from in the respective healthcare facilities. Female gender represented the greatest proportion of admitted patients (fig. 1), with people between 41-50 years being the best represented age group, while two aggregated age groups (51-60 years and 61-70 years) were approximately equal with the 31-40 years age group.



Figure 1. Distribution of in-patients by gender



Figure 2. Distribution by age groups

Sixty-eight percent of patients considered the access to the hospital they have chosen was easy, and only 32% encountered problems.



Figure 3. Patients' perception on hospital access

Ninety-one percent of patients were prior hospitalised in the same facility, as those hospitals are located in their town of residence, being thus the first choice in emergency situations, but also following recommendation of medical personnel in the outpatient setting.



Figure 4. History of admissions in the same healthcare facility

Patients' own choice for the same hospital was seen in only 42% of cases.



Figure 5. Patients' choice for the same healthcare facility

Eighty-eight percent of patients were admitted to hospital based on referral by family or specialist physician and only 12% through the emergency room.



Figure 6. Types of patient admission

Most patients consider the accommodation in the health facilities as good and very good.



Figure 7. Opinions on accommodation services in healthcare facilities

However, most of them are dissatisfied and very dissatisfied with hospital rooms and adjacent areas hygiene.



Figure 8. Room hygiene

Quality of meals provided by health facilities is low, which was negatively judged by the hospitalised patients.



Figure 9. Meals quality

Regarding the general evaluation of the hospital, most patients proved to be dissatisfied and very dissatisfied.



Figure 10. General evaluation of hospital

Provision of information by authorised personnel and ease of access to information is deemed by 86% of patients as unsatisfactory.



Figure 11. Access to requested information

DISCUSSIONS

The first barometer regarding citizens' opinion on the status of Romanian healthcare system was conducted in 2002, with emphasis on access to healthcare services, both in urban and rural areas^[13]. In 2003, the questions relating to health issues from people's perspective, the ways by which the health system might address those issues, the degree of awareness of new structures and mechanisms involved by the introduction of health insurance system in Romania, the degree of insurance and healthcare services covering, and the barriers to access to healthcare services were reiterated.

In the 2006 opinion barometer, answers to questions regarding hospital hygiene and meals provided to patients showed that 9.9% and 3.4% of patients, respectively, consider these should be changed^[14]. In our study, 55% are dissatisfied with hospital hygiene and 64% with the quality of meals. On the opposite, regarding the

CONCLUSIONS

Most patients show their dissatisfaction in the general evaluation of the hospital they were admitted in, mainly because of the lack of information, the quality of meals

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accommodation (room appearance, furniture), 74% declared themselves content, in accordance with the national study that found 8.7% of patients would change these features..

and hygiene provided by the health facility where they were hospitalised.

The choice of the same healthcare facility is mostly due to the lack of alternatives and the need to solve their personal health issues.

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MALE CIRCUMCISION: A REVIEW OF RECENT DATA CONCERNING THE EFFECTS OF THE PROCEDURE ON SEXUAL TRANSMITTED DISEASES AND SEXUAL FUNCTIONING



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ABSTRACT

Male circumcision is a surgical procedure performed on a large scale for cultural, religious and medical reasons, consisting in removal of the foreskin, with consequent penile glans exposure. Even if the procedure is employed for thousands of years, the benefits and the risks of circumcision are still subject to intense debate in the medical world. While, recently, it has been proved that the procedure determines a decrease in the risk of HIV infection and also reduces the risk of developing penile squamous cell carcinoma, the relation between circumcision and the risk to acquire sexual transmitted infections is still subject to debate. With respect to sexual function, the effects of removing the foreskin on the sensibility on the glans and on the sexual act in itself are still now well established. The article is focused on presenting the recent data in the medical literature regarding this subject. **Key words:** circumcision, HIV infection, sexual dysfunction

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INTRODUCTION

The foreskin protects the sensitivity of the penian glans and defends it from various irritating agents such as urine, feces or mechanic external factors (1). Circumcision is, as generally accepted in present days, the surgical removal of the prepuce with penile exposure of the glans. Circumcision can also be encountered in females, in certain African cultures with customs of ritual genital mutilations. While in males circumcision is limited to the removal of the foreskin covering the glans, in females ritual circumcision covers an extremely wide range of interventions, from the removal of the prepuce of the clitoris to the total excision of the clitoris or even the excision of the clitoris associated with the narrowing of the vaginal introitus (infibulation) (2)

Circumcision has been practiced for approximately 5000 years in Western Africa and for almost 3000 years in the Middle East (3). It was also used in Ancient Greece and Rome (4). The reasons for circumcision are usually religious, cultural or medical. In present days, al global scale, approximately 25% of the male individuals are circumcised (3). In the United States approximately 80% of the male newborns are circumcised; the percentage varied between 60% and 80% during the last decades (3); a study conducted by Introcaso and published in 2013 analyzed the data from the National Health and Nutrition Examination Surveys 2005-2010 and estimated prevalence the а of circumcised males aged between 14 and 59 years of 80.5% (5). It is also considered that approximately 110 millions of women are circumcised globally, most of them being found in Equatorial Africa; 90% of the women in Somalia and only 10% of the women in the Arab countries are circumcised (2).

Circumcision complications include cutaneous infections, edema, incomplete excision associated with scarring of the residual prepuce skin, stenosis, bleeding, keloid formation and anesthetic risk, and are estimated to approximately 5.1% (6,7). Even rarer complications have also been described, such as penile elephantiasis or penile gangrene (8,9)

THE EFFECTS OF MALE CIRCUMCISION ON THE RISK OF CONTRACTING SEXUAL TRANSMITTED DISEASES (STDs)

Circumcision as a protection factor against HIV infection.

Male circumcision decreases the risk of HIV infection, herpes simplex 2 virus infection, human papilloma virus (HPV) infection and reduces the risk of the female partner of the circumcised male to develop bacterial vaginosis, trichomoniasis and HPV infection, decreasing, as a consequence, her risk of developing cervical cancer (10). Three randomized studies were conducted to establish the efficiency of male circumcision in the transmission of HIV.

A first study conducted in South 2005 Africa in included 3274 uncircumcised males aged between 18-24 years, randomized into two groups; the participants from the first group were circumcised at the beginning of the study, while the male sublects from the second group were circumcised at the end of the study (month 21). The study was interrupted at month 18 for ethical reasons, when the data analysis showed a protection rate against HIV infection of 60% in the circumcised subjects group, as compared to the control group (11).

A study conducted by Kisumu, Kenya, and published in 2007 included 2784 males aged 18 to 24, divided into two groups: one group in which the male participants were subjected to circumcision (n=1391) and a control group composed of uncircumcised male subjects (n=1393), subsequently followed at months 1, 3, 6, 12, 18 and 24. Adverse reactions of the procedure were encoutnered in 1.5% of the circumcised males, all of these reactions being self-limiting. An HIV infection rate of 2.1% (95%CI 1.2-3.0) was observed in the circumcised group, as compared to an infection rate of 4.2% (95% CI 3.0-5.4) in the control group (p=0.0065). The study was ceased for ethical reasons, considering the high rate of the infection among the uncircumcised subjects. The protection against HIV infection rate was calculated to approximately 60%, the study concluding that the circumcision intervention has an important protective role and should be included in the panel of protective measures against HIV. (12).

In the same year, a study performed on 4996 uncircumcised HIV-negative males aged 15 to 49 years, randomized into a group of subjects who were circumcised (n=2474) and a control group where the circumcision was postponed (n=2522) showed a periprocedural adverse reaction rate of 3% in the circumcised individuals and a protection rate against HIV infection of 55% (13).

Therefore, a WHO release in 2007 recognizes male circumcision as an effective approach to reduce the risk of HIV infection and admits the introduction of this procedure among other well-established anti-HIV strategies (14).

World Health Organization and Joint United Nations Program on HIV/AIDS intend to achieve an 80% rate of male circumcision in the countries endemic for HIV virus infection (10). At present, the American Academy of Pediatrics also recognizes the benefits of the procedure and recommends it (10), while in the 70s, in lack of solid evidence to support the benefits of the procedure, the American Academy of Pediatrics has opposed to routine circumcision and, in 1989, adopted a neutral position towards the intervention, in the light of new evidence to support its advantages (3). Podder et al. consider, after the analysis of mathematical dynamic transmission modeling, that even though the procedure does not exclude risk of HIV infection, the the combination represented by circumcision and antiretroviral treatment is even more efficient in reducing the HIV reservoir in the population than the combination represented by circumcision and the use of condoms (15).

As a result of reducing the risk of HIV infection and therefore decreasing the costs necessary to diagnose and treat the affliction, male circumcision is considered to be cost-effective (16).

However, the exact mechanism through which male circumcision prevents HIV infection is still subject to debate. Szabo and Short have asserted that Langerhans cells from the prepuce could represent an entry portal for HIV, especially since the prepuce skin is extremely thin (17), while White et affirm that Langerhans cells al. produce a substance - langerin- which inhibits HIV infection (18). Nowadays, it is considered that the existence of a wider prepuce surface with a thin epithelium, especially since this area is rich in Langerhans cells that capture the HIV virus and then present it to the T-lymphocytes, an area frequently exposed to mechanic trauma during sexual intercourse, represents a risk factor to develop HIV infection (19).

Some authors are concerned that risk compensation might occur as a result of HIV prevention technologies, including circumcision. In their opinion, circumcision has the potential to lower perceptions of risk regarding HIV infection and circumcised men might have a high risk sexual behavior, a particular concern being a decrease in the use of condoms. As a result, their risk of acquiring ulcerative sexually transmitted infections, such as herpes simplex 2 virus, would increase and, as a result, the risk of acquiring HIV would increase (20, 21). Recent studies however, showed that circumcised males understand that circumcision only offers partial protection against HIV and, according to them, there is little suggestion of risk compensation following circumcision (22).

Circumcision effects on the decrease in the risk of other STDs.

Howe shows in a meta-analysis that there exists no real correlation between circumcision and the risk of infection with non-HIV sexually transmitted disorders (syphilis, gonorrhea, chancroid) (23). Other studies also support this idea; thereby, a study published in 2009 shows that male circumcision does not decrease the risk of infection with Neisseria gonorrhoeae (24).

Circumcision may also be practiced a treatment method for certain as dermatologic disorders, such as lichen fact, sclerosus; in phimosis (impossibility of mechanical retraction of the prepuce) exclusively appears in uncircumcised males, and so does (defined paraphimosis as the impossibility to reduce a proximally positioned foreskin over the glans) (25). Furthermore, circumcision determines the healing of the affliction in over 75% of the cases, even though recurrences of lichen sclerosus on the glans of the penis are possible (25). Lichen sclerosus evolves towards squamous

cell carcinoma in 5.8% of the cases; the evolution is slow, the mean latency period until the appearance of a squamous cell carcinoma being around 17 years (26).

Circumcision reduces the risk of genital squamous cell carcinoma in males.

Together with maintaining a proper local hygiene, giving up smoking and protection against HPV, circumcision contributes to a reduction in the risk for penile cancer (27). Penile cancer is extremely rare in circumcised A systematic individuals. review conducted by Larke et al. in 2011 showed that men who were circumcised during childhood/adolescence present a lower risk for penile cancer as compared to individuals who were circumcised during adulthood; it is possible that these results might be a consequence of the fact that circumcision at a younger age prevents phimosis development (28). Also, precarious genital hygiene, a risk factor for penile squamous cell is more carcinoma, frequently uncircumcised encountered in individuals (26%), as compared to the circumcised ones (only 4%) (27).

Moreover, *circumcision reduces the risk of urinary tract infections in children*, especially in the ones who are predisposed to the affliction; however, circumcision should not be routinely performed for this purpose, because, statistically, at a population level, a numeber as high as111 circumcisions would be necessary to prevent a single inferior urinary tract infection in predisposed children (29).

CONTROVERSIES REGARDING THE EFFECTS OF CIRCUMCISION ON SEXUAL FUNCTION

The sensibility of the foreskin and its erogenous importance is another subject to intense controversy. A metaanalysis performed by Morris and Krieger and published in August 2013, which included 2675 publications regarding the effects of circumcision on sexual function, showed that circumcision does not impair sexual functionality, sensibility, sexual sensations and/or sexual satisfaction (30).

However, Bronselaer et al showed, in a study published in the that included same year 1059 uncircumcised male participants and 310 circumcised male subjects that the preputial skin plays a very important role in the sexual act. Circumcised individuals reported a decrease of sexual pleasure and intensity of the orgasm; also, they reported that a greater effort is necessary to reach orgasm and an important percentage of the circumcised respondents accused irritation sensations, pruritus and paresthesia of the glans; postpubertal circumcised men reported a decrease in the sexual pleasure as compared to the prepubertal circumcised men and a higher rate of unpleasant sensations on glans and the shaft of the penis (31).

A study performed by Kim et al in 2007 which included 373 sexually active men of whom 138 were sexually active before circumcision, 117 were circumcised but not sexually active before circumcision and 118 were not circumcised, showed that there was a decrease in the masturbatory pleasure and sexual enjoyment after 63% circumcision and of the

CONCLUSIONS

Circumcision is a procedure performed on a large scale for cultural, religious and medical reasons. The procedure determines a decrease in the risk of HIV infection; since the procedure not devoid from is complications, it should only be performed on a large scale in countries where HIV infection is endemic. While it has been proven that circumcision

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respondents reported an increased masturbatory difficulty. (32) However, prior studies that recorded the sensibility of the glans showed that there existed no significant differences between circumcised and uncircumcised individuals (33).

In respect to the adulthood psihosexual impact of performing circumcision in the phallic period (3-6 years), no negative effects were recorded, as shown by Armagan et al. in a study published in 2013; no significant differences were reported with respect to orgasm, erectile response, satisfaction succeeding sexual act between the individuals circumcised in the phallic period of development as compared to the ones circumcised outside of this age period (34). Hoschke et al also showed that male circumcision is not associated with a higher prevalence of erectile dysfunction (35). As for circumcision effects on premature ejaculation, it seems like the risk of premature ejaculation is higher in male individuals who were circumcised after the age of 7 years (36).

reduces the risk of developing penile squamous cell carcinoma, the relation circumcision and the between acquire possibility to sexual transmitted infections is still subject to debate. With respect to sexual function, the effects of removing the foreskin on the sensibility on the glans and on the sexual act itself are still subjects to controversy in the medical world.

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PREDICTION OF TREATMENT POSSIBILITIES IN INTERVERTEBRAL DISC DEGENERATION



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ABSTRACT

One of the first degenerative diseases of the lumbar spine is the subchondral sclerosis from which other degenerative complications can occur. The subchondral sclerosis is associated with obesity, high body fat index and high stress on the vertebral spine. This paper presents a fuzzy inference system based prediction and a fuzzy expert system that predicts the optimal treatment of a patient suffering with intervertebral disc degeneration. The expert system correlates the body mass index (BMI) with the body fat (BF) percentage and the daily activity expressed by the consumed calories. In total 60 inference rules were created and the first results present a correlation of 0.91 with the results from the control group. Using this system a compliant patient can avoid serious spinal cord problems. The system infers three possible actions: 1) spinal cord surgery, 2) medication combined with exercises and 3) no action needed. The system takes in consideration the age and sex of the patient, a pain intensity parameter, the metabolic rate of the patient and mobility parameters measured by Zebris Mobility system. In total 243 rules have been formulated but only 21% of the rules suggest surgery. The initial results are promising; there is a correlation of 0.83 between the control results and the results from the system.

Key words: Expert system, prediction, subchondral sclerosis, lower back pain, medication, surgery, fuzzy systems, quality of life

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Dr. Diana Andrei PhD student Address: "Victor Babeş" University of Medicine and Pharmacy, Timisoara, Romania E-mail address: <u>andreidiana81@gmail.com</u> Intervertebral disc degeneration is characterized by dehydration of the pulposus nucleus and annulus fibrosus wear as a result of multiple mechanical and biochemical factors. A number of degenerative changes can be described as processes of destabilization followed by re-stabilizing processes.

Initially, the lesions of annulus fibrosus result in the loss of the pulposus nucleus contention ability. The internal concomitant changes of pulposus nucleus the lead to obstruction of the joint space and to a reduced loading capacity of that segment. The vertebral nuclear material is not firmly contained within the intervertebral disc and will migrate in the direction of least resistance, which is usually towards posterior or posterolateral.

This migration leads to a "prominent" or "encapsulated hernia" of the annulus fibrosus towards the vertebral hole or root canal. If the means of the ring contention lose their stability, the nuclear material can herniate. This is the so-called "real hernia" or "non encapsulated hernia". (1,2)

It is important to note that both types of hernia are the result of a degenerative process. In a disc that has not suffered degenerative from processes, the rupture after a trauma typically occurs at the cartilaginous vertebral plaque level; a normal intervertebral disc, which is traumatized, will rarely herniate (3). After internal disjunction of the intervertebral disc, the loss of the disc height and the reduction of the annulus fibrosus stabilization capacity represent the main mechanisms through which the stability of the mobility segment affected is (segmental instability) (4). As a result of this situation, on the margins of the vertebral body and the vertebral arch there is a process of reactivate bone formation that leads to the classic radiologic appearance of osteophytosis and subchondral sclerosis (5).

Essentially, an early diagnosis, a compliant patient and a competent physician can substantially influence of the result disease ("disease outcome") and its quality of life (6-9). The treatment remains at the boundary between internal medicine, surgery, medical rehabilitation and requires knowledge of pathogenesis and the natural development of osteonecrosis. The therapeutic option depends upon disease stage, which can be best assessed by further investigations (10, 11). Typically, patients with lumbar disc herniation are treated in a conservative way (12). However, medical treatment alone only helps some patients for several years. The recoverv treatment should be considered in the surgical therapy context, preceding it and continuing it, adapted in scale and intensity to the degree of suffering evolution/ severity and to the evolutionary stage and context term, psychological, social, family, educational, professional or associated pathology of each case (13). Pre and postoperative recovery is a clear advantage compared to recovery only in terms of pain and functionality control. The fundamental idea on which we rely in specialized assistance for the recovery of patients with osteonecrosis surgery or not are, for them at the moment and in the future, it will be possible to "normal life", fulfilled and independent.

The question is why do we want a soft prediction? That soft prediction system is necessary For a more accurate diagnosis and a quicker and safer decision of a certain treatment.

AIM AND OBJECTIVES

The main objective of this study is to make a correct and accurate diagnosis in patients with degenerative spine injuries that require surgical treatment. Another objective is to compare BMS, daily activity, lumbar spine mobility (flexion, extension and rotation measured by Zebris) and pain

questionnaire.

MATERIAL AND METHODS

1.Fuzzy inference system:

Fuzzy logic extends the Boolean logic by introducing a degree of uncertainty (14). The fuzzy logic maps a numerical to a linguistic value. This is fuzzy done using membership functions which indicates a degree of appurtenance to a fuzzy set. A degree of 1 indicates a full membership to the fuzzy set and a degree of 0 indicates that the element is not part of the fuzzy set. The Fuzzy logic allows a partial membership that takes on a value between 0 and 1.

The fuzzy inference system is constructed form four major parts: the fuzzification system which converts the numerical data in linguistic data, the linguistic variables, the inference rules data base which infer a result and the defuzzification process.

The fuzzy inference rules are created in such a manner that they will cover as many possible options as they can. These rules are very similar to the natural language communication. They can be compared with instructions coming from one person to another. In their general form they have an antecedent and а consequence separated by the "THEN" statement. The antecedent is a conjunction of several fuzzy terms (using the statement IS) and several logical operators (AND, OR, NOT) between them.

For example: "IF LV1 IS FS1 AND LV2 IS FS3 AND LV3 IS FS2 THEN R1 IS FS2"

Our system bypasses the defuzzification process and gives the result in linguistic form. The used inference system is a Sugeno type inference system (15) because the system returns 2 crisp possibilities: healthy patient or predisposed patient.

By changing the linguistic variables and inference rules we have made 2 prediction systems. One prediction system infers the possibility of appearance of the subchondral sclerosis based on clinical data and the second inference system to predict using Para-clinical data if the patient how suffers from low back pain needs a surgery or not.

2. BMI (Body Mass Index)

Body Mass Index is an internationally accepted weight indicator that is used to classify weight stages at adults (16). It is calculated using the following formula:

BMI = m/h^2 (1)where *m* is the mass of the patient in kg and *h* is the height of the patient in meters.

Table 1.	BMI	categories
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ivii cutegories	
Classification	BMI value
Underweight	<18.50
Normal range	18.50 - 24.99
Overweight	≥25.00
Obese	≥30.00

BMI values are independent of age and sex. However, BMI may not correspond to the same degree of fatness due, to different body proportions. The health risks associated with increasing BMI are continuous and the interpretation of BMI grading in relation to risk may differ for different populations.

2.2. BF (Body Fat)

The body fat percentage of a human or other living being is the total mass of fat divided by total body mass. Body fat percentage index includes essential body fat and storage body fat. Essential body fat is a type of fat that is necessary to maintain life functions. The percentage of essential fat is 3–5% in men, and 8–12% in women. Storage body fat is the accumulation of adipose tissue, which partially protects internal organs in the chest and abdomen and partially creates weight problems. The body fat percentage is a measure of fitness level; it is the only body measurement which directly calculates a person's relative body composition without regard to height or weight. The BF percentage is in relation with the BMI (17).

Table 2. The formula's that are used to calculate the BF percentage are the following

Deurenberg formula(18) #1:	Adult Body Fat % = (1.20 x BMI) + (0.23 x Age) - (10.8 x gender) - 5.4
Deurenberg formula(19) #2:	Adult Body Fat % = (1.29 x BMI) + (0.20 x Age) - (11.4 x gender) - 8.0
Gallagher formula(20):	Adult Body Fat % = (1.46 x BMI) + (0.14 x Age) - (11.6 x gender) - 10
Jackson-Pollock formula(21):	Adult Body Fat % = (1.61 x BMI) + (0.13 x Age) - (12.1 x gender) - 13.9

where BMI is the calculated body mass index, the Age is the age of the patient and gender is for male = 1 and female = 0.

A BF percentage of 25% for men and 30% of BF for women can be

considered as the lowest point for obesity.

RESULTS

Case study one: Detection of the subchondral sclerosis

1.1 The fuzzy inference rules

To detect the subchondral sclerosis 4 linguistic variables were defined. One of the variables describes the sex of the patient and three of the variables describe the physical constitution of the patient using the BMI (Body Mass Index) (22), BF (Body Fat Index) (23) and the daily burned calorie

The linguistic variables are constructed according to the following list:

- SEX: Male Female represented by singletons;
- BMI: 0-18 Underweight, 18–25 Normal, 25-29 Overweight And 30-50 Obese
- BF: 0-10 Low, 10-20 Normal, 20-30 Medium, 30-60 High;
- Calories: 1500-1800 Low, 1700-2500 Normal, 2400-4000 High;

Except for the sex, each linguistic variable is constructed using trapezoidal membership functions. In this case study 60 rules were computed taking in consideration the relation between the BMI and the BF (24).

Several of the inference rules are presented below:

IF SEX IS MALE AND BMI IS UNDERWEIGHT AND BF IS LOW AND CALORIES ARE HIGH THEN PREDISPOSITION IS HIGH

IF SEX IS MALE AND BMI IS OBESE AND BF IS MEDIUM AND CALORIES ARE HIGH THEN PREDISPOSITION IS HIGH

IF SEX IS MALE AND BMI IS NORMAL AND BF IS NORMAL AND CALORIES ARE NORMAL THEN PREDISPOSITION IS LOW

44 of the rules indicates the need to start an early prevention if the there is no LBP and 16 of the rules indicates a healthy patient. The clinical trial of the system is a work in progress and is developed in Visual Studio.NET 2013 using C# language and the AForge.NET open source software platform (25).

1.2 The results:

The test was realized using a group of 201control patients. Form the group 147 patients are diagnosed with subchondral sclerosis and the rest were healthy patient. A comparison between the results of the control group assessed by the MD and the assessment of the same group made by the fuzzy system is presented in Figure 1 In 5 situations there was a difference between the results of the control group and the fuzzy system. In 2 situations the fuzzy system indicated that a diagnosed patient is healthy and in 3 cases indicated that a healthy patient will develop subchondral sclerosis.



Figure 1. Initial results of the fuzzy prediction system, Results: 1-predisposition, 0- healthy patient

These differences appeared in patients that were at the limit of overweight and high BF percentage. The correlation index between the results of the control group and fuzzy system is 0.91. The clinical testing of the systems is in progress, but the initial results are encouraging.

Case study two: treatment prediction in low back pain

2.1 Linquistic variables and inference rules:

In our case we have used 7 linguistic variables. Two of the variables describe the demographic data of the patients described by the sex and age, two variables describe the quality of life by the mean of the pain questionnaire and the consumed calories and the rest describe the range of motion measured with the ZM.

The linguistic variables are constructed according to the following list:

• SEX: MALE – FEMALE represented by singletons;

• AGE: TEEN 10-18, YOUNG 17-32, ADULT 30-60, OLD 58-100;

• PAIN: 0-20 LOW, 18-40 MEDIUM, 38-50 HIGH;

• CALORIES: 1500-1800 LOW, 1700-2500 NORMAL, 2400-4000 HIGH; • FLEXION: 60-80 LOW, 78-92 NORMAL, 90-100 HIGH;

• EXTENSION: 10-20 LOW, 18-30 NORMAL, 28-40 HIGH;

• ROTATION: 15-30 LOW, 28-45 NORMAL, 43-60 HIGH;

Except for the sex each linguistic variable is constructed using trapezoidal membership functions.

In our case 243 rules were computed. Several of the inference rules are presented below:

IF AGE IS ADULT AND SEX IS MALE AND FLEXION IS LOW AND EXTENSION IS LOW AND ROTATION IS LOW AND CALORIES IS HIGH AND PAIN IS NORMAL THEN OPERATION

IF AGE IS ADULT AND SEX IS MALE AND FLEXION IS LOW AND EXTENSION IS LOW AND ROTATION IS NORMAL AND CALORIES IS HIGH AND PAIN IS LOW THEN MEDICATION

IF AGE IS ADULT AND SEX IS MALE AND FLEXION IS LOW AND EXTENTION IS NORMAL AND ROTATION IS NORMAL CALORIES IS NORMAL AND PAIN IS LOW THEN HEALTY

51 of the rules send the patient to operation and 159 rules indicates the

need of medical recovery by treatment and 33 rules indicates a healthy patient.

2.2 The results of the prediction:

The first test of the system was realized using a group of 26 control patients. All patients were adults, 16 male and 10 female patients with divers' numerical results. The results are presented in Figure 2.



Figure 2. Initial results of the SpineFIS system, Results: 1-surgery, 2-medication, 3-healthy patient

In two situations the FIS suggested that surgery is preferred instead of medication and in one situation FIS suggested to start the

medication in a healthy individual. There is correlation of 0.88 between the results of the M.D. and the results of the SpineFIS.

CONCLUSIONS

The system has the ability to identify the adequate treatment in patients with degenerative disc pathology. With this software we can ensure the quality of the treatment and

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the quality of life. The patients will follow a correct treatment and will return quickly to an independent and fulfilling life.

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BUTYRYLCHOLINESTERASE, DIFFERENTIATION FACTOR BETWEEN BENIGN PROSTATIC HYPERPLASIA AND PROSTATIC ADENOCARCINOMA



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ABSTRACT

Prostate tissue is under the action of androgen hormones, noradrenergic nerve endings and cholinergic receptors.

Purpose: The purpose of this paper was represented by the investigation of acetylcholine status in patients with prostatic pathology with highlighting the correlations between cholinergic imbalances and inflammatory process and the degree of disease activity assessed by the level of prostate specific antigen.

Material. Method: The present study was performed on a prospective analysis of patients with prostatic pathology between 2011-2013. The study included 84 normal weight men with adequate nutritional status without treatment administered in the last two months in which acetylcholine was assessed by determining the status of butyrylcholinesterase activity.

Results: There were obtained statistically significant differences between groups with prostate diseases and the control group, concerning creatinine, C reactive protein, prostatic specific antigen and butirylcholinesterase. Statistically significant changes were obtained in the butyrylcholinesterase activity between benign prostatic hyperplasia and prostate cancer (p < 0.05). A special attention was given to the existant relationship between serum changes in butyrylcholinesterase activity and creatininemia, between butyrylcholinesterase and C reactive protein levels between butyrylcholinesterase and prostatic specific antigen.

Conclusions: These results draw attention to the fact that butyrylcholinesterase could be a possible factor in differentiating patients with benign prostatic hyperplasia of those with prostate cancer.

Key words: benign prostatic hyperplasia, prostatic adenocarcinoma, butyrylcholinesterase, prostatic specific antigen, tumorigenesis

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Dr. Ene Cosmin Address: Urology Department, "Sf. Ioan" Hospital,. Sos.Vitan-Barzesti 13, Bucharest Phone: +4 0721182156 E-mail address: cosmin85_ene@yahoo.com The prostate is a gland on which acts several types of mechanisms. Prostate tissue is under the actions of androgens, noradrenergic nerve endings and cholinergic receptors.

There were studies that appeared constantly that evaluated the effect of cholinesterase inhibitors in benign prostatic hypertrophy (BPH). BPH is characterized by decreased availability of acetylcholine in the prostate tissue, blocking enzymes of metabolism, being a method of increasing the level of secondary, acetylcholine and of cholinergic activation, by relieving symptoms benign in prostatic hyperplasia.

Cholinergic fibers innervate both bladder (detrusor muscle of the and prostate. Distigmina, bladder) inhibitor of cholinesterases, is one of many molecules being evaluated for the treatment of BPH in patients with impaired detrusor bladder. Some studies indicate significant а improvement in urinary flow in patients with BPH, other ones indicate significant systemic side effects of this type of treatment (bradycardia tachypnea, pulmonary edema). These substances act through acetylcholine at the level of the five subtypes of muscarinic receptors (M1-5). Muscarinic receptors are G protein coupled receptors and are activated by the action of acetylcholine. They can be grouped into Gq/11 protein coupled receptors that act via inositol phosphate, such as receptors type M1, M3 and M5 and receptors coupled to Gi/o protein acting via inhibition of adenylate cyclase, such as M2 and M4 receptors. In prostatic glandular epithelium, the action of cholinergic system on muscarinic receptors occurs on the secretion of prostatic fluid [1].

In the prostate, the studies on several animal species, including humans, have shown an important cholinergic action on prostatic glandular component and a weaker action in the prostate stromal component with physiological variations from species to species [2].

The existence of cholinergic innervation in the prostate, is linked in studies with many immunohistochemical presence of the enzyme that degrades acetylcholine, named acetylcholinesterase. This enzyme doesn't have a high specificity due to the fact that it is also found in the nerve fibers, and in the cholinergic system. There are markers such as choline acetyltransferase or vesicular acetylcholine transporters that have a higher specificity for cholinergic system, but have been rarely used in the human prostate. In the cultures of prostatic cells, in prostatic stromal tissue, it was determined by PCR, mRNA only for muscarinic receptors type M2, M3 and M4, with the predominance of M2 receptor at this level of the prostate. The M2 receptor is the most abundant in the prostate and mediates decreasing of cAMP accumulation [3]. In prostatic epithelium it was determined mRNA for M1, M3 and M5 receptors. Compared to the number of adrenergic receptors, studies have shown a higher prevalence of muscarinic receptors both in the normal prostate and prostatic adenoma, more pronounced in prostate epithelial tissue. This location is different from that of the alpha - receptors, which are found in a more important extent at the stromal level and in blood vessels. Also, some studies have shown the involvement of receptors M1, M2, M3 in the process of oncogenesis [4], with a greater density of M3 receptors in tumors, where it can stimulate the proliferation and division of prostatic cell lines [5]. Acetylcholine can be binded on M3 receptors

in the tumor and is produced by tumor cells that stimulates in this way the growth of the tumor, existing at this level there is an increase in the level of M3 correlated with VEGF (also

known being implicated as in neovascularization and in tumor development) [6,7]. On the other hand, the receptor type M 2 can be found in prostatic stromal level, even in a higher density in the normal prostate gland and is involved in the secretory and contractile function of the prostate. The M1 receptor type has been studied in animals and was observed an involvement in mediating the neurotransmition of acetylcholine and of carbachol in muscle tissue of the prostate, with assumptions that a similar action occurs in the human prostate in glandular epithelium, where it is mostly located [8, 9].

The role of muscarinic receptors in the prostate is to response to signal transmission (increased intracellular Ca or inhibiting cAMP), smooth muscle contraction or prostatic growth.

At the cellular level, there are several models of action of cholinergic system:

Calcium is released from intracellular stores under the action of phospholipase C, involving Gq/11 protein in the signaling model for the receptors type M1, M3, M5. Calcium the bladder from enters the extracellular to intracellular space through voltage-gated Ca channels. Several studies have shown increases of the Ca when muscarinic receptor are stimulated in an agonist way in the prostate and, there are assumptions that it would stimulate prostatic secretion.

cAMP inhibits prostate contractility are inhibited on Gi protein activation, representing the signaling pathway for M2, M4 receptors.

MATERIAL AND METHODS

This study was based on prospective analysis of patients with prostatic pathology between 2011-2013. Were included in the study 84 normal weight men with adequate nutritional status without treatment administered Muscarinic receptor agonists inhibit the formation of cAMP, which leads to the stimulation of prostate contractility. This contractile mechanism of the prostate has proven its function in different animal species (mice, guinea pigs), but it was poorly functional in human level and totally dysfunctional in patients with prostatic adenoma.

At the tissue level , muscarinic receptors are located in the nerve endings where controls the release of acetylcholine and norepinephrine. Acetylcholine produces a significant contractile response in the prostatic capsule, the response being inhibited by parasympatholytics like atropine [10]. There are substances such as acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) which are anticholinergic, preventing binding of acetylcholine at nerve endings. Studies have shown the presence of hydrophilic monomers of AChE or BChE in the hyperplastic prostate tissue, respectively in neoplastic tissue, but without significantly influencing of the level by histological type of prostatic tissue changes. Moreover, AChE and BChE are also found in seminal fluid and sperm fluid in a major amount, their enzyme activity decreasing proportionally with the quality of sperm fluid [11].

The purpose of this paper is the investigation of acetylcholine status in patients with prostatic pathology and highlighting the correlations between cholinergic imbalances and the inflammatory process, respectively, the degree of disease activity assessed by prostate-specific antigen level.

in the last two months grouped as follows:

- 30 patients diagnosed with benign prostatic hyperplasia (BPH);
- 24 prostate adenocarcinoma (ADK);

• 30 healthy volunteers without prostate dysfunction (control).

All participants at the study entry signed an informed consent according to the declaration of Helsinki.

There were excluded from the study the patients with: malignant diseases, inflammatory diseases, renal failure, nervous anorexia, parenteral and enteral nutrition, liver diseases, AIDS, metabolic syndrome, or obesity.

There were no cases of exclusion from the study because of the compliance of the patients.

RESULTS

Investigation of serum activities of the BChE in patients with prostate diseases and in the control group required selection of similar groups of study with the same demographic and biological characteristics. The analysed groups (benign prostatic hyperplasia, prostate cancer and control group) are similar in terms of age, lifestyle, blood pressure, hemoglobin and glucose concentrations, the tests of liver function, as well as lipid profile (Table 1). There were obtained statistically significant differences between groups with diseases of the prostate and the control group concerning creatinine, CRP, PSA and BChE (Table 1). As compared to control (0.78 \pm 0.1 mg / dl) serum creatinine was elevated in patients with BPH $(1.47 \pm 0.54 \text{ mg} / \text{dl})$, p <0.05) and also in patients with prostate cancer $(1.53 \pm 0.46 \text{ mg} / \text{dl}, \text{p})$ <0.05). Compared to the values obtained from the control (0.26 ± 0.26) mg / dl), CRP was elevated, with statistical significance in patients with BPH (0.38 ± 0.31 mg / dl, p < 0.05) and in patients with prostate cancer (0.89 \pm 0.81, p < 0.05). The variation of CRP presents а statistical significance between patients with BPH and ADK (p < 0.05). As compared to control (0.87 ± 0.87 ng / ml), PSA was elevated in patients with BPH $(3.77 \pm 0.25 \text{ ng} / \text{ml})$ p <0.05) and also in patients with prostate cancer (8.36 \pm 6.35, p <0.05).

All patients were examined clinically and at the laboratory at the enrollment.

The performed laboratory bioassays were: complete blood count, lipid profile, liver function tests, blood sugar, kidney tests, tests of inflammation, PSA.

Acetylcholine was assessed by determining the activity of butyrylcholinesterase (BChE) by standard spectrophotometric methods. All clinical and laboratory data were statistically processed (SPSS software).

Statistically significant differences were obtained for PSA between BPH and ADK groups (p <0.05).

Compared with the control group $(5728 \pm 1107 \text{ U} / \text{ l})$ there were obtained low serum values for butyrylcholinesterase activity in patients with BPH (5249 \pm 1102 U / l, p <0.05) and ADK (4028 ± 865 U / l, p < 0.05). Statistically significant differences were obtained in the butyrylcholinesterase activity between benign prostatic hyperplasia and ADK (p <0.05) (Figure 1).

A special attention was given to the existant relationship between seum variations of butyrylcholinesterase activity and creatininemia (Figure 2), between the BchE level and CRP (Figure 3), between BChE and PSA (Figure 4).

In normal serum creatinine (0.6 to 1.3 mg / dl), there was no significant relationship between BChE activity and creatinine in any of the studied groups. For creatinine values ranging from 1.3 to 2.0 mg / dl and BChE, it was obtained a weak negative correlation in patients with BPH (r = -0.17, p = 0.05), and a strong negative correlation in patients with ADK (r = -0.52, p < 0.05) (Table 2).

For values of CRP smaller than 0.30 mg / dl, there was no significant relationship between serum CRP and BChE activity. For the range 0.31-0.6

mg / dl of CRP, it was a negative correlation statistically significant between CRP and BChE in patients with BPH (r = -0.37, p <0.05) and in patients with ADK (r = -0.48, p <0.05). For CRP >0,60 mg/dl, it was observed a negative correlation, statistically significant between CRP and BchE in patients with HBP (r=-0,54, p<0,05) and also for patients with ADK (r= -0,72, p<0,05) (Table 3). In PSA serum level ranged between 0.0 to 1.0 ng / ml and 1.01 to 4.0 ng / ml and serum BChE activity there was no relationship in patients with BPH, even in those with ADK. Between PSA values > 4 ng / ml and the activity of BchE it was obtained as a statistically significant negative correlation both in patients with BPH (r = -0.14, p <0.05) and ADK patients (r = - 0.19, p <0.05) (Table 4).

Table 1. Clinical parameters and laboratory parameters in patients with prostate diseases and control

Variables	BPH (n=30)	ADK (n=24)	Control (n=30)
Age	57,3±8,2	59,2±9,1	58,9±8,5
Smoker/Non-smoker	5/25	6/19	4/26
Alchool/ Non-alchool	3/27	2/22	3/27
Systolic tension (mmHg)	133,2±2,1	131,1 ± 2,6	137,3±1,9
Diastolic tension (mmHg)	61,2±1,0	67,4±1,3	69,4±0,7
Haemoglobin (g/dl)	13,9±1,2	14,3±1,4	14,1±1,1
Glycemia (mg/dl)	87,9±11,1	79,4±10,3	84,2±8,7
Creatinine (mg/dl)	1,47±0,54 ¹	1,53±0,461	0,78±0,1
AST (U/l)	22,8±6,1	25,1±5,3	22,8±4,5
ALT (U/l)	19,6±5,8	22,5±6,3	18,3±4,1
Triglicerides (mg/dl)	88,3±15,8	79,9±11,2	84,7±16,3
Cholesterol (mg/dl)	161,4±27,2	156,3±31,1	161,9±24,5
CRP (mg/dl)	0,38±0,31	0,89±0,811,2	0,26±0,26
PSA (ng/ml)	3,77±0,251	8,36±6,35 ^{1,2}	0,87±0,87
BChE (U/l)	5249±11021	4028±8651,2	5728±1107

1 – p< 0,05 statistical significative variation between BPH and control, respectively between ADK şi control;

2 – p< 0,05 statistical singnificative variation between ADK and BPH;

AST – aspartat aminotransferase; ALT – alanin aminotransferase; CRP – C reactive protein; PSA – prostatic specific antigen; BChe – butirilcholinesterase; HBP – benign prostatic hyperplasia; ADK – prostate cancer;



Figure 1. Graphical representation of BChE (U/l) in patients with benign prostatic hyperplasia (BPH), prostatic cancer (ADK) and control (p<0,05)

Study group	Variables	Creatinine (mg/dl)	
		0,6-1,3	1,31-2
	n	30	-
Control	r	0,14	-
	р	0,92	-
	BChE (U/l)	5728±1107	-
	n	12	18
BPH	r	0,10	-0,17
	р	0,28	0,05
	BChE (U/l)	5597±972	5018±1106
	n	5	19
ADK	r	-0,08	-0,52
	р	0,04	0,00
	BChE (U/l)	4625±411	3869±1403

Table 2. Corelations between BChE and creatininemia in patients with prostatic diseases and control

BChE - butirilcholinesterase; HBP – benign prostatic hyperplasia; ADK – prostate cancer; n – number of cases; r – correlation coefficient; p- threshold of statistical signification;



Figure 2. Graphical representation of BChE (U/l) depending on seric concentration of creatinine (mg/dl) in patients with benign prostatic hyperplasia (BPH), prostatic cancer (ADK) and control

Studiy group	Variables	CRP (mg/dl)		
		0,0-0,3	0,31-0,60	>0,60
	n	24	6	-
Control	r	0,10	0,19	-
	р	0,89	0,33	-
	BChE (U/l)	5736±1099	5699±430	-
	n	11	14	5
BPH	r	0,26	-0,37	-0,54
	р	0,61	0,04	0,00
	BChE (U/l)	5711±1080	5081±812	4693±432
	n	4	9	11
ADK	r	-0,19	-0,48	-0,72
	р	0,09	0,04	0,00
	BChE (U/l)	4782±207	4207±688	3625±512

Table 3. Corelations between BChE and CRP in in patients with prostatic diseases and control

CRP – C reactive protein; BChE - butirilcholinesterase; BPH – benign prostatic hyperplasia; ADK – prostate cancer; n – number of cases; r – correlation coefficient; p- threshold of statistical signification;


Figure 3. Graphical representation of BChE (U/l) depending on seric concentration of CRP (mg/dl) in patients with benign prostatic hyperplasia (BPH), prostatic cancer (ADK) and control

Table 4. Corelations between BChE and PSA in patients with prostatic diseases and control

Studiy group	Variables	PSA (ng/ml)		
		0,0-1,0	1,01-4,0	>4,0
	Ν	24	6	-
Control	R	0,04	0,09	-
	р	0,89	0,41	-
	BChE (U/l)	5799±1100	5429±211	-
	n	2	19	9
BPH	r	0,01	-0,14	-0,27
	р	0,99	0,16	0,05
	BChE (U/l)	5811±119	5482±1117	4799±706
	n	-	5	19
ADK	r	-	-0,19	-0,44
	р	-	0,07	0,00
	BChE (U/l)	-	4502±108	3901±1103

PSA – prostatic specific antigen; BChE - butirilcholinesterase;HBP – benign prostatic hyperplasia; ADK – prostate cancer; n – number of cases; r – correlation coefficient; p- threshold of statistical signification;



Figure 4. Graphical representation of BChE (U/l) depending on seric concentration of PSA (ng/ml) in patients with benign prostatic hyperplasia (BPH), prostatic cancer (ADK) and control

As mentioned in the introduction, the cholinergic system is well represented in the prostate. There are a number of reports which have noted the existence of cholinergic fibers in the prostate and in the urinary bladder detrusor muscle, the presence of muscarinic and adrenergic receptors glandular (M1-M5), in prostatic epithelium, the existence of cholinergic innervation in the glandular and stromal component of the prostate, the presence of cholinacethyltransferase activity in the prostate stroma. Cholinesterase activity (AChE and BChE) was detected in the prostate tissue, in spermatic fluid and seminal fluid, influencing the number and the motility of spermatozoons.

In assessing the cholinergic imbalance in patients with prostate diseases, the authors started from the premise that butyrylcholinesterase activity may be useful in identifying patients with BPH and ADK.

Investigation of butyrylcholinesterase activity in patients with prostate diseses and control, showed a low levels of enzyme activity in patients with BPH, respectively with ADK versus control (p < 0.05) (Table 1). IT was obtained statistical significant differences of BchE activity between patients with BPH and ADK (p < 0.05) (Figure 1). These results draw attention to the fact that BChE could be a possible factor in differentiating between patients with BPH and ADK.

Other experimental results presented this study, which in reconfirm the possible involvement of cholinergic stimulation the in pathophysiology of BPH and ADK are the negative correlations obtained between the BChE activity and creatinine level (Table 2), between BChE and CRP (Table 3) between BChE and PSA (Table 4). As a result, a significant decrease in the activity of BChE was observed in chronic inflammatory conditions in patients with BPH and ADK (Figure 3). CRP evolves with low BChE activity. An important reduction of BChE activity was recorded in patients with elevated PSA (Figure 4). These findings seem to be in agreement with the hypothesis that a reduction in the activity of BChE, coupled with increasing the amount of acetylcholine, may be associated with the prostate tumorigenesis. There are recent reports suggesting that cholinergic stimulation participates in uncontrolled growth of skin tumors [14,15].

For a correct interpretation of variations inBChE activity, the authors recommend the establishment of reference intervals for a control group, similar to groups with prostatic pathology as age, habitat, food habits, anthropometric characteristics, with haematological and biochemical common values (Table 1).

For sustaining this observation, we bring a series of arguments showing that a large number of factors affect the activity of BChE [14-21]. It is known that BChE [1,3,8,12,16,19] is a glycoprotein encoded by the genes located on chromosome 3 (3q26.1 -3q26.2), with half-lives of 12 days, which is not inhibited by high А concentrations of acetylcholine. of studies have number noted associations between BChE activity and the parameters: cholesterol, next triacylglycerols, transferrin, albumin, prealbumin, C - reactive protein, retinol binding protein, interleukin- 6 (IL-6), tumor necrosis factor alpha (TNF alpha), insulin , HOMA - R , C peptide, stress, inflammation, Gleason score, the number of total lymphocytes aminotransferases, the blood. in glutamyl transpeptidase, complement C3, IgA titer, magnesium ion, mercury, cadmium, copper, zinc, aluminum. Changes in the serum BChE are also caused by anabolic steroids, carbamates, cimetidine, cyclophosphamide, estrogens, glucocorticoids, neostigmine, oral

CONCLUSIONS

The results obtained in this study showed low levels of cholinesterase activity in patients with prostate pathology and significantly different values between patients with BPH and ADK. The level of BChE activity was influenced by CRP and PSA. The

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authors attributed to BchE a possible role in differentiating patients with BPH of those with ADK.

Conflict of interests: There is no conflict of interests between the authors.

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RECENT ADVANCES IN THE MODERN TREATMENT OF PSORIASIS VULGARIS: THE USE OF BIOLOGICALS



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ABSTRACT

Psoriasis is a chronic recurrent dermatosis characterised by well-defined infiltrated erythematous papules and plaques, covered by thick white to yellowish scales occurring mostly on the elbows, knees, sacral area and scalp. It is a physically, emotionally and socially invalidating disorder which affects 1-2% of the population. Traditional topical agents are cosmetically unacceptable, messy, treatment administration is time consuming and are associated with low adherence to treatment. Systemic treatments on the other hand are limited by side effects, incomplete effectiveness and demanding treatment schedules, resulting in decreased patient compliance. As a result of continuous progress and advances in molecular biology of psoriasis, biologic treatments, designed to block specific molecular steps in the pathogenesis of psoriasis were developed. An overview of these new therapeutic agents is vital for the dermatologist in order to master the whole spectrum of modern therapeutic measures that could be employed in psoriasis treatment.

Key words: psoriasis, biologicals, TNF-a blockers

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Mircea Tampa MD, PhD Address: Sos. Mihai Bravu 281, 3rd District, Bucharest, Romania Phone: +4 0726382600 E-mail address: tampa_mircea@yahoo.com Psoriasis is a chronic recurrent dermatosis characterised by a T-cellmediated inflammatory reaction and subsequent epidermal hyperproliferation, leading to welldefined infiltrated erythematous papules and plaques, covered by thick white to yellowish scales affecting mostly the elbows, knees, sacral area and scalp; however, quasitotal skin surface involvement is not rare, as well as joint and nail involvment [1].

In ancient times, the disease was confused with leprosy and with other scaly eruptions, hindering the development of an adequate treatment. [2, 3] The Papyrus of Ebers, written around 1500BC, describes the earliest topical treatments for skin disorders, including psoriasis, which had not yet been separated from other skin conditions. It consisted in concoctions with cat and dog faeces and mixtures of onions, sea salt, urine, goose oil, semen, and wasp's droppings in milk of sycamore. [2, 4]. Another treatment for psoriasis, used even from prebiblical times, was exposure to sunlight. It was then noted that what people at that time considered as "leprosy" improves after sun exposure. It is now believed that at least some of those patients had, in fact, psoriasis. [3] Galen (AD 133-200) recommended a soup made from boiled vipers as a remedy for the disease. [2, 4].

Other historical treatments for psoriasis included Fowler's solution (potassium arsenite, 1% KAsO₂ in aqueous solution), green rays (ultrasoft X-rays or Bucky rays), sulphur, chrysarobin, pyrogallol, β -naphthol, injections of adrenal cortical extracts, fever induction, intramuscular injections of milk and fat-free diets. [2, 3]

At present, a repertoire of therapies is available for the treatment of psoriasis, both topical and systemic. Therefore it is important to individualise the treatment depending on the patient's measurable severity of the illness and on his own perception of the disease. [3, 5]

The topical treatment at present times consists in keratolitycs (salicylic (cignolin), acid. urea), anthralin vitamin D analogues, corticosteroids, retinoids, topical coal tar and emollients. They have the advantage of low risk of systemic side effects but patients often find these topical agents cosmetically unacceptable, messy, and administration time treatment consuming. In spite of literature data about topical treatment adherence being scarce and very heterogenous, non-compliance is usually reported in most studies around the value of 40%. [1, 3, 5, 6]. A systematic review conducted by Devaux et al. in 2012 showed also that not only the adherence of psoriatic patients to topical treatment is low, but the doses of topical agents employed in the treatment by patients are less with one to two thirds of the dose prescribed by the dermatologist; usually adherence issues were encountered more frequent in young patients, in male patients, in patients with early onset of the condition and in individuals with higher self-assessed severity [7, 8].

Phototherapy, the treatment of the condition by skin exposure to ultraviolet (UV) light, is a first line treatment in moderate to severe psoriasis, either as monotherapy or in combinations with various topical and/or systemic agents. There are many types of phototherapy: natural sunlight, UVB phototherapy, photochemotherapy (PUVA), photodynamic treatment, excimer laser and/or narrow-band UVB. It is however associated with an increased risk for skin cancer, which recent systematic reviews proved to be more significant for PUVA therapy; even if the lack of prospective studies in patients following narrow-band UVB impedes the correct assessment of carcinogenicity of this treatment, a reasonable concern accompanies this therapeutic method, also. [1, 3, 5, 6, 9].

Systemic treatment in psoriasis is indicated in patients with severe forms of disease (erythrodermic, pustular or psoriatic arthritis), when topical treatment failed or when the lesions are physically, socially or emotionally invalidating. [10]

Methotrexate is the main antipsoriatic drug and its effectiveness has been proven in over 30 years of experience. (braunfalco) It is indicated for long-term management of severe forms of psoriasis. However, it has been associated with hepatotoxicity, hematopoietic suppression and digestive side effects. Therefore, a complete blood count, hepatic and renal function testing need to be performed regularly. [5, 10]

Systemic retinoids can be also used in severe forms of psoriasis. They are contraindicated in pregnancy because of their teratogenicity. The side effects include dry lips, skin xerosis, hair loss, elevated cholesterol and triglyceride levels and abnormal liver function tests. [6]

Unlike methotrexate and retinoids, cyclosporine does not alter keratinocytes'proliferation directly, but inhibits IL-2 production by T helper lymphocytes and the release of various cytokines, resulting in decrease of the recruitment of antigen presenting cells to the epidermis [11]; the drug can be employed in severe forms of psoriasis but it is not recommended for long term treatment because it has been associated with an increased risk of skin non-melanoma cancer; the carcinogenic risk is furthermore increased in patients following PUVA therapy. The main problems cyclosporine poses treatment are nephrotoxicity and arterial hypertension. Therefore laboratory assessment should include creatinine levels prior to treatment and regularly afterwards on the duration of the therapy. [5, 6]

Conventional systemic treatments are limited by side effects, incomplete effectiveness and demanding treatment schedules, resulting in decreased patient compliance.

As a result of continuous progress and advances in molecular biology of psoriasis, new agents, designed to block specific molecular steps in the pathogenesis of psoriasis were developed. [5] They were called biologic therapies and, in order to understand how they work, it is important to look over the main cytokines involved in the pathogenesis of psoriasis.

CELLULAR AND MOLECULAR BASIS OF THE PATHOGENY OF PSORIASIS

Large numbers of CD4⁺ and CD8⁺ T-cells are found in the epidermis and dermis of a psoriatic lesion. CD4+ Th1 cells are mostly found in the dermis and produce INF-y. Activated T-cells and dendritic cells produce TNF-a. INF-y amplifies the production of IL-23 in the dendritic cells and IL-23 expands subsets of CD4+-T cells subsets (Th17 and Th22), which produce interleukin IL-17, IL-21 and IL-22, with an important role in maintaining inflammation. IL-17 plays an important role in neutrophil chemotaxis and angiogenesis, IL-21 is involved in naïve

T cells differentiation to Th17, while IL-22 acts as an important agent leading to hyperproliferation of the keratinocutes [12, 13].

CD8⁺ cells, mostly located in the epidermis of the psoriatic lesion, produce IL-17, IL-22 and INF- γ , which promote the production antimicrobial peptides hBD-2, chemokines, growth factors (TGF- α , AREG, IL-19, IL-20), therefore promoting epidermal hyperplasia and activation of the keratinocyte innate defense response. Keratinocites produce IL-7 and IL-15 which influence the turnover of CD8 cells and IL-8 which increases production of $INF-\gamma$ by T cells and

attracts neutrophil granulocytes to epidermis. [5, 6].



Figure 1. Molecular and cellular network and pathways involved in psoriasis pathogenesis; Th: T helper lymphocyte; IFN: interferon; TNF: tumor necrosis factor; IL: interleukine; PMN: neutrophils; K: keratinocyte (authors'schematic representation)

The biologic agents used in psoriasis can be categorised as agents inhibiting T-cells (*efalizumab, alefacept*), agents inhibiting tumor necrosis factor alpha TNF-a (e.g. *infliximab, adalimumab, etanercept*) and IL-12 and IL-23 blockers (*ustekinumab*). [14]

1. Agents inhibiting T-cells

Efalizumab is a humanised monoclonal antibody to the subunit of the integrin LFA-1 (CD11a) and was used to treat severe and therapy refractory forms of psoriasis. It targets pathogenesis at multiple psoriasis levels, by inhibiting the T-cell the lymph activation in nodes, presenting binding of the T-cells to endothelial cells and blocking trafficking of T-cells from the circulation into the psoriatic skin. In 2009 it was taken off the market after 3 cases of progressive multifocal leukoencephalopathy (PML) were reported. PML is а serious demyelinating disease of the central nervous system produced by John Cunningham virus (JCV), a type of human polyomavirus usually affecting immunocompromised patients. [15, 16]

Alefacept was the first biologic introduced for the treatment of moderate to severe psoriasis. It is a human fusion protein combining the Fc portion of the human IgG1 and LFA-3 (lymphocyte-function-associated antigen-3) located on antigenpresenting cells. It blocks the activation of T cells and induces apoptosis of memory T cells. Clinical trials showed a PASI75 of 28% of treated patients. Studies show that it is the least prescribed biologic agent. [17, 18, 19]

<u>2. TNFa inhibitors</u>

TNFα inhibitors have been approved in Europe for the treatment of adults with moderate to severe plaque type psoriasis for whom phototherapy or conventional systemic treatments have been inadequate or inappropriate.

In Romania patients who have a medical insurance can benefit from

biologic therapies (Infliximab, Adalimumab, Etanercept) through the National Programme for Psoriasis free of charge, provided that they fulfil certain inclusion criteria, as follows:

- patient has been diagnosed with moderate or severe psoriasis
- previous standard treatment, including methotrexate and phototherapy have failed, are inadequate or inappropriate
- the patient is eligible for biologic treatment
- at least one of the following:
- development or high risk to develop toxicity to the treatment used and standard alternative therapies cannot be used;
- intolerance or contraindication of standard systemic treatments (acitretin, methotrexate, phototherapy);
- unresponsiveness to standard therapies (failure to achieve PASI 50 and improvement of the DLQI score of under 5 points after 3 months of treatment);
- the disease can only be controlled with repeated hospitalisations;
- comorbidities that exclude the use a systemic treatments;
- severe, unstable, critical disease; [20]

The choice of the biologic treatment depends on clinical manifestations of the disease, comorbidities and patients or doctors preference.

Infliximab is recombinant а immunoglobulin IgG1 chimeric antibody composed of human constant and murine variable regions that specifically blocks membrane-bound and soluble TNFa. [21] It helps control angiogenesis by down-regulating angiopoietin and its receptor and normalises hormone levels (eg, hypothalamic - pituitary - adrenal axis), thus decreasing inflammation. Infliximab normalizes keratinocyte differentiation and induces apoptosis of lesional keratinocytes therefore speeding up clinical improvement. [22]

Infliximab has been approved for the treatment of rheumatoid arthritis, ankylosing spondylitis, Crohn's disease, chronic ulcerative colitis, psoriatic arthritis and psoriasis. It has also been successfully used in several off label indications like hidradenitis supurativa, pityriasis rubra pilaris and pyoderma gangrenosum. [21]

The recommended regimen for Infliximab is 5 mg/kg body weight intravenous infusion, at weeks 0, 2, 6 and every 8 weeks thereafter and a clinically significant response is expected after 1-2 weeks. The expected response rate after 10 weeks of treatment is PASI 75 in approximately 80% of treated patients. [23]

Infliximab has the advantage of rapid and marked clinical efficacy. Its disadvantage consists in the chimeric structure which promotes formation of neutralising antibodies, associated with a decrease in long-term response to treatment. Concomitant administration of Methotrexate is recommended to decline neutralising antibody formation. [5]

It is contraindicated in patients who have a known active infection (viral, tubercular, bacterial or atypical), patients with class II/IV congestive heart failure, central nervous system demyelinating syndromes or current malignancy other than non-melanoma skin cancer. [24]

Adalimumab is a recombinant human immunoglobulin (IgG1)monoclonal antibody containing only human peptide sequences that blocks both soluble and membrane bound TNFa [25, 26]. It is indicated in the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis and Chron's disease. [27] It has been successfully used off-label for the treatment of hidradenitis suppurativa, pyoderma gangrenosum, sarcoidosis, vasculitis, pemphigus, systemic multicentric reticulohistiocytosis and aphthous stomatitis.

The recommended dosage of adalimumab in plaque psoriasis is 80 mg subcutaneously at week 1 followed by 40 mg every other week. [25]. The clinically significant response is expected after 4 weeks. Studies show a PASI 75 response rate of 53 to 80% after 12 to 16 weeks of treatment. [26]

Anti-adalimumab antibodies can occur with the treatment and several authors report that they are associated with lower serum concentrations of the drug and lack of adequate response. [28]

The use of Adalimumab is contraindicated in active tuberculosis, serious infections, reactivation of hepatitis B and moderate to severe heart insufficiency (NYHA III/IV) [25]

A study performed in 2013 by Gerd R Burmester et al, that included 23 458 patients from global clinical trials, aiming to analyse the long-term safety of the drug, showed that the most frequently reported adverse events were infections; the overall malignancy rates for the patients with psoriasis were similar to the ones expected for the general population; the incidence of non-melanoma skin cancer was raised; death rates were lower than or equivalent to those expected in the general population. [27]

Etanercept is a dimeric fusion protein consisting of the extracellular ligand-binding protein of the human 75 kDa (p75) tumour necrosis factor receptor linked to the Fc portion of a human IgG1. It inhibits the activity of TNF by competitively binding it, thus antagonizing interactions with TNF receptors cell surface, and on preventing activation of the inflammatory cascade. It prevents the binding of free, soluble TNFa but not that of membrane-bound TNFa. [29]

It is indicated in the treatment of rheumatoid arthritis, psoriasis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis

The recommended dosage for etanercept is 25 mg or 50 mg

subcutaneously twice a week. The clinically significant response is expected after 6-8 weeks. The expected response rate after 12 weeks of treatment is PASI75 in approximately 33% of patients treated with 50 mg weekly and 49% of patients treated with 100 mg/weekly. [30, 31]

It is the only anti-TNF agent licenced for the treatment of paediatric patients with psoriasis and juvenile idiopathic arthritis. [5, 14, 25]

Although anti-etanercept antobodies were detected in some patients, they were non-neutralising and their development was not correlated with decreased blood level of the drug or clinical efficacy. [33]

Etanercept is contraindicated in chronic, active, serious, and recurrent infection, active tuberculosis, hepatitis multiple sclerosis and В, other demyelinating disease, NYHA class III or IV congestive heart failure, pregnancy or lactation, and hypersensitivity to etanercept or its ingredients. [14]

<u>Safety issues concerning TNFa</u> <u>blockers</u>

Biologic therapies are usually well tolerated. However, like all drugs, these therapies can be associated with adverse reactions, some of them severe.

The most common adverse events for all biologic agents are injection site reactions (erythema, oedema, pruritus) and infections. [5, 14]

Serious infections due to bacterial, viral, mycobacterial, fungal or opportunistic infections have been associated with anti-TNF biologic use. Some studies showed an association between the initiation of biologics and the risk of herpes zoster. Therefore, the risk and benefits should be considered when prescribing biologic treatments to patients with recurrent infections or with an increased risk of infections (e.g poorly controlled diabetes) [5, 34, 35]

An increased risk for tuberculosis has also been reported in patients receiving biologic therapies. However, most cases develop in areas where the infection is endemic. It occurs shortly after the initiation of the treatment therefore suggesting a reactivation of a latent infection. Over 60% of the cases are extrapulmonary and 25% of the patients have a disseminated disease. The risk of tuberculosis seems to be higher in patients treated with Infliximb and Adalimumab than in those treated with Etanercept. [5, 35, 36]

The risk of malignancies has been reported in patients treated with biologic therapies. Although it is too early to make a definite conclusion, it seems like non-melanoma skin cancers are the most frequently encountered malignancies, followed by an increased risk of lymphoma [5, 35, 37]

The use of TNFa-inhibitors can lead to new onset or exacerbation of congestive heart failure in elderly patients. Demyelinating disease was associated with biologic therapies. Therefore, they should not be used in those patients or in first degree relatives of patients with demvelinating diseases, such as multiple sclerosis. [5, 14, 35]

As regard to the use of TNAainhibitors in pregnancy, the data from clinical studies to this point is insufficient to make a firm conclusion. A study that followed the outcome of 130 pregnancies in women with rheumatologic disorders who were treated with anti-TNF before or during pregnancy showed an increased risk of spontaneous abortion as compared to general population and a small number of congenital malformations. However, guidelines suggest that these drugs should be avoided during pregnancy. [38] In order to minimise the risk associated with the treatment, before prescribing biologic therapies the patients must be screened for latent tuberculosis, active infections including HIV, HCV, HBV, demyelinating disease, malignancy, congestive heart failure and pregnancy.

Patients should be monitored and re-evaluated every 3 months to decide if the treatment should be continued. The therapy is considered adequate if, after 3 months of treatment, the PASI score decreases with 50% and the DLQI score decreases with at least 5 points as compared to the initial moment. [20]

3. IL-12 and IL-23 blockers

Ustekinumab is an anti-IL12/23 kappa human monoclonal IgG1 antibody which targets the p40 subunit of IL-12 and IL-23, prevents their interaction with the receptor, thereby blocking subsequent signalling, differentiation and cytokine production. [39] It has been approved for the treatment of moderate to severe psoriasis in 2009.

The dosing regimen is 45 to 90 mg subcutaneously (depending on the body weight) at weeks 0, 4 and every 12 weeks after that.

A PASI 75 was achieved by 73.8% of patients receiving 45 mg and 67.5% of patients receiving 90 mg after 12 weeks of treatment.

The most common adverse reactions are upper respiratory tract infection, headache, nasopharyngitis, injection site erythema, and arthralgias.

Prior to treatment, patients should be screened for tuberculosis.

There is not enough data to establish the risk for malignancies and serious infections. [5, 14]



Figure 2. The administrations regiment for biologicals, from moment zero of treatment initiation (time is represented in weeks)

<u>Biosimilars in the treatment of</u> <u>psoriasis</u>

As the patent for many of the branded biologics will soon expire, generic versions of these agents will soon enter the market. [40]

According to the European Medicines Agency, a biosimilar is a biological medicine that is similar to another biological medicine that has already been authorised. [41]

Biosimilars are different from chemical generics because, while chemical generics have an identical structure to the original product, biosimilars are high molecular weight compounds with a fragile threedimensional structure, impossible to accurately reproduce since the manufacturing process of innovator

CONCLUSIONS

Psoriasis is a chronic, debilitating disease affecting approximately 2% of the population. During time, patients suffering from this condition were marginalised and stigmatised, as they were confused with lepers. Today, the disease remains physically, emotionally and socially invalidating. It is therefore important to develop specific new drugs to increase the quality of life of those patients; the products is a proprietary knowledge. During the manufacturing process, primary aminoacid sequences can become modified through glycosylation, changing the shape of a protein because of alterations in the way it folds. These alterations may significantly impact receptor binding, stability, pharmacokinetics and safety. [40, 42].

As to the cost of biosimilars, it is expected to be smaller than the cost of the original product. However, as compared to generics and their original products, the price difference between biologics and biosimilars is likely to be smaller because the production of biosimilars incurs higher research and development costs. [43]

regarding knowledge psoriasis pathogenesis improves rapidly, supporting the development of new agents, biological with increased tolerability and greater efficacy. An overview of these new therapeutic agents is vital for the dermatologist in order to master the whole spectrum of modern therapeutic measures that could be employed in psoriasis treatment.

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CLINICAL STATUS IN HEART FAILURE WITH PRESERVED EJECTION FRACTION



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ABSTRACT

Background : Quality of life is one of the important aspects in chronic pathologies. So far, therapeutic strategies have focused on improving paraclinical parameters and increasing survival. Heart failure with preserved ejection fraction (HFPEF) is a complex disease that adversely affects patient well-being.

Aim and methods : The aim of this study is to assess the quality of life in patients suffering from heart failure with preserved ejection fraction and to determine the extent to which this parameter is influenced by other clinical elements, comorbidities and paraclinical parameters. We included patients with a first diagnosis of heart failure were evaluated quality of life by Minnesota Living with Heart Failure questionnaire (MLHFQ), exercise capacity by 6 minutes walk test (6MWT), the risk of depression by scale of depression Fahrenberg. These parameters were reassessed after 1 year and compared with prognostic markers and with comorbidities. Were formed two groups: patients with HFPEF NYHA class II (group 1) and patients with HFPEF NYHA class III (group 2). The statistical methods used are Pearson's correlation coefficient and multiple linear regression.

Results : After one year of disease evolution, there is a much stronger correlation between the two clinical parameters, namely the quality of life and the exercise capacity ($r^2=0.431$, p<0.001), as compared with a weak correlation recorded at patient inclusion.

As predictors of quality of life were identified both clinical and paraclinical parameters: presence of diabetes (r = 0,43, p = 0,003) and risk of depression in group 1 and NT-proBNP value (r = 0,62, p < 0,001), presence of hypertension (r = 0,34, p = 0,04) in the group of patients in NYHA class III.

Conclusion : the evolution of heart failure with preserved ejection fraction patients' quality of life is correlated with the evolution of prognostic markers (proBNP and NT-proBNP) and, in disease evolution, with their exercise capacity.

Key words: quality of life, exercise capacity, comorbidities, prognostic marker

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Adina Bucur Address: University of Medicine and Pharmacy "Victor Babes", Timisoara Phone: +4 0723786442 E-mail address: <u>adina.bucur@gmail.com</u> Heart failure is a chronic disease that affects all aspects of patients' lives and impacts on the quality of life. Although its incidence is high, which involves increased costs in the healthcare system, current therapeutic strategies did not show significant improvement in the long-term prognosis of this pathology.(1)

Bv now, the therapeutic management goals in heart failure aimed at improving symptoms and prognosis. Improving patients' quality of life should be at least an equally important goal. Quality of life is one person's perception his/her on physical and psychical status. How the patient perceives his/her own health status is important in both disease evolution and patient's compliance to treatment. Many of the quality of life measurement tools are based upon a health status model primarily focusing on objective assessment methods, paying less attention to subjective assessment.

Moreover, not all the methods developed for research are easily applicable in the clinical setting. There

MATERIAL AND METHOD

is a growing interest in developing custom-tailored tools at the expense of standard ones. (2)

Recent studies revealed that a poor quality of life in heart failure patients is associated with unfavourable prognosis and survival reduction. These data particularly relate to patients with systolic dysfunction heart failure. (3, 4)

There are studies, however, proving that a poor quality of life does not always correlate with unfavourable prognosis of heart failure. (5) This is also possible since some of the quality of life assessment questionnaires used were not specific to a certain clinical pathology.

The aim of this study is to assess the quality of life in patients suffering from heart failure with preserved ejection fraction and to determine the extent to which this parameter is influenced by other clinical elements (NYHA class, exercise capacity), comorbidities and paraclinical parameters with proven prognostic role in heart failure with preserved ejection fraction.

Eighty-one patients admitted to Ascar Cardiology Clinic in 2011/2012 with clinical signs of heart failure and who received a primary diagnosis of heart failure with preserved ejection fraction were included.

> Inclusion criteria: Sinus rhythm

Clinical signs and symptoms of heart failure according to Framingham criteria

> $FE \ge 45 \%$ E/E' ≥ 15 Pro-BNP >150pg/ml Exclusion criteria: Atrial fibrillation

Acute coronary syndrome within the last 30 days

Cardiac stimulator pacemaker Severe valvular heart diseases Severe respiratory dysfunction Chronic kidney disease ≥4

KDOQI Mont

Mental disorders Cancer

All patients have signed the Informed Consent.

Quality of life was assessed by Minnesota Living with Heart Failure questionnaire (MLHFQ) and risk of depression was assessed by Fahrenberg scale.

Laboratory values were determined at hospital admission. BNP has been determined by MEIA Abbott method, NT-proBNP by Roche electrochemiluminescence.

Cardiac ultrasound assessment has been performed by the means of a Vivid S5 cardiac ultrasound system:

- assessment of LVTD, LVTS and LV wall thickness in M-Mode,

- measurement of ejection fraction by Simpson method,

- assessment of transmitral diastolic flow (E and A waves, e/a ratio, EWDT- E wave deceleration time, IVRT - isovolumetric relaxation time), assessment of pulmonary venous flow,

- tissue Doppler with recording of early and late diastolic mitral annulus velocities (E´ - maximum early diastolic velocity and A´ - maximum late diastolic velocity)

- assessment of left atrium dimensions- determination of LA area in apical 4-chamber

Minnesota Living with Heart Failure questionnaire and Fahrenberg depression scale were filled in by patients the day before discharge.

Minnesota Living with Heart Failure questionnaire comprises 21 items, each quantified on a 0-5 scale. Some of the items assess the physical status (8 items: 2-7, 12-13), while 5 items assess patient's emotional status (17-21).

At the same time, the risk of depression has been assessed by the means of Fahrenberg scale.

The 6-minute walk test (6MWT) was performed the day before discharge. The patient walked for 6 minutes on a flat surface at his own pace. Blood pressure and heart rate were measured before the test; if BP>180/100mmHg or/and HR>120b/minute, the test was not performed.

Twelve months after patients' inclusion, elements of clinical status (exercise capacity and quality of life), along with biological markers (proBNP, NT-proBNP) were assessed again. Cardiovascular and noncardiovascular cause admissions of patients were monitored within the same period of time.

Pearson's correlation coefficient and multiple linear regression have been used for the analysis of statistical series corresponding to the pair of statistical variables, the dependent variable being expressed as a linear combination of independent variables. The used algorithm was backward stepwise regression.

RESULTS

Two groups of patients have been formed, depending on NYHA class to which they were assigned at admission (47 patients in NYHA class II and 34 patients in NYHA class III). I must mention that none of the cases was assigned to NYHA I or IV classes of heart failure. Table 1 shows the main characteristics of the two groups. The distribution of patient by age groups is represented by fig. 1

Table 1. Characteristics of patient groups

	r		
	Group I	Group II	р
	N=47	N=34	
Age	66±9.8	68±8.1	0.33
Males	11 (23%)	11 (32%)	0.51
Ischemic cardiopathy	29 (62%)	23 (67%)	0.81
Hypertension	43 (91%)	32 (94%)	0.93
Diabetes	16 (34%)	10 (29%)	0.81
Obesity	25 (51%)	17 (50%)	0.89
Metabolic syndrome	26 (55%)	19 (56%)	0.89
Chronic kidney disease	13 (27%)	16 (47%)	0.10
Body mass index	32.2±4.9	30.6±5.8	0.18

GFR 1	80.7±52.4	65.0±24.0	0.10
BNP	428.75 ± 189.4	536.62±296.8	0.0495
NT-proBNP	1731.02 ± 751	908.29±499.85	< 0.0001
Minnesota score	45.58 ± 11.49	53.81±12.92	0.0034
M_e ²	11.34 ±3.81	14.12±3.66	0.0015
M_ph ³	18.93±7.44	22.72±7.78	0.0293
Walk distance 6MWT	263.39 ± 58.97	236.33±74.06	0.07
Depression score	7.73± 2.27	8.69±2.20	0.06
Readmissions	17 (36%)	24 (70%)	0.0052
FEVS	56.17±10.91	53.66±8.27	0.26

1: Glomerular filtration rate

2: *emotional score from MLHFQ*

3: physical score from MLHFQ



Figure 1. Distribution of patients by age groups

It can be seen that statistically significant differences in the value of diagnostic markers (pro-BNP and NTproBNP), quality of life scores as assessed by Minnesota questionnaire and number of readmissions were recorded between the two groups. A weak, inverse correlation with statistical significance (r^{2} - 0.184, p <0.001) has been evidenced at inclusion between the two markers of clinical status: quality of life and exercise capacity (fig.2).



Figure 2. Correlation between score of quality of life MLHFQ and walk distance at inclusion (6MWT)

A weak correlation ($r^2 = 0.189$) with statistical significance (p< 0.001) has been evidenced between quality of life Minnesota score and pro-BNP value (fig.3).



Figure 3. Correlation between Minnesota score of quality of life MLHFQ and pro-BNP value measured at *inclusion*

The same type of correlation ($r^{2}=$ 0.229) with statistical significance (p<0.001) has been evidenced between

Minnesota score and NT-proBNP value at inclusion (fig.4).



Figure 4. Correlation between score of quality of life MLHFQ and NT-proBNP at inclusion

One year after the inclusion, a strong, statistically significant correlation is seen between reevaluated quality of life, and pro- BNP (r^{2} = 0.559, p < 0.001) (fig.5) and NT - proBNP values (r^{2} = 0.439 and p<0.001) (fig.6).



Figure 5. Correlation between score of quality of life (MLHFQ 1) and pro-BNP after one year (pro-BNP1)



Figure 6. Correlation between score of quality of life (MLHFQ1) and NT-proBNP after one year (NT-proBNP1)

At inclusion, the exercise capacity, as assessed by 6 minute walk test, is in weak, inverse, statistically significant correlation with pro-BNP value (r^{2} = -0.273, p<0.001) (fig.7), while no correlation is seen between exercise

capacity and NT-proBNP value (r^{2} = -0.093).

One year after the inclusion, the direct correlation between Minnesota score and pro-BNP value is much stronger (r^2 = 0.559, p<0.0001) (fig.8)



Figure 7. Correlation between exercise capacity (6MWT) and pro-BNP, at inclusion



Figure 8. Correlation between quality of life (Minnesota1) score and pro-BNP (BNP1) after one year

The same situation in the case of correlation between Minnesota score

and NT-proBNP value after one year (r²=0.431 and p<0.0001).

As regards the exercise capacity assessed one year after, it does not correlated with the pro-BNP (r^{2} = 0.060 with p = 0.26) or NT-proBNP values (r^{2} = 0.03 and p =0.140).

After one year of disease evolution, there is a much stronger correlation between the two clinical parameters, namely the quality of life and the exercise capacity ($r^{2}=0.431$, p<0.001), as compared with a weak correlation recorded at patient inclusion.

At the one year re-evaluation, statistically significant differences can be seen between the two groups in the same parameters as at the time of inclusion. NT-proBNP value, depression risk score, assessed by Fahrenberg scale and emotional score from MLHFQ are the parameters with significant statistically differences between the two groups after one year, compared to the time of inclusion. (Tab. 2).

Table 2. Evolution of clinical and paraclinical parameters after 1 year in the two study groups

Comparison after 1 year	Group I	Group II	р
	N=47	N=34	
BNP	401.18±234.46	551±337.46	0.0208
NT-proBNP	1886.36±806.23	866.42±564.87	< 0.0001
-			
Minnesota score	46.97±19.61	57.93±19.53	0.0150
(MLHFQ)			
M_e	10.60±3.90	13.12±3.89	0.0052
M_ph	18.90±8.57	27.93±36.20	0.12
Walk distance (6MWT)	264.87±73.28	251.43±93.28	0.47
Risk of depression	7.40±2.83	8.53±1.66	0.0406
-			

By multiple regression analysis, having the quality of life score as variable dependent, the independent variables with predictive power at inclusion for the patients from the first group are: presence of diabetes mellitus ($r^2=0,43$, p=0,003) and the components of emotional and physical status ($r^2 = 0,75$, p<0,001) of the Minnesota questionnaire for assessing quality of life.

One year after the inclusion, predictor values for quality of life are: depression risk score and the two components for assessing the physical (Mph) and emotional (Me) status of the quality of life score (p<0,0001), as assessed by Minnesota questionnaire.

Regarding the NYHA III heart failure patients, predictors of the quality of life at study inclusion are pro-BNP and blood pressure values ($r^2=0,34$, p=0,04), as well as the components for assessing the physical (Mph) status of the quality of life score, as assessed by Minnesota questionnaire ($r^2=0,87$, p < 0,001).

Predictors of the quality of life for NYHA III heart failure patients one year after the inclusion are: NT-pro-BNP value after one year, emotional status component of Minnesota questionnaire for assessing quality of life and exercise capacity (fig.9).



Figure 9. Predictors of the quality of life for NYHA III heart failure patients (group 2) , one year after the inclusion

DISCUSSIONS

NYHA class the is most frequently used parameter for assessing clinical status of heart failure patients. It is determined by the physician through subjective assessment and it has proven to be a predictor for heart failure evolution. (6) Being a subjective assessment, NYHA classification is dependent on the physician ability to determine the impact of symptoms on patient's daily activity. Significant differences in NYHA class assessment have been shown between clinicians, as well as between physician's and patient's assessment, respectively, regarding patient's limitation of daily activity. (7) NYHA classification is a subjective parameter, determined by the physician, often inconsistent with the quality of life as assessed by the patient himself. (8) For an adequate and as real as possible assessment of NYHA class, this should be done together with the patient, as NYHA classification is performed according to patient's clinical symptoms and may be misinterpreted by the physician.

Quality of life is the emotional, physical and social wellbeing as perceived by a person. Its perception is rather subjective, depending on each individual's beliefs, expectations, intelligence and personality. Physicians tend to objectively assess a disease evolution and rely less on subjective characteristics. Quality of life questionnaires measure disease or effects from treatment patient's perspective. Several quality of life aspects can be affected in heart failure, both physically and psychologically, as well as by the side effects of a treatment or by social limitations. lead These factors may to the family worsening of and social relationships, depression, anxiety and decrease in treatment compliance.

Quality of life is different from health status, as it assesses the way the patient perceives it emotionally, physically and as regards his/her own expectations. Not infrequently, answers are surprising for the treating physician.

The heart failure patients often tend to be compliant to a

cardiovascular medication that improves their quality of life, but not to the medication or therapeutic conduct that increase their survival. (9) Various quality of life questionnaires have been used in the clinical studies performed so far in patients with cardiovascular pathology, that а correlation so between these studies cannot be due dissimilar established to assessment means.

Quality of life assessment started to play an increasingly important role in the management of heart failure patient. A low quality of life leads to an hospitalisations increase in and mortality of heart failure patients. The quality of life assessment is therefore important in secondary prevention, actually helping the identification of patients who need adjuvant psychological therapy even or medication for favourable evolution. At the same time, it is extremely important assess clinical to implications of a therapeutic approach over patients' quality of life.

A series of clinical studies have shown that some emotional status components (anxiety, depression) may negatively impact on the evolution of heart failure patients' quality of life, most of them being performed in the outpatient setting. (10)

Exercise capacity is both an assessment tool of clinical status, and a component of the therapeutic management of heart failure patients.

Although there are studies in which no correlation between quality of life and exercise capacity has been

CONCLUSIONS

In conclusion, the evolution of heart failure with preserved ejection fraction patients' quality of life is correlated with the evolution of prognostic markers (proBNP and NTproBNP) and, in disease evolution, with their exercise capacity.

Although in the case of heart failure with preserved ejection fraction

shown (11), in the present study we found a correlation between these two components of clinical status, the difference between these studies consisting in the quality of life evaluation tool (SF-36 questionnaire for HFREF and MLHFQ for HFPEF)

high incidence The of comorbidities in heart failure with preserved ejection fraction is well known. Even though no significant correlation of quality of life associated with various comorbidities has been established. presence of diabetes mellitus in NYHA II patients and high blood pressure in NYHA III patients influences their quality of life.

Similar to the PROTECT study, in which the evolution of the quality of life in HFREF patients has been assessed by monitoring the NTproBNP evolution, and in which it has been shown that NT-proBNP reduction correlates with significant improvement in the quality of life, a significant correlation between the evolution of the quality of life and NTproBNP evolution in NYHA III heart failure patients has been shown in our study.

Emotional status component in the Minnesota questionnaire and the depression risk are predictors influencing patients' quality of life both at heart failure onset, and in this pathology evolution.

No connection between ejection fraction and quality of life has been established; hence, left ventricle dysfunction does not impact the HFPEF patients' quality of life.

patients the comorbidities incidence is much more increased than in heart failure with systolic dysfunction, no statistically significant differences in clinical status have been evidenced in patients with various comorbidities (ischemic cardiomyopathy, metabolic syndrome, chronic kidney disease), except for diabetes mellitus and high blood pressure.

To date, treatment goals in heart failure consisted in the reduction of hospitalisations and mortality. However, quality of life improvement has an equal importance.

Even though there is a trend to consider that improvement of patients' exercise capacity is the main factor contributing to the quality of life improvement, this study proves the importance of emotional status in the evolution of quality of life in heart failure with preserved ejection fraction patients.

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Clinically, we can conclude that quality of life assessment may provide better monitoring of HFPEF patients. Therapy of non-physical aspects in chronic diseases should be considered an integral part of the main disease treatment in order to reduce anxiety, depression and social functioning disturbances, which can lead to improved treatment compliance and better social integration of these patients. The routine use of quality of life questionnaires could aid in the identification of patients who need further support to improve their quality of life.

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DIAGNOSTIC AND PROGNOSTIC ROLE OF MAGNETIC RESONANCE IMAGING IN ACUTE CERVICAL SPINAL CORD INJURY



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ABSTRACT

Objectives: the aim of this study is to correlate the clinical neurological impairment and magnetic resonance imaging in acute patients with cervical spinal cord injury (SCI)

Material and methods: we analyzed the MRI images of 43 patients with acute cervical SCI, admitted and surgically treated. On MRI spinal cord edema, hemorrhage and cerebrospinal fluid flow, after surgical decompression, at SCI level was observed.

Results: all the patients with SCI presented spinal cord edema, the hemorrhagic lesion was present in all patient with complete SCI and in 21.4% in patient with incomplete lesion.

Conclusions: the spinal cord edema, hemorrhage and the absence of CSF flow are directly correlated to neurological impairment and the recovery rates of the patient with acute cervicalSCI.

Key words: magnetic resonance images, spinal cord injury, cerebrospinal fluid

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The computerized tomography (CT) is today a standard investigation for cervical spine injury. The present fracture classification is based on the morphology of the lesions. However CT can not determine the presence or extend of spinal cord injury (SCI). Magnetic resonance imaging (MRI) allows better visualization of SCI, soft tissue damage, discs. ligaments, vessels, of extradural presence compressing bleeding, muscle concussions, lacerations and edema associated even with small bony fracture.

There has been used many MRI technical modalities to visualize spinal cord injury. The most used sequences T1-weighted and T2-weighted are sagittal views. New sequences like diffusion-weighted MR images (DWI) are developed to a better visualization of spinal cord changes, early in the secondary injury faze.[1] Considering T1-weighted and T2-weighted images, there was described three signal patterns for describing the spinal cord injury: hemorrhage in the cord, edema of the cord and a combination of hemorrhage and edema.[2] Even if regarding studies there are the diagnostic and prognostic role of MRI in acute SCI, these studies are done

with too many differences regarding the stimulation and release times of sequences, the time interval after the injury, investigation before or after the surgery. The hemorrhage in the cord is relatively constant described in millimeters, but edema is evaluated different millimeters or number of levels involved.[3]

In compression lesions the STSG (Spinal Trauma Study Group) published a spinal cord compression measurement (Spine, Volume 31, Number 5, 2006) like percent (1di/(da+db)/2) x 100 of reduction in spinal cord diameter. There is no possibility to determine the percentage of swelling. There have not been published studies with correlation of the traumatic spinal cord swelling and the presence of cerebrospinal fluid (CSF) in the subarachnoidian space adjacent to the lesion, on MR images after the surgical decompression.

The objective of this study is to analyze the correlation between the spinal cord hemorrhage, edema, the presence or absence of CSF in subarchnoidian space at the lesion site (after the surgical decompression), with the clinical diagnostic findings and the recovery rate.

MATERIAL AND METHOD

There has been included in the study the patients with cervical SCI admitted in Polytrauma Compartment Casa Austria, County Hospital 2012-2013. Timisoara between Exclusion criteria were cervical spine injury without SCI, patients without control after surgical MRI decompression and fixation, in the first two weeks after injury. All the patients were surgically treated in the first 24 hours or, in polytrauma patients with systemic inflammatory response syndrome, after the day five.

Neurological evaluation was made at the admittance and after one month. We used the ASIA (American Spinal Cord Injury Association) motor and sensory score and also the AIS (ASIA Impairment Scale).[4] For recovery rate motor and sensory we use the Lucas and Ducker formula recovery percent %= [(Final Score -Initial Score) \div (100 – Initial Score)] x 100. [5]

The MRI investigations were performed on 1.5T, GE device. The spinal cord edema is defined as high

intensity signal in T2-weighted sagittal images, measured in millimeters (mm) cranial-caudal. Hemorrhage is defined as low intensity signal in T2-weighted images, surrounded by high intensity signal (edema). The measurement of hemorrhage was done in mm on sagittal images, cranio-caudal. In post surgical decompression images, it has been also noted the presence or absence of CSF continuity in the subarachnoidian space around the injured spinal cord, in T2-weighted sagittal images, both anterior and posterior to the spinal cord.

Statistical analysis was done with Sofa Statistics version 1.4.0 for mac os x. There was analyzed diagnostic value aspects: 1) correlation of the variation

RESULTS

There was 43 patients with SCI, 30 male and 13 female with age range from 21 to 73 years, mean age 43.26, median age 44 years. AIS was A for 15 patients (34.9%), B for 9 patients (20.9%), C for 8 patients (18.6%) and D for 11 patients (25.6%). in length of edema and hemorrhage; 2) correlation between AIS score at admittance and distinctly length of edema, length of hemorrhage; 3) correlation of the presence / absence of CSF with the variation of edema and hemorrhage, also with the AIS score. Regarding the prognostic value statistics we analyzed: 1) correlation of AIS score at admittance and one month after injury; 2) correlation of AIS at admittance and recovery rates; 3) correlation between the variation of spinal cord hemorrhage, edema and the recovery rates; 4) significance of presence / absence of CSF around the injured cord correlated to the recovery rate, AIS score at one month.

All the patients with SCI have spinal cord edema present. The hemorrhage is present in all cases with initial AIS score A, in 44,4% cases with AIS B, in 25 % cases with AIS C and no patient with AIS score D has spinal cord hemorrhage. (Table I)

Table I. CSF presence at the site of SCI, the length in mm, maximal values, minimal values, median values, range of spinal cord edema and hemorrhage distributed according to initial neurological AIS

			Edema (mm)				Hemorrhage (mm)					Hemorrhage Present	C No.	CSF Cases
		Median	No.Cases	Min	Max	Range	Median	No.Cases	Min	Max	Range	No.Cases	Present	Absence
	Α	73.30	15	47.8	120.4	72.60	9.60	15	6.3	11.1	4.80	15 (100%)	1	14
AIS	В	33.20	9	23.1	58.1	35.00	0.00	9	0.0	6.0	6.00	4 (44,4%)	4	5
initial	С	32.50	8	12.7	61.3	48.60	0.00	8	0.0	3.1	3.10	2 (25%)	7	1
	D	13.20	11	8.4	38.1	29.70	0.00	11	0.0	0.0	0.00	0 (0%)	11	0

Runing ANOVA test for the correlation of the AIS with edema and hemorrhage is possible altered because

of a less "normality" of the data. (Table II).

Table II. results for ANOVA test regarding the hemorrhage variation in the AIS (A to D) group patient. P abnormal provides a single measure of normality. The p value for test is < 0.001, F is 30.95

Group	N	Mean	CI 95%	Std. Dev.	Min	Max	Kurtosis	Skew	P abnormal
А	15	9.067	8.310 - 9.824	1.496	6.3	11.1	-1.093	-0.451	0.376
В	9	1.767	0.251 - 3.282	2.320	0.0	6.0	-0.961	0.741	0.415
С	8	0.775	-0.219 - 1.769	1.435	0.0	3.1	-0.667	1.155	0.159
D	11	0.0	0.000 - 0.000	0.000	0.0	0.0	-3.000	0.000	0.589

The CSF in subarachnoidian space at the site of SCI is present in only one case (6.7%) with AIS A, in

four cases (from eight) with AIS B, in all cases except one of AIS C and in all cases of patient with AIS D. (Table III).

Table III. Variation of CSF presence in subarachnoidian space at the site of SCI, with AIS score at admittance

				No.Cases	Col %
AIC	Δ	CCE	No	14	93.3%
	A	CSF	present	1	6.7%
	В	CCE	No	5	55.6%
AI5 Initial		CSF	present	4	44.4%
Intitut	С	CCE	No	1	12.5%
		Cor	present	7	87.5%
	D	CSF	present	11	100.0%

There is a strong correlation of the edema and hemorrhage regarding the length of the lesions. (Fig 1) There is also a correlation between the length of the lesions and AIS score. (Fig 2).



Figure 1. Spearman's test of linear correlation edema (mm) vshaemorrhage (mm), p value < 0.001, slope 0.136



Figure 2. Correlation of spinal cord edema and hemorrhage with initial AIS. (p value < 0.001)

Statis	stic	analyze	with	Mann-	
Whitnet	U	test	and	t-test	

(independent), we find a significance difference between the group with

absent or present CSF at the site of injured spinal cord, regarding the

extend of edema and hemorrhage. (Table IV, V).

Table IV. Result of Independent Sample t-test of average edema for presence versus absence of CSF at the site of SCI. p value <0.001, t statistic: 7.76

Group CSF	N	Mean	CI 95%	Standard Deviation	Min	Max	Kurtosis	Skew
NO	20	70.27	59.928 - 80.612	23.596	33.2	120.4	-0.593	0.363
Present	23	25.713	20.285 - 31.141	13.281	8.4	54.3	-0.485	0.597

Table V. Result of Independent Sample t-test of average hemorrhage for presence versus absence of CSF at the site of SCI. p value < 0.001; t statistic: 9.01

Group	N	Mean	CI 95%	Standard Deviation	Min	Max	Kurtosis	Skew
NO	20	7.385	5.959 - 8.811	3.253	0.0	11.1	-0.501	-0.801
Present	23	0.452	-0.213 - 1.117	1.626	0.0	7.3	12.272	3.648

Statistically significant (p value < 0.001) correlation was determined with Pearson's Chi Square test between the AIS at admittance and presence/absence of CSF (at the SCI level), and between the presence of hemorrhage and absence of CSF, the last one being the most significant.

Neurological recovery was evaluated by recovery rates calculated from ASIA score with the presented formula. There are registered recoveries even for AIS A, but no patient with AIS A changed the AIS classification and two patientshas vital complications. There was two patient from AIS B who became AIS C, also two patients changed from AIS C to D. (Table VI) None of the patients from AIS D became E in the one month follow up.

The poor recovery rates are correlated with the edema, hemorrhage and more significant with the CSF absence. (Table VII, VIII).

The recovery rates are also correlated with the initial AIS score at the admittance. The Pearson's test of linear correlation is shown in Fig 3.

				No.	Col %	%	recovery	rate
				Cases		Median	Mean	StdDev
	٨	AIC Einal	А	13	86.7%	0.00	1.07	1 50
	A	AI5_Final	mortality	2	13.3%	0.00	1.07	1.39
	В	AIS_Final	В	7	77.8%	2 50	6.81	8.84
AIS_initial			С	2	22.2%	2.50		
	С	AIC Final	С	6	75.0%	0.00	0.10	7 09
		AIS_Final	D	2	25.0%	9.00	9.10	7.08
	D	AIS_Final	D	11	100.0%	16.00	16.39	5.90

Table VI. The recovery regarding AIS classification and recovery rates

Table VII. Results of ANOVA test of average recovery rates for groups with and without CSF presence at the SCI site. (p value < 0.001; F: 49.27)

Group CSF	No. Cases	Mean	CI 95%	Standard Deviation	Min	Max	Kurtosis	Skew
Absent	18	1.061	0.368 - 1.753	1.498	0.0	5.0	0.390	1.116
Present	23	13.444	10.441 - 16.447	7.347	0.0	25.0	-1.120	-0.188

without presence of hemorriage in spinal cold at SCI site. (p value < 0.001, F. 02.25)								
Group	No.	Mean	CI 95%	Standard	Min	Max	Kurtosis	Skew
Hemorrhage	Cases			Deviation				
Absent	22	14.055	11.173 - 16.937	6.896	2.43	25.0	-1.172	-0.151
Present	19	1.005	0.341 - 1.669	1.476	0.0	5.0	0.579	1.196

Table VIII. Results of ANOVA test of average recovery rates for groups with and without presence of hemorrhage in spinal cord at SCI site. (p value < 0.001; F: 62.25)



Figure 3. Results of Pearson's test of linear correlation for recovery rates with hemorrhage (left) and edema (right)

DISCUSSIONS

The SCI is an anatomical lesion with a functional effect. AIS and ASIAscore can measure the neurological impairment motor and sensory. The MRI is able to offer a better view about extend of the lesion in term of hemorrhage and edema. If we interpret the table II the CI 95% (confidence interval of 95%) is that for present hemorrhage lesion the patient is with AIS C, at length of 3.2 mm AIS scale is D and after 8.3 mm the lesions is complete. In the same manner we can interpret the edema and we found that lesions of 23.309 - 46.966 mm are 95% AIS C, 28.649 - 45.351 mm AIS B and AIS A between 67.554 - 88.779 mm. Regarding diagnostic value of MRI we found edema in all cases with SCI, hemorrhage is present from AIS C and extend in length is well correlated with neurological impairment. the The neurological recovery in term of changing the AIS score was not present in lesion with hemorrhage present or absence in post surgical images of the CSF at the SCI level.

Our results agree with previous studies in tern of neurologic recovery with respect to MRI changes. [6,7]The recovery in term of motor and sensory score is present in 7 patients (36.8%) from the 19 patients with hemorrhagic lesion. There are similar results regarding the recovery present in 7 patients (38.8%) from 18 with absence of CSF at the SCI level. Only one patient with hemorrhagic lesion has present CSF at the injury level and one patient without hemorrhagic lesion has absence of CSF at the injury level. Considering the CSF that was evaluated after surgical decompression fixation, and so no extradural compression was present, the cause of compression was intradural. In our study the absence of CSF is better correlated with the presence of hemorrhage than with the length of edema.

CONCLUSIONS

The	The clinical		neurological		
impairment	can	be	correlated		

gradually with the edema length, hemorrhage length and absence of CSF

in subarachnoidian space at the SCI level. prognostic regarding The having recovery is the same correlation. The absence of subarachnoidian CSF flow at the SCI level after the surgical decompression is highly correlated with the presence of hemorrhagic lesion and can be

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explain by intradural regional elevated pressure. Further study could be necessary to measure the intradural pressure on the level of SCI and to develop strategies for lowering this pressure in order to influence of the neurological recovery.

INSIGHT IN ACUTE AND TRANSIENT PSYCHOTIC DISORDERS AND PARANOID SCHIZOPHRENIA



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ABSTRACT

Introduction: Insight is a multidimensional concept that has been studied mainly in subjects with schizophrenia.

Objectives: Comparing the level of insight of a sample of subjects with acute and transient psychotic disorder to a sample of subjects with paranoid schizophrenia.

Material and method: Two samples of 41 subjects each have been selected: one sample with a diagnosis of acute and transient psychotic disorder (ATPD) and another with paranoid schizophrenia. Each subject was applied The Birchwood Self-Report Insight Scale, after a five years of evolution period and the results have been compared.

Results: The application of The Birchwood Self-Report Insight Scale revealed statistically significant differences between the two samples for the proportion of subjects having a good level of general insight and for the average of scores of the subscale that appreciates the awareness of the symptoms in favor of those with acute and transient psychotic disorder.

Conclusions: There are statistically significant differences in insight when comparing acute and transient psychotic disorder diagnosis with paranoid schizophrenia, suggesting the need to approach insight in psychosis also from a categorical point of view.

Key words: insight, significant differences, categorical approach

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Address: Clinica de Psihiatrie "Eduard Pamfil" Timisoara, 21 I. Vacarescu, Str., 300 128, Timisoara, Romania E-mail address: <u>papavaion@yahoo.com</u> The conceptualization of insight in psychosis has evolved over time. Initially described as a unidimensional concept, it involves now multiple dimensions and is seen as a continuous variable which is present in varying degrees. (Amador & Kronengold, 2004). (1)

Insight is describes most commonly as having three aspects: illness awareness, the ability to re-label symptoms as part of the illness and the appreciation of the need for treatment. These aspects may be present or not in some degree, at the same time. (MA Cooke et al., 2005; McGorry & McConville, 1999; Osatuke et al., 2008). (2,3,4)

Traditionally, lack of insight was seen as inherent to the psychopathology of psychotic disorders and distinctive а characteristic between the psychotic disorders and the so-called neurotic disorder. (David, 1990). (5)

Generally, insight has been considered a cornerstone of recovery and improved well-being. Clinical insight in psychosis is considered extremely important for issues such as reahabilitation, (Stefanopoulu et al, 2009), social functioning and quality of life (Drake et al, 2007), adherence to treatment (Buckley and al, 2007, Lacroute and al, 2002), number of relapses and readmissions (Drake et al.

MATERIAL AND METHOD

The two samples of our study included 41 subjects who each had their first admission in Timisoara Psychiatric Clinic between 2005 -2008. One sample comprised subjects diagnosed with Acute and transient psychotic disorder (ATPD), and the other subjects with Paranoid Schizophrenia. Sample size has been selected based on the number of subjects with ATPD, who had the first 2007 Pijnenborg et al, 2013) (6,7,8,9,10). Insight is overall considered as an important factor for the prognosis and the outcome of psychosis.

The link between insight and psychopathology was and remains controversial. A meta-analysis on 40 studies, Mintz (2003) concluded that there is indeed an association between insight and psychopathology, but weak and dependent on illness phase and patient age at onset of symptoms. (11)

Thompson (2001) compared patients with first-episode psychosis with patients with multiple episodes and noticed that the former group had a lower insight than the latter. This suggests that insight may improve during the disease's course, following the first episode. (12)

Insight, in general, has been developed and studied especially in patients with schizophrenia and far less in other psychotic disorders. Therefore, there is a very limited body of literature on the other psychotic disorders in general. Low insight was seen as a defining feature of schizophrenia compared with other psychoses.

In the present study we aimed to assess the insight of certain diagnosis groups, namely acute and transient psychotic disorders and paranoid schizophrenia after a 5 years clinical course.

admission in period mentioned above, and maintained their diagnosis after five years of evolution.

Therefore inclusion criteria for this study were:

- Age at first hospitalization between 18-65 years;

- Diagnoses, according to ICD 10 WHO, of Acute and transient psychotic disorder for the first sample and Paranoid schizophrenia for the second; diagnosis maintained during five years of clinical course;

-All of the subjects must be active outpatients of Timisoara Mental Health Center or of other psychiatric ambulatory services in Timisoara;

-Voluntary participation from subjects without any kind of motivation from the investigators;

Subjects having a history of alcohol or drugs abuse or dependence have been excluded from our research.

None of the subjects was being hospitalized during the assessment.

For each of the subjects was applied the Self-Report Insight Birchwood Scale, after five years of clinical course of the illness (1994)(13). It consists of eight items and measures three dimensions of insight: awareness of symptoms (two items), awareness of the disease (2 items) and awareness of the need for treatment (4 items).

The Self-Report Insight Birchwood Scale is a self-evaluation scale with three possible answers in relation to each of the existing statements: agree, disagree and unsure. There is a grid listing for each of the 8 statements and a score is given:

- Between 0-8 points insight is low

- Between 9-12 points insight is medium

- Between 13 to 16 points insight is high

This scale also includes three subscales:

1. Awareness of symptoms

2. Awareness of the disease

3. Awareness of the need for treatment

For these subscales a score of 3-4 points means a good insight and a score of 1-2 points means a low insight.

Birchwood insight scale has been applied to all subjects, collecting data on awareness of symptoms, awareness of the disease (the fact that he is ill), awareness of the need for treatment and the overall score indicating the insight.

The average scores obtained by the subjects in the two samples were compared and also the percentage with a degree of insight in order to establish the existence of statistically significant differences between the two groups. For comparing the averages we have used the non-parametric Mann Whitney comparison test. The limit of statistical significant was p<0.05. The existence of differences between proportions has been verified as well.

RESULTS

The sample of subjects with acute and transient psychotic disorder included 22 women (53.6%) and 19 men (46.4%) and the sample with paranoid schizophrenia included 23 women (56.1%) and 18 men (43.9%).

After applying the Birchwood scale to the first sample (TPAT), only 17.1% of subjects had low insight on awareness of symptoms, while 82.9% of subjects had increased insight for this subscale.

In the group of subjects with paranoid schizophrenia, 34.1% of subjects had low insight, and 65.9% has increased insight for the awareness of symptoms subscale.

The difference between the proportion of subjects who had a good or low awareness of the symptoms is not significant between the two groups (p = 0.08).

As regards the awareness of the disease, 56.1% of subjects from the ATPD sample had poor insight and 43.9% has good insight. In the second samples, 41.5% of subjects with paranoid schizophrenia had low insight and 58.5% had good insight.

Again the differences between the proportion of subjects who had a good or low awareness of the disease is not significant between the two groups (p = 0.189).

Regarding the awareness of the need for treatment, we obtained a low insight in 41.5% of subjects with ATPD and 31.7% of subjects with paranoid schizophrenia and good insight in 58.5% of the subjects in the former sample and 68.3% in the latter.

In this case as well the difference between the proportions of the number of subjects who have a good awareness of the need for treatment or a low one is not significant between the two groups (p = 0.36).

In terms of general insight we obtained the following results:

Table I. Result	ts				
Birchwood Scale-	Paranoid Schiz	zophrenia Sample	ATPD Sample		
general insight	Number of	%	Number	%	
	subjects		of subjects		
Absence of insight	0	0.0	0	0.0	
(score 0-2)					
Low insight (score	2	4.9	1	2.4	
3-5)					
Medium insight	9	21.9	2	4.9	
(score 6-8)					
Good insight	30	73.2	38	92.7	
(score 9-12)					

The difference between the percentage of subjects with a good insight in the two groups is statistically significant (p = 0.02): the percentage of subjects with acute and transient psychotic disorders who have good general insight is significantly higher

than the proportion of subjects with paranoid schizophrenia with a good general insight.

In both groups, the application of the insight scale yielded the following average values:

Tuble II. Average values						
Birchwood	Paranoid Schizophrenia		ATPD Sample		Average	The statistical
Scale	Sample		_		difference (Z)	significance of the
	Average	Std.Dev.	Average	Std.Dev.		difference
Awareness of	2.8	0.99	3.2	0.73	Z = -2.15	P=0.03
symptoms						Stat.sign.
Awareness of	2.3	1.04	2.4	0.89	Z = -0.38	P=0.70
the disease						Stat.non-sign.
Awareness of	2.9	0.91	3.0	0.78	Z = -0.35	P = 0.72
the need for						Stat.non-sign.
treatment						
General Score	11.00	2.67	11.8	1.96	Z = -1.45	P = 0.15
						Stat.non-sign.

Table II. Average values

The application of the Mann-Whitney comparison test indicates a statistically significant difference between the two groups in terms of the

DISCUSSIONS

In clinical practice, we noticed that after a first psychotic episode with complete recovery of symptoms, most patients believe that this episode was accidental, unique and are convinced that it will not happen again. So they average scores for the subscale of awareness of symptoms of the Birchwood insight scale.

believe that this episode was not due to a disease and that they not need longterm medication. This applies particularly to Acute and transient psychotic disorders where the functional and symptoms recovery is

usually complete after each episode. These observations would be translated to the present study through the large percentage of the subjects in this sample (ATPD), above average, who do not have a proper insight of their disease (56.1%). Also in favor of these observations comes the high percentage of subjects from the ATPD sample considering that treatment is not necessary for their condition (41.5%). Regarding the awareness of symptoms, a very high percentage of the subjects of this group have a good insight and are aware of their pathological nature, but further they have not considered their symptoms as being that relevant for stating that they have a mental illness or that treatment is necessary for their condition.

Overall the number of subjects in the first group (ATPD) who had a good insight was very high (38 of 41 subjects), which could lead to the conclusion that subjects with acute and psychotic disorders transient are characterized by a good general insight. The difference between the percentages of subjects with a good insight of the two groups was statistically significant in favor of the ATPD. Generally studies have identified low insight as a defining feature of schizophrenia versus other psychoses. Amador (1994) and Pini (2001) found a lower insight in schizophrenia compared with monopolar psychotic depression and schizoaffective disorders. (14.15)

In some cases, for schizophrenia, the improvement of insight is related to the occurrence of depressive symptoms. (16) The awareness of psychosis is also related to an increased risk of suicide (Drake 1986). (17)

As mentioned before, the research on insight in psychoses was concentrated particularly on schizophrenia and less on other psychoses. In these circumstances the approach focused more on the strictly psychotic symptoms, rather than on diagnostic categories. Therefore there is a poor body of literature centered on the insight for other diagnostic categories that we can relate to.

Our study, even if comparing insight of awareness of symptoms did show statistically significant not differences between the two samples in terms of the proportions of subjects with low or good insight, indicates, however, that in the paranoid schizophrenia sample the percentage of subjects with low insight is twice as big as in the ATPD sample (17.1% versus 34.1%). Lack of statistical significance is probably due to the small number of cases assessed.

Regarding the awareness of the disease we found it interesting that although the differences are not statistically significant we can still observe that that in the ATPD sample the percentage of subjects with low disease insight is higher than in the group with paranoid schizophrenia. The fact that those with paranoid schizophrenia assume much more easily the term mental illness than with and those acute transient psychotic disorders we believe is due to the higher renown in general population of the term schizophrenia which is far more associated with mental illness and also because the recovery of the symptoms is with a certain degree of defect than in ATPD. Stigma and negative visions of society make the diagnosis can of schizophrenia one full of suffering for the patient, that automatically attracts a higher insight, as has been demonstrated in previous studies. Also the shorter duration of relapses for those with ATPD can contribute to the fact that this entity is not associated with the general sense of illness by those who experience it. Plus, it is a polymorphic entity that does not have a history as long and as clear as schizophrenia.

Regarding the awareness of the need for treatment, in both samples more than half of the subjects had a good insight on it. However, its need
and its importance are more acceptable to those with ATPD than those with schizophrenia. To this may probably contribute the more favorable outcome in case of ATPD. Their states of wellbeing may, however, be a cause for further non-adherence; they may interrupt treatment arguing they are feeling good and they don't need it anymore and because they know they will never again experience a new episode "of mental breakdown".

Although, on the subscales the differences between percentages were not generally significant, the percentage of subjects with a good insight of the ATPD sample was significantly higher than the proportion of subjects with good insight in the paranoid schizophrenia

CONCLUSIONS

The application of the insight scale revealed that the percentage of subjects with acute and transient psychotic disorders who have a generally good insight is significantly higher than the proportion of subjects with paranoid schizophrenia with the same degree of insight. Also, subjects

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sample. This was expected due to the fact that ATPD are considered as psychoses with a better outcome than schizophrenia (18) and the clinical insight is directly correlated with this factor (Lincoln et al, 2007) (19).

As regards the strictly the average values obtained with Birchwood scale, although significant differences were found only on the awareness of the symptoms subscale, the mean values were higher in the ATPD sample for all of the subscales and for the total score, however without being statistically significant. Thus, the degree of insight was increased for those with ATPD, both in the awareness of symptoms and necessity of the treatment and in total as well.

with acute and transient psychotic disorders have a significantly higher degree of awareness of symptoms than subjects with paranoid schizophrenia.

Further studies are needed to research the insight in psychoses based on a categorical approach and not only on symptoms.

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FIRST-LINE TREATMENT IN ADVANCED HODGKIN LYMPHOMA



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ABSTRACT

Introduction. Hodgkin lymphoma is the malignant proliferation of the lymphoreticular system, either localised or disseminated, initially involving the lymph nodes, spleen, liver and bone marrow. ABVD polichemotherapy (doxorubicin, bleomycin, vinblastine and dacarbazine) is the standard therapeutic scheme; BEACOPP polichemotherapy (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone) may also be used. Hodgkin lymphoma is the result of clonal alteration of B cells that leads to the appearance of pathognomonic binucleated Reed-Sternberg cells. Chemotherapy either alone or in combination with radiation therapy leads to complete remission in over 75-80% of patients.

Aim. To assess the response of patients with advanced Hodgkin lymphoma to polichemotherapy.

Material and method. We have conducted a retrospective analytical study of 80 patients diagnosed with Hodgkin lymphoma in the Haematology Department Timisoara between May 2008 and April 2013. The main diagnostic method used was biopsy, followed by the histopathological and immunohistochemistry exam of the harvested tissue. Staging was performed by computed tomography (CT). The polichemotherapy and the number of cycles have been decided based on the disease histological stage and grading. Patients' data regarding medical history and laboratory tests performed have been extracted from each patient's medical record.

Results. Patients' mean age was 50 years; out of the 80 patients, 60 (75%) were men and 20 (25%) women. The most frequent sign was lymph nodes hypertrophy, especially those in the cervical area. Sixty-eight (85%) patients in our study had hypertrophy of several lymph node groups; splenomegaly was seen in 25 (31.25%) patients, followed by hepatomegaly by a much smaller percentage. Seventy-two (90%) patients underwent ABVD and 8 (10%) BEACOPP polichemotherapy. As the staging concerns, 2 (2.5%) patients had IV Bx stage, 9 (11.25%) IV B, 4 (5%) IV A, 10 (12.5%) III Bx, 16 (20%) III B, 14 (17.5%) III A, 3 (3.75%) II Bx, 9 (11.25%) II B, 10 (12.5%) II A, and 3 (3.75%) I B. According to histological grading, 47 (58.75%) had nodular sclerosis form, 26 (32.5%) mixed cellularity and 7 (8.75%) lymphocyte depletion. Six ABVD and 6 BEACOPP polichemotherapy cycles were applied on average. Up to April 2013, 60 (75%) patients were in complete remission, 10 (12.5%) in partial remission, in 3 (3.75%) patients the disease has progressed, 4 (5%) patients died, and 3 (3.75%) were lost to follow-up.

Conclusions. This study shows the efficacy of ABVD polichemotherapy in advanced Hodgkin lymphoma. *Key words:* Hodgkin lymphoma, polichemotherapy

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INTRODUCTION

Hodgkin lymphoma is the malignant proliferation of the lymphoreticular either system, localised or disseminated, initially involving the lymph nodes, spleen, liver and bone marrow. ABVD-type polichemotherapy is the standard therapeutic scheme; BEACOPP polichemotherapy may also be used. ABVD regimen was first introduced in the 1970s for patients not responsive to MOPP treatment (chlormethine, vincristine, procarbazine, and prednisolone) [1-5,12] and in which the first-line treatment could not be used anymore, especially because the ABVD regimen drugs induce infertility and secondary leukemia to a smaller degree than those in the MOPP regimen. ABVD has been often combined with MOPP or a new therapeutic regimen in the hope that the use of several drugs on short periods of time would decrease the development of tumour resistance. A series of randomised trials [6-9] established ABVD treatment as the gold standard, taking into account both the efficacy and the reduction of toxic effects on the long term. A German study [10] compared standard therapeutic regimen the (COPP and ABVD) with increased hybrid doses in the regimen (BEACOPP) ^[13]. The use of increased doses of BEACOPP requires routine

MATERIAL AND METHOD

We have conducted а retrospective analytical study of 80 patients diagnosed with Hodgkin lymphoma in the Haematology Department Timisoara between May 2008 and April 2013. The main diagnostic method used was biopsy, followed by the histopathological and immunohistochemistry exam of the harvested tissue. Staging was performed by computed tomography

administration of granulocyte colony stimulating factor. Results showed significant improvement of treatment results with the decrease of 5-year relapse rate in patients treated with BEACOPP versus those treated with COPP and ABVD (76% vs. 69%), as well as in patients treated with high doses of BEACOPP in which the 5-year relapses decreased by over 87%. [10] An improved 5-year survival rate has been also evidenced in patients treated with both **BEACOPP-based** regimens compared with those treated with COPP and ABVD, no significant differences between the two BEACOPP regimens being recorded [11]. Nine cases of acute myeloid leukemia and myelodysplastic syndrome were reported in patients treated with increased-dose compared with those treated with standard-dose BEACOPP and one case only in patients treated with COPP and ABVD. [10]

Hodgkin lymphoma is the result of clonal alteration of B cells that leads to the appearance of pathognomonic binucleated Reed-Sternberg cells. Chemotherapy associated or not with radiation therapy leads to complete remission in over 75-80% of patients.

The aim of this paper is to assessthe response of patients with advancedHodgkinlymphomapolichemotherapy.

(CT). The polichemotherapy and the number of cycles have been decided based on the disease histological stage and grading. Patients' data regarding medical history and laboratory tests performed have been extracted from each patient's medical record.

Data were collected in a Microsoft Excel 2007 database and processed by the means of SPSS 17.0 statistical programme and Microsoft Excel 2007

Patients' mean age was 50 years, with intervals between 20 and 79 years (figure 1); out of the 80 patients, 60 (75%) were men and 20 (25%) women (figure 2). The most frequent sign was lymph nodes hypertrophy, especially those in the cervical area. Sixty-eight (85%) patients in our study had hypertrophy of several lymph node groups; splenomegaly was seen in 25 patients, followed (31.25%)by hepatomegaly by a much smaller percentage (figure 3). Seventy-two (90%) patients underwent ABVD and 8 (10%) BEACOPP polichemotherapy (figure 4). As the staging concerns, 2 (2.5%) patients had IV Bx stage, 9

DISCUSSIONS

multicentre studies. Many starting from the de la Rey histological classification, have evidenced that the histopathological subtypes with mixed cellularity and lymphocyte depletion are correlated with а more unfavourable evolution. The nodular sclerosis histological subtype has a better prognosis than the former ones, the 5-year complete remission duration being greater. It seems that histopathological aspect has an influence over an adequate therapeutic response rate, complete remission being achieved in over 85% of nodular sclerosis cases and in less than 70% of the lymphocyte depletion and mixed cellularity histological subtypes. A

CONCLUSIONS

The current study proves the efficacy of ABVD polichemotherapy in advanced Hodgkin lymphoma.

(11.25%) IV B, 4 (5%) IV A, 10 (12.5%) III Bx, 16 (20%) III B, 14 (17.5%) III A, 3 (3.75 %) II Bx, 9 (11.25%) II B, 10 (12.5%) II A, and 3 (3.75%) I B (figure 5). According to histological grading, 47 (58.75%) had nodular sclerosis form, 26 (32.5%) mixed cellularity and 7 (8.75%) lymphocyte depletion (figure 6). Six ABVD and 6 BEACOPP polichemotherapy cycles were applied on average. Up to April 2013, 60 (75%) patients were in complete remission, 10 (12.5%) in partial remission, in 3 (3.75 %) patients the disease has progressed, 4 (5%) patients died, and 3 (3.75%) were lost to follow-up (figure 7).

prevalence of 58% in nodular sclerosis form is noticed in our study; this suggests a favourable prognosis in case treatment, of proper which is reinforced by the fact that 75% of the patients in our study have complete remission. A series of randomised trials ^[6-9] established the ABVD treatment as the gold standard, taking into account both the efficacy, with the significant increase of survival rate as compared with other therapeutic regimens, and the reduction of toxic effects on the long term. Our study shows complete remission in 75% of the studied patients and partial disease remission in 12.5% of the patients.



Figure 1. Age group distribution of patients



Figure 2. Gender distribution of patients



Figure 3. Main signs present during patients' examination



Figure 4. Recommended polichemotherapy



Figure 5. Disease staging



Figure 6. Patient classification according to histological grading of disease



Figure 7. Status of monitored patients

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PREDICTIVE FACTORS OF CERVICAL METASTASES IN LARYNX SQUAMOUS CELL CARCINOMA



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ABSTRACT

The aim of this paper is to evaluate potential predictive factors for cervical metastases in larynx squamous cell carcinoma.

Material and methods. We describe the markers according to their activity and their prognostic or predictive contributions.

We performed a retrospective analysis of 60 retrospective cases of supraglottis laryngeal scuamous cell carcinomas (SCC) treated surgically.

Results. Tumor and lymph nodes histopathologic characteristics were evaluated in the context of finding a correlation with the metastatic potential.

In our group all SCC, we noted the prevalence of poorly differentiated non keratinized in 23(38.33%) and 13(21,66%) with low tendency of keratinization, 2(3.33%) cases of spindle cell and 2 (3.33%) cases of basaloid and 20(33.3%) cases keratinized. These patients developed cervical metastases: 3 nonkeratinized SCC, 2 SCC with low tendency of keratinization, 1 spindle cell carcinoma and 2 keratinized SCC G2. The average time for local recurrence was 4 months (1–8 months).

We attempted to correlate SCC type with supraglottic localization to emphasize a predictive marker for the prevalence of cervical metastases, P = 0.4271.

Conclusion. Quantification of localization, SCC type, capsular effaction, inflammatory response and perineural, perivascular invasion in larynx squamous cell carcinomas may be useful in identifying groups of patients at high risk of tumor recurrence and in conducting a correct therapy.

Key words: laryngeal cancer, prognostic factor, cervical metastases

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Mihaela-Cristina Prodea Address: University of Medicine and Pharmacy "Victor Babes" Timisoara, Eftimie Murgu Square, no. 2A, RO-300041, Timisoara Phone: +4 0723036805 E-mail address: <u>mihaelaprodea@umft.ro</u>; <u>mihaelaprodea@gmail.com</u> All though of the surgical treatment is improving, multidisciplinary treatment approaches are ,more complex and dynamic, complementary therapies and integrated modern treatments, the (Head and Neck Squamous Cell Carcinoma) HNSCC survival has been almost the same in the last 30 years.[1,2]

Histopathology features of SCC are studied with the objective to value

MATERIAL AND METHOD

We selected for present study 213 retrospective cases of laryngeal scuamous cell carcinomas (SCC) surgically treated in the ENT Clinic Timisoara. We analized the patients charts, biopsies and histopathologic exams from the surgery pieces.

We examined the biopsy exams of all 213 patients and we found SCC different grades of differentiation: 7 SCC keratinized G1, 141 SCC keratinized G2, 2 SCC keratinized G2/G3, 1 SCC keratinized G3, 20 SCC with keratinization tendency, 30 SCC nonkeratinized SCC G2, 1 nonkeratinized G2/G3, 1 verrucous, 3 basaloid type, 3 with papillary pattern and 4 spindle cell carcinoma.

The influence of grading in the tumor prognostic was the object of numerous studies with very different results. For defining 4 degrees of Grading [**3.'4**, 3, 4]

(cytological grading) and a nuclear grading (only aspects of the nucleus), WHO takes into consideration the degree of keratinization, number of beads corneas, mitotic activity, correlations with tumor evolution and metastatic potential. Determining (molecular) markers in order to obtain a more complex TNM staging would give a better prognostic stratification and most relevant: an appropriate treatment could be decided.

Aim and objectives

The aim of this paper is to evaluate potential predictive factors for cervical metastases in larynx squamous cell carcinoma.

presence of intercellular junctions, nucleus-plasma ratio and the presence of anaplastic cells.

The vast majority of all laryngeal malignancies (95%) are conventional squamous cell carcinomas (SCC) and they vary according to their degree of differentiation to well, moderate and poor carcinomas. Poor differentiation carcinomas are negative prognostic factors.

It is now solidified the concept that the presence of lymph node metastasis is linked with negative prognosis. Clinic evidence of cervical lymph node metastasis in HNSCCs represents an important prognostic factor, being correlated with regional recurrence and distant metastases, with impact on overall survival (OS) and disease free survival (DFS).[1][2][8][12]. Studies from 20 years ago show that the presence of lymph node metastasis will influence the prognostic in a negative way. The capsule rupture of the lymph node on the tumor side is a particular sign of negative prognostic. [3.'4]

RESULTS

In our cluster of 213 patients analyzed from 2008 till 2010 we noted the specific features. At presentation it was performed the objective exam, inspection, palpation we noted 13 cases

with clinical N1 (cN1), 11 cN2, 6 cN3 and 183 cN0.

The N+ patients at presentation were stadialized: 8 stage III: 4 T2N1, 3 T3N1, 1 T1N2 and 22 stage IV: 1 T2N2, 2 T3N1, 2 T3N2, 3 T3N3, 4 T4N1, 7 T4N2, 3 T4N3.

Tumor and lymph nodes histopathologic characteristics were evaluated in the context of finding a correlation with the metastatic potential.

Studies from literature show that non-keratinizet poorly differenciated SCC with subglotic localization have a more aggressive local manifestation [5]

And in our group we noted at supraglotic level, from the 60 cases we noticed the prevalence of poorly differenciated non keratrinized SCC in 23 patients and 13 patients with SCC with low tendency of keratinization, 2 cases of spindle cell SCC and 2 cases of basaloid SCC and 20 cases keratinized

DISCUSSIONS AND CONCLUSIONS

Puri et al. noted in their study that the presence of cervical lymph node metastasis remains the most significant prognostic indicator of survival and disease recurrence in patients with HNSCC. With the development of lymph node metastasis it is seen an approximately 50% reduction in 5-year survival rate in these patients. A further precipitous and significant decline in survival and an unacceptably high rate of localregional and distant failure occurs when extracapsular spread of lymph metastasis node is present. Extracapsular spread is noted in a majority of the lymph nodes larger than 3 cm and in a significant number of nodes less than 2 cm and it has been demonstrated in lymph nodes measuring less than 1 cm. They concluded that extracapsular spread, thus, is the most important predictor of survival, local-regional recurrence, and distant metastasis [11]. Various studies concluded that extracapsular invasion

SCC. At supraglottis level we had 8 cervical metastases: 3 nonkeratinized SCC, 2 SCC with low tendency of keratinization, 1 spindle cell carcinoma and 2 keratinized SCC G2. We performed a Chi square test and we correlated different SCC with supraglottic localization to emphasize a prognostic factor for the prevalence of cervical metastases, P = 0.4271. Further analyze is needed on bigger groups of patients to find a correlation between cellular differentiation, localization and cervical metastases potential. The average time for local recurrence was 4 months (1-8 months).

So far the cellular differentiation was not considered a meaningful factor in tumor stadialization, but there have been reported correlations with cervical metastasis probability [6, 7, 8, 9], well acknowledged for the impact on survival [10].

represents a poor prognostic factor for OS for the following sites: oral cavity [12], oral cavity and oropharynx [53], supraglottic larynx [13], hypopharynx and larynx [14] and all sites [**60**, 15]. In our study we examined only 7 lymph nodes with extracapsular spread and we couldn't establish a correlation between extracapsular spread and local-regional recurrence.

Selective neck dissection may be sufficient for many N+ patients with SCC of the oral tongue, but some patients with extensive nodal disease may benefit from more aggressive treatment of the neck. Radiotherapy may be beneficial for all of the positive lymph node patients, but further studies are needed to be done. Prospective, randomized clinical trials will be useful in further defining the role of selective neck dissection in the clinically N2 neck and radiotherapy in the N1 neck for patients with SCC of the larynx [16].

However, the patients that are diagnosed with positive lymph nodes or extracapsular spread should be considered for a more complex and aggressive therapy, because they are at risk for regional and distant metastases. **[2, 59]**

It is of main importance the identification of subgroups of patients with primary head and neck squamous cell carcinomas that are at high risk of tumor recurrence. By considering localization, cellular differentiation of the squamous cell carcinoma (SCC),

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There have been found correlations between molecular markers and invasiveness, aggressiveness, degree of differentiation, tumor stage, and potential for metastases, but only in a few clinical studies it is demonstrated the impact on prognosis. To establish clinical implications of these results it is needed to realize studies on larger number of patients.

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COMPOSITE MATERIALS USED FOR ESTHETIC ADHESIVE. INDIRECT RESTORATIONS: A REWIEW



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ABSTRACT

Aesthetic expectations and demands of the patients are steadily growing, both related to the anterior area, as well as the posterior area. Adhesive "tooth-like" inlay/onlay-type restorations placed in the posterior areas of the oral cavity become an interesting alternative for the teeth with extensive coronal lesions. This option represents a conservative intervention, if compared to crowns, providing the advantage of maintaining pulp vitality, through less invasive dental preparations in comparison with tooth grinding. Indirect realization of such restorations, by means of dental laboratory, implies not only a good team-work of the dentist and the technician, but also a rigurous pass through all clinical and laboratory stages to achieve a final result according to the clinical principles. The existence of a multitude of materials that can be used for manufacturing such inlays makes it difficult for the dental practitioner to choose the optimal type of material. Thus, the present article intends to highlight some issues regarding some specific composite materials that can be used for indirect restorations inlay-type.

Key words: adhesion, esthetic indirect restorations, composite, class II cavities

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INTRODUCTION

If today's treatment of lesions with loss of hard dental tissues in anterior teeth is no longer a problem, composite materials allowing to solve this problem easy enough, with good esthetic results, we cannot say the same about the restorations of posterior teeth, especially in cases of extensive restorations; dental practitioners tried and still try to find solutions more resistant over time and also esthetic, allowing the maintenance of stable occlusal stops [1]. One of the solutions represented is by esthetic inlays/onlays, which can be made of

INDIRECT COMPOSITE MATERIALS

1. The first generation of materials used

Touati and Mörmann have introduced the first generation of indirect composites used for the manufacturing of inlays in the 1980s. These were made of an organic resinbased matrix, inorganic fillers and a coupling agent. The polymerization of these composite was light-induced and the photo-initiator used was camphorquinone. An aditional extra-oral curing of composite inlays was recommended for further reducing the polymerization contraction. We'll mention two of the materials belonging to the first generation: Concept and Sculpture.

Concept presents an array matrix formed of urethane dimetacrilat, butanediol-dimethacrylat and dimethacrylat-decanediol, and 73-76% comprising inorganic area silica particles ytterbium-trifluoride and particles (particle sizes range between 0.01 and 0.04 µm). Polymerization method consists in heat treatment under presure (121° C and 85 psi). The hardness of the material is 500-600 N/mm² and clinical surface loss over a period of five years is 25.3 µm.

Sculpture (Jeneric/Pentron Inc.) has resin monomers dimethacrylate-

composite or ceramic materials. The esthetic composite inlays are preferred the ceramic ones by to many practitioners, because of their require minimal advantages: they the preparations, manufacturing technique is easier, due to the userfriendly composite material handling and radioopacity, future adjustments of the occlusal surface are allowed without need of laboratory intervention, thev can be easily repaired and, last but not least, have a lower cost.

polycarbonate and Bis-GMA etoxylate; the filler contains barium-borosilicate particles and amorphous silica (78.5% content, particle sizes being 0.6 μ m). The polymerization is accomplished using a QTH curing unit with an intensity of 600 mW/cm² (Optilux 400) for 20 seconds. The hardness of the material is 80 N/mm², and the clinical surface loss over a period of five years is 15 μ m.

However, it has been mentioned that the first generation of indirect composites showed improved properties only in the laboratory, with failures in clinical trials. The first generation's clinical failures have led to the development of an improved generation of composite materials. The improvements have occurred mainly in three areas: structure and composition, polymerization technique and strengthening fibers.

2. The second generation of materials used

A development of composite materials used for indirect restoration was achieved by the introduction of the second generation of composite "Poly-glass" materials known as [2]. During recent years, materials several composite resins with

indications for indirect restorations have been used: Artglass (Heraeus Kulzer), Belleglass HP (Belle de St Claire/Kerr) and Targis (Ivoclar). In spite of the different techniques and formulas, all three materials are polymer-based that promise to reduce the clinical surface loss of opposing teeth, easier and faster an manufacturing, and an easier repair compared to porcelain restorations [3]. Artglass, introduced in 1995 as a "Polymaterial. glass" contains 70% (percentage of mass) filling and 30% (percentage of mass) organic resin. The filling consists of barium-aluminasilicate medium-sized glass with particles of 0,7 µm, and a moderate amount of colloidal silica particles. "Poly-glass" Artglass is unique because in addition to conventional bifunctional monomers, the resin matrix contains new polyfunctional methacrylates monomers, bis-glicidiltrietylen-glycolacrylates, and dimethacrylates. Artglass was marketed as a product without metal support in total restorations fillings (inlays, onlays, veneers), but also in restorations with metallic infrastructure (bridges, crowns, Maryland bridges), or in implantsupported restorations.

"poly-glass" In other cases, Artglass appears alongside the metal structure, for example in the case of "Kevloc" system that involves applying of an acrylo-nitrate copolymer primer and of an urethane resin on the grinded metal surface, before the application and the curing of composite material. This material shows a hardness of 380 MPa and a clinical surface loss at five years about 40% [4].

Belleglass HP was introduced in 1996 by Belle de St Claire (now the trademark belongs to Kerr Hawe). Resin matrix is based on conventional monomers of composite resins: uretanand aliphatic dimethacrylates. The material contains "barium glass", 78% (percentage by mass), particles of 0.6 μm size-dentine material and "borosilicate glass", 74% (percentage by mass)-enamel material. Belleglass uniqueness lies in the mechanism of polymerization: the material is polymerized under a pressure of 5 bar (80 psi) at a high temperature $(140 \circ C)$, in the presence of nitrogene. The high temperature is used to achieve a high level of conversion. Nitrogen rules out the inhibition due to the oxygen within process of polymerization, the degree resulting in a high of conversion of the resin matrix, obtaining a material with improved properties. The intrusion of a quantity as low possible of oxygen leads to a superior translucency of the restorative material [5].

The manufacturer cites for **Belleglass** a 890 Mpa hardness and a clinical surface loss of 6,3 μ m, within a period of five years. The **Belleglass** material is marketed as system without metallic structure (inlays, onlays, veneers and crowns) for anterior teeth, with metallic reinforcement, or as a fiber-reinforced structure, used for dental bridges.

1996, Ivoclar introduced In Targis, so-called "ceromer" (optimized polymer with ceramic particles). These ceromers combine the advantages of ceramics with those of good quality composites [6]. Ceromers are special compounds, made presenting а padding with fine ceramic particles of submicron size (77% percentage by mass), well condensed (approximately 75-85% weight), embedded in an matrix of advanced organic polymers (23% percentage by mass). The filling consists of "barium glass" with the particle size of 1 µm, sferoidal silica particles of 0,25 µm, and colloidal silica whose dimensions vary between 0.015 and 0.05 µm. The resin matrix consists of conventional Bis-GMA monomers, decandiol-dimethacrylates and urethane-dimethacrylates. The superior properties of the Targis product are the result of "optimal chemical composition" and of "optimized polymerization process" [7].

The manufacturer cites as clinical surface loss phenomenon a value of 85 μ m, within a period of five years ("in vivo" studies).

Due to their composition and structure, the ceromers combines the advantages of ceramics (durable esthetic quality, abrasion resistance and high stability) with those of composites (simple handling, easy adjusting, easy finishing and polishing, chemical bond with glass ionomer cements used as bases, low risk of fracture, as well as the possibility of repairing the restorations in a singleappointment clinical approach). As long as the ceromer restorations have very good esthetics, they also preserve tooth structure. Moreover, the adhesive luting with dual composites ensure their stability.

Targis is used for veneers and indirect restorations (inlay/onlay), for crowns and short bridges (no more than three elements), reinforced with composite units (**Vectris**) and for crowns and bridges, in cases of implant-supported restorations. **Targis** restorations with metallic support are fixed through conventional cementation technique, and the metalfree ones through adhesive luting technic.

Targis Kit contains many shades and products for characterisation, allowing natural-looking restorations. The shade system, combined with "Chromascop" System, gives the possibility to achieve harmonious restorations, with exquisite esthetics.

Other advantages of Targis translucency and system are: similar fluorescence to enamel. characterisation, abrasion and hardness similar to the enamel, flexural strength, adhesive cementation, easv high degree of biocompatibility.

Knoblock and coll. (1999) [8] have studied the degree of conversion and the degree of clinical surface loss for inlays made from the same material (table I). **Belleglass**, **Artglass** and **Targis** systems have been used for this purpose. None of the three composite from the second-generation did not show an increased degree of polymer conversion and no increased abrasion resistance, compared to the results of previous studies carried out with materials from the first generation (**Concept**) [6,9].

Table I. The degree of conversion and the atrition of composite used for inlay restoration (Knoblock and collab., 1999) [8]

	, , , , , ,	
Material	Degree of conversion	Atrition surface loss
	(%)	(µm/resolution)
Belleglass	74	0,35
Artglass	54	0,46
Targis	48	0,46

60 inlays from each of the following composites: Artglass, Belleglass and Targis were made in more specialized centres (Christensen and collab., 1999) [10]. A year later, the three materials' clinical surface loss was higher than the one observed for Brilliant DI and **Concept** inlays. Artglass crowns cemented with Denthesive II adhesive agent showed a high frequency of cementation failure

(42%). **Targis** presented an incidence of failure of 28% [6].

Postoperative sensitivity was frequent with the three systems. The opposite teeth clinical surface loss has not been a problem, but occlusal contact between two **Artglass** crowns has led to a high degree of usage of the material.

Table II shows the results of studies "in vivo" and "in vitro" for three composite systems. Dyer and Sorensen (1998) [11] have mentioned the flexural and fracture strength of some composite systems used for inlay manufacturing.

Table II. Abrasion and atrition of composite resins used for inlays and enamel surface loss (Sorensen and Dyer, 1998) [11]

Material	Abrasion (µm)	Atrition (µm)	Enamel surface loss (mm²)
Belleglass	10 ± 8	32 ± 7	4 ± 1
Targis	23 ± 8	54 ± 19	4 ± 1
Artglass	30 ± 9	92 ± 29	8 ± 1

As mentioned by the manufacturer, Artglass has shown a high degree of conversion of monomers, greater fracture toughness, and a lower rigidity and hardness. However, resistance to clinical surface loss through abrasion and atrition of Artglass was significantly lower than the same resistance of other materials, perhaps as a result of a lower Young modulus and a lower hardness. The authors concluded that Artglass cannot be recomended for restoration in the

posterior areas with high occlusal stress.

Table III compares Artglass, Belleglass and Targis with а composite material for used inlays, maerial from the first generation, **Concept.** There were minor differences in terms of resistance to bending, although Belleglass had greater resistance than Concept. Concept showed the greatest resistance to while Artglass fracture, the was weakest.

Table III. Flexural strength and fracture resistance of composite resins for inlays (Dyer and Sorensen, 1998) [11]

Material	Flexural strength (Mpa)	Fracture toughness (MN m ^{-3/2})
Concept	130 ± 18	$2,3 \pm 0,2$
Artglass-dentin	132 ± 14	$1,4 \pm 0,2$
Targis-dentin	135 ± 14	$1,9 \pm 0,2$
Belleglass	150 ± 16	$2,0 \pm 0,1$

Other studies (Pallensen and collab.) over a period of two years included inlays, onlays and metal-free crowns infrastructure were completed.

The failure rate of **Artglass** restorations was 20% after two years, considered by Pallensen [12] as

CONCLUSIONS

Patients' esthetic requirements increasing. are constantly The restoration of posterior teeth with extensive coronal lesions raises significant problems and is still searching for the ideal material for indirect techniques. Composite inlays represent a treatment option for Class Π cavities. Second generation unacceptable even in circumstances where they have replaced direct composite restorations. The causes of failure: the destruction of the adhesive attachment (10%), fracture (5%) and pulpal complications (5%).

composites like Belleglass and Targis proved higher qualities compared to Artglass: clinical surface loss through abrasion and atrition of these two being lower than the other. The properties of materials used for inlays are different, making difficult the choice of the optimal material that can ensure the longevity of the restoration. Based upon the above results, future research may try to improve the next generation of composite materials, in order to obtain superior clinical results. The clinician is the one who must

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THE INTERDISCIPLINARY MANAGEMENT OF UPPER LATERAL INCISORS-HYPODONTIA – CASE REPORT



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ABSTRACT

Introduction: The most frequent cases of hypodontia (except the third molars) involve the upper lateral incisors and often require a multidisciplinary treatment approach, targeting the management of maintaining, closure and redistribution of space. The treatment options discussed in the literature are: orthodontic space closure, tooth-supported prosthodontic treatment and implant-supported crowns.

Case report: A 13 year old girl was diagnosed with Angle Class II malocclusion and a mild Class II skeletal pattern. A diastema and tremas were present in the maxillary arch. Radiographic examination confirmed that 1.2 and 2.2 were missing. A combined orthodontic-restaurative-surgical treatment approach was adopted. Space opening in the maxillary arch and the replacement of the maxillary lateral incisors with future implants was the treatment of choice. Before the brackets were applied, a Distal Jet appliance with precalibrated 240 g coil springs was activated for 4 months. After two years, the brackets were debondedand two Maryland bridges have been cemented, replacing 1.2 and 2.2, until the patient will reach 18 years of age, being able to receive two dental implants.

Treatment results:We obtained an average of 3.2 mmof distalization for each hemiarch. All the orthodontic objectives were achieved.

Conclusions: Orthodontic treatment can be an effective treatment option in patients with congenital hypodontia, favouring the redistribution of space, teeth alignment and the correction of malocclusion. The interdisciplinary treatment approach was essential in order to maintain the stability of the orthodontic treatment outcome and to improve aesthetics. The Distal Jet achieved the simultaneous distalization of the maxillary first and second molars into a bilateral neutral relationship.

Key words: hypodontia, upper lateral incisors, interdisciplinary management, Distal Jet

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INTRODUCTION

The term hypodontia is used when one to six teeth are missing, while the term oligodontiais used when more than six teeth are absent third (excluding the molars). Anodontia is an extreme case of tooth agenesis, denoting complete absence of teeth. Tooth agenesis is one of the most dental developmental common abnormalities which occurs as a result of disturbances during the initial stages of tooth formation. Tooth agenesis has an unclear etiology and may occur isolated (familiar or sporadic) or as a part of a syndrome. Familiar tooth agenesis can be transmitted as an autosomal recessive, autosomal dominantor X-linked genetic inheritance pattern[1-4].Screening the affected families is essential to ensure the proper diagnostic and the adequate timing for treatment. The sporadic tooth agenesis occurs with no hereditary history [5].

Hypodontia in the maxilla is more frequent than in the mandible. Many studies reported that, with the exception of thethird molars, the most frequent cases of hypodontia involve the upper lateral incisors, followed by the upper and lower second premolars. In European populations, the most frequently missingteeth (after the third molars) arethe mandibular second premolars, followed by the maxillary lateral incisors and the maxillary second premolars[<u>6</u>].

The incidence of maxillary lateral incisors hypodontia is 1% to 2% in white populations [7].This type of hypodontia usually affects both maxillary hemiarches.

Maxillary incisors lateral hypodontiaoften requires amultidisciplinary treatment approach, targeting the management of maintaining, closure and redistribution of space. In most cases, several factors should be taken into account: patient motivation, compliance with orthodontic treatment, age, type of malocclusion, skeletal pattern, facial profile, degree of crowding andnumber of absent teeth[8].

In the literature, a few possible treatment options are discussed: orthodontic space closure [9, 10], tooth-supported prosthodontic treatment[11-14] and implant-supported crowns [12, 15, 16].

CASE REPORT

A 13 year old adolescent girl presented for orthodontic treatmentin the Department of Pedodontics and Orthodontics, at the Faculty of Dental Medicine, "Victor Babeş" University of Medicine and Pharmacy Timişoara. The patient was diagnosed with Angle Class II malocclusion and a mild Class II skeletal pattern, with a lowFrankfurtmandibular plane angle (FMA) and reduced anterior face height. The patient had no facial asymmetry, a slightly convex facial profile, competent lips and a low smile line (Figure 1).



Figure 1. Extra-oral examination (frontal view)

Intra-oral examination revealed a Class II malocclusion,a diastema and

tremaspresent in the maxillary arch (Figure 2).





Figure 2. Intra-oral examination: a) frontal view; b) right lateral view; c) left lateral view

Radiographic examination confirmed that the upper lateral incisors 1.2 and 2.2 were missing.

Nonintervention was not an option.With the consent of the patient, a combined orthodontic-restaurativesurgical treatment approach was adopted.The main objectives of the orthodontic treatment were to correct the malocclusion, to redistribute the space and to align the teeth in preparation for the later prosthodontictreatment phase.

Space opening in the maxillary arch and the replacement of the maxillary lateral incisors with future implants was the treatment of choice.

Because orthodontic fixed braces alone could not solve the problem of space redistribution, a Distal Jet appliance with precalibrated 240 g coil springs was used before the brackets were applied (Figure 3). The Distal Jet was activated for a period of 4 months.



Figure 3. Distal Jet appliance

The Distal Jet appliance had a dual role:

- to obtain neutral molar relationships bilaterally;
- to obtain the necessary space for the distalization of the canines and to create space for future implants

in order to replace the missing teeth 1.2 and 2.2.

After the sagittal expansion (Figure 4), the Distal Jet screws were locked and the appliance was left in place in order to maintain anchorage.



Figure 4. Intra-oral view after 4 month of active treatment using the Distal Jet appliance

Roth OMNI (GAC) brackets (0.22 inch slots) were applied using the straight wire technique(Figure 5).Overbite reduction started slowly at the beginning of the treatment.



Figure 5. Intermediate treatment phase after the bracketswere applied

After two years of active orthodontic treatment, the brackets were debonded.In order to maintain space and tooth stability and to temporary restore the esthetics, two Maryland bridges have beencemented (Figure 6), replacing 1.2 and 2.2, until the patient will reach 18 years of age and will be able to receive two dental implants.The Maryland bridges also function as an orthodontic retainer. Because of the lack offrontal maxillary alveolar bone height and width, bone augmentation of the alveolar processwill probably be neededbefore implant insertion.



Figure 6. Maryland bridges cemented, replacing 1.2 and 2.2

TREATMENT RESULTS

All the pretreatment orthodontic objectives were achieved and both arches were correctly aligned, with coincident midlines.

For each millimeter of bodily distalization and uprighting of the molars, 2 mm were gained in arch length. Over a four-month period, the Distal Jet achieved an average of 3.2 mm/hemiarch of distalization, moving the crowns of the maxillary first molars into a Class I relationship.

The orthodontic objectives during both the active and retentive phases were achieved with good treatment outcome(Figure 7 and 8).



a)







Figure 7. Treatment results (intra-oral examination): a) frontal view; b) right lateral view; c) left lateral view



Figure 8. *Treatment results (extra-oral examination)*

DISCUSSIONS

The general dental practitioner is usually the first to diagnose hypodontia, but the final treatment involves a multidisciplinary approach.

Regarding the multidisciplinary management of hypodontia, several treatment options are considered[<u>17</u>]:

- maintaining the space, using a prosthodontic/restaurative treatment approach;
- orthodontic space closure;
- orthodontic redistribution of space (space opening).

When the hypodontia produces minimal spacing that is of no aesthetic concern to the patients (especially when the spacing is posterior to the canines), or the patients refuse the orthodontic and restorative treatment options, we should provide only preventive maintenance. Anterior spacing can be aesthetically managed using bonded restorative techniques (veneers and composite build-ups)[<u>18</u>].

Another treatment alternative is orthodontic space closure and the enameloplasty of the canine to resemble a lateral incisor. Although this treatment option is acceptable in patients with low smile lines, the orthodontic patient opted for redistribution of space, in order to achieve a lower discrepancy in the

levels of the gingival margins between the central incisors and the canines.

Another advantage of space opening is the proper positioning of the canines, allowing canine guidance in mandibular lateral movements. Space opening also benefits patients by favouring good intercuspation in the posterior region[<u>19</u>].

The major disadvantage of this treatment choice is that the patients require permanent dental prostheses that maintain a correct arch form and continuity.

Two factors influence the space required for the future prostheses: the occlusion and the aesthetics. In ideal circumstances, the orthodontic treatment should achieve a normal overbite and overjet, coincident midlines and a neutral occlusion [8, 20].

At the end of the growth period, the insertion of narrow diameter implants (3-3.3 mm) will be taken into account. Dental implant treatment is a good therapeutic option if sufficient bone volume is present, otherwise augmentative bone procedures have to be provided to the patient. This will prolong the treatment time with a minimum of 3 months. Regarding the aesthetics factor, very often soft tissue volume is insufficient and therefore connective tissue grafts have to be

CONCLUSIONS

- Orthodontic treatment can be an effective treatment option in patients with congenital hypodontia, favouring the space, redistribution of teeth alignment and the correction of malocclusion.
- The interdisciplinary treatment approach, in our case, was essential in order to maintain the stability of the orthodontic treatment outcome and to improve aesthetics.
- The individual characteristics of the patient and the patient preferences

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placed in order to regain the buccal contour.

play an important role in the interdisciplinary treatmentof hypodotia cases.

• The Distal Jet appliance was successfully used for the simultaneous distalization of the maxillary first and second molars into a bilateral Class I molar relationship.

Resin-bonded Maryland bridges and future implant-supported prostheses were the preferred restorative optionsin our case.

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UNILATERAL ECTOPIC CANINE THERAPY- CASE REPORT



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ABSTRACT

Introduction

Dental ectopia is a rare clinical finding characterized by a change in the normal tooth eruption pathway. In more severe cases, nontreated ectopia may develop into either partial or total transposition. Patient, aged 15, described in this case report, presents a unilateral canine ectopia, tooth number 2.3, combined with an inverted dental engrenage at dental level 1.2 and 2.4.

Objectives

In this article, our aim is to obtain tooth alignment on the upper and lower dental arch and to realize a Class I Angle occlusion, that is both functional and stabile.

Material and method

We applied an orthodonthic fixed appliance on dental arches, Roth 3B, slot o. 2.2, using straight wire technique. The patient was treated for 15 months. At the treatment beginning, it was imposed to realize an elevated occlusion in order to align the inverted lateral incisor 1.2.

Results

After 15 months of treatment, we obtained occlusal relationships AngleClass lat molar and canine level, dental alignment, correct medial line and leveling of the occlusal dental outline. At the end of treatment, the patient received fixed contention, bimaxillary.

Conclusions

Early treatment of canine ectopia with fixed dental appliances is important in order to obtain correct occlusion and to improve the esthetic appearance by correct alignment of teeth.

Key words: canine ectopia, inverted dental engrenage, dento-alveolar incongruency, fixed orthodontic appliance

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INTRODUCTION

The superior permanent canines develop in the depth of the maxillary bone, the dental development ends late and then they erupt in the oral cavity in the remaining space between the lateral incisor and the first premolar. The eruption disturbances appear more often involving the upper canines[1] and the wisdom teeth. Ectopic eruption is an orthodontic and surgical issue, because of possible dental inclusion, radicular pathologic resorbtion of the adiacent teeth or other septic The maxilar complications. canine dental follicle appears as an extension of the dental palatine lamina of the deciduous lateral incisor. The mineralization of the canine dental crown starts at 4-12 months and is completed around the age of 6-7 years. During dental eruption, we assist at the extension of the gubernacular channel. The dental germs are placed, generally, in contact with the apex of the temporary canines[2], lateral incisor and first premolar. During the eruption process, the canine migrates along the distal margin of the lateral incisor, to this particular tooth[3]. close Previous studies have shown that the lamina dura is often absent in this eruption stage[4]. Because of this intimate contact, the lateral incisors may easily bend distally in their apical third.

The period between the loss of the deciduous canine and the eruption

MATERIAL AND METHOD

Patient, aged 15, is presented with Angle class I molar relationships,

of his successor is long, approximately 139 days. Cases have shown that this period may grow up to 955 days.

Clinically, the palpation of the vestibular surface of the alveolar process may show the presence of the maxillary canine 1, 11/2 years before his eruption. This fact has clinical and diagnostical value[5].

During the active fazes of eruption, the dimension of the canine dental follicle grows[6], while, in cases of canine inclusion, this dimension is diminishing.

Dental ectopia involves often the upper canine because of the dental eruption chronology. The causes of this may activate long before[7], but the anomaly becomes manifest at a relatively high age. The incidence of this anomaly varies linked by age particularities the examined of patients. observed We patients collectivity with ages between 7-14 years, that present a canine ectopia frequence of 2, 7%[8]. Examining the same collectivity separately aged 12-14, the frequency rises at 12, 4%. The studied anomaly, alone or associated with other dento-maxilary disorders[9], is found around 15% of the patients. Regarding the localization, prior dental literature[10]shows the following proportions: bilmaxillary ectopia 9%, upper vestibular ectopia 61%, upper palatal ectopia 24%, vestibular inferior ectopia 5%, lowe lingual ectopia 1%.

inverted dental engrenage at the level of 1.2 and 2.4, and canine ectopia 1.3.



a.Intraoral frontal picture b.Intraoral lateral left c.Intraoral lateral right picture picture figure 1. Patient O.N., 15, is presented in our service in September 2012

The intraoral examination shows the following:

- Permanent dentition
- Overbite 1/3
- Dento-alveolar incongruency with dental crowding both maxillary and mandibular
- Inverted dental engrenage 1.2/2.4
- 1.3 and 3.2 positioned vestibular

- The sagital outline shows frontal overjet of 2 mm and in the molar and canine area occlusion Angle class I
- The vertical/ frontal outline presents overbite of 1/3.
- The medial line is 2mm deviated towards left.

Examination of the study model and the paraclinical examination confirm our clinical diagnostic.



a.Study model



b. Orthopantomography

Figure 2.

We proceeded in the placement of a fixed orthodontic appliance, bimaxillary, using brackets roth 3B, slot 0, 22mm. the dental occlusion had to be

DISCUSSIONS

The straight wire technique is often used in orthodontic therapy. In has been described by Andrews in 1972. The premise he followed is that a preadjusted system in the correct position allows the teeth to be aligned with a right arch in dental occlusion contact, having a perfect mesio-distal declention. elevated during the first month of treatment, in order to align the left upper lateral incisor 1.2. The technique we used in this case is straight wire.

All the information that is necessary for the positioning of the affected tooth in all three outlines is offered by positioning of the bracket at the intersection of the facial axis of the clinical dental crown. Andrews' system has been through several modifications during 40 years, improvements have been attached; no arch bending, for ideal dental alignment, but the initial fixation of the bracket remains the most important treatment step.

The patient was treated for 15 months.



a. Frontal view

b. Left lateral view

c. Right lateral view

Figure 3. Intermediary aspect after 11 months of treatment

After treatment finishing, we obtained correct relationships in all three outlines of interest:

- Molar relationship Angle class I
- Canine relationships Angleclass I
- Medial line corresponds on both maxillaries
- Alignment of teeth prior malpositioned
- In the lateral area, every tooth has contact with two antagonists
- Overbite 1/3
- Overjet 2mm



a. Frontal view

b. Left lateral view Figure 4. Treatment results



We applied fixed contention canine-canine on the maxillary dental

arch aswell as on the mandibular dental arch.



a. Intraoral aspect

b.Fixed maxillary contention *Figure 5.*

c. Smile

CONCLUSIONS

- Unilateral canine ectopia, with medial line deviation may be solutioned by extraction of 4 premolars, but cases exist where extractions can be avoided.
- Suplimentary paraclinic investigations (besides orthopantomography and lateral

skull) are needed in order to trace eventual root resorbtion at lateral incisor level.

- Teenagers respond very rapidly to correct treatment
- Fixed contention is always imposed in order to prevent and avoid relapse.

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OCCUPATIONAL HAZARDS AMONG DENTAL LABORATORY TECHNICIANS



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ABSTRACT

Introduction: Dental laboratory technicians have multiple occupational exposures, which may have adverse effects on their health.

The aim of the study was to obtain information about the nature and prevalence of occupational health problems (hazards) and their attributed causes, among a group of dental laboratory technicians in Timisoara.

Material and method:40 dental technicians from Timisoara, aged between 24 and 53 years, were taken into study. They were selected from Faculty of Dentistry and from private laboratories. All subjects filled in a questionnaire, focusing on occupational health complaints and their cause.

Results:90% of dental technicians consider they have a stressful job. 35% of dental technicians worked in dental laboratories with air vacuum. None of the investigated laboratories had autoclave or dry heat oven for infection control. 65% of laboratories used disinfection methods (bath immersion or spraying). The occupation related complaints were dermal reactionsusually located on hands & fingers including the nails and the nail borders(50%);musculoskeletal reactions in both neck and hands (65%); systemic reactions- headache& fatigue (75%).

Conclusion: Dental laboratory technicians in Timisoara exhibit a high frequency of occupational health problems, attributed to different aspects of pollution in their work environment.

Key words: occupational health problems, dental technician, working environment

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INTRODUCTION

The work in dental technology laboratory implies а series of occupational hazards of chemical, ergonomic and stress like nature, with the possibility of developing physical and psychological reactions¹. Musculoskeletal pain has been documented as a problem among dental practitioners for many years, and oral health care population is risk considered at greater for development of musculoskeletal disorders. These injuries result rather from chronic, repetitive movements of the hand or wrist and the cumulative work stress^{2,3}.

Dental materials have different composition, being diversified in metals, resin-based synthetic polymers, cements, or impression materials. The transfer of potentially allergenic components from such materials carry the risk of hypersensitive reactions among both patients and dental personnel². Inhalation of volatile substances, such as methylmethacrylate (MMA), implies the risk of producing pathogenic changes of the central nervous system⁴, lungsand liver.⁵ Direct handling of (MMA) without protection may lead to axonal degeneration of distal nerves.⁴ Later reactions to metals chromium,cobalt and nickel also reported.^{1,6}

Dental technicians are potentially exposed to various occupational dusts and chemicals.Grinding dusts from metals, resins, ceramics and plaster may cause silicosis like lung diseases.⁴

Technicians and other personnel who spend many hours in noisy dental laboratories may be at risk of developing hearing problems if they choose not to wear ear protection^{2,7}.

It is generally accepted that the practice of dentistry is characterized by stress.Work-related stress is believed to lead to high rates of cardiovascular disease,suicide,alcoholism and drug abuse. Major stressors may include time-related pressures, high case-loads, financial worries, staff problems, or equipment breakdowns^{1,8}.

Nevertheless, cooperation between the dentist and the technician is important, with benefits for dental practice⁹.

The aim of the studywas to determine noxious factors, that dental laboratory technicians from Timisoara face, to facilitate taking measures for the prevention and elimination of these noxious factors by implementing optimal hygienic conditions/ working environment.

MATERIAL AND METHOD

40 dental technicians from Timisoara, aged between 24 and 53 years, were taken into study. They were selected from Faculty of Dentistry private laboratories.All and from participants filled in а questionnaire(focusing on occupational health complaints), which included:

- Demographic data including age, sex, employment status.
- Work-related data including duration of practice in years.
- Work environment: type of ventilation; lighting and space of

the laboratory; condition of instruments and equipment.

- Safety precaution measures, like use of fire pump, warning alarm.
- Infection control measures: use of • paper mask, face shield, gloves, mask, protective glasses, immunization against virus hepatitis B,hand washing (frequency, use of disinfectant soap), proper handling of sharps, dry heat oven, autoclave, and uniform.

- General (systemic) reactions, like feeling of headache, vertigo, nausea, fatigue or others; and attributed causes;
- Musculoskeletal reactions in the neck & hands(tension, rigidity, pain with reduced mobility in the muscle) and attributed causes;
- Neurological & vasomotor finger's reactions: manifestation and attributed causes;
- Respiratory tract reactions, in the nose, throat and lungs.
- Mucosal reactions: manifestation (running nose or impaired sense of smell) and attributed causes;
- Eye reactions, its manifestation (conjunctival eye reactions, dry or running eye); Functional eye disturbances.

- Dermal reactions (finger and nail border): symptoms and attributed causes;
- Hearing problems: impaired hearing, increased noise sensitivity.
- Carpal tunnel syndrome (left hand or right hand): symptoms
- Stressors: the technicians were asked if they thought that their work is stressful, and were also asked to choose the stress factor or factors: variety of work (7 factors), working conditions (5 factors), interpersonal relationship (4 factors).

Yes or no answer was used for each item. All participans were assured that responses would remain anonymous confidential.The and participants were also asked to describe their health complaints with their own words.

RESULTS

Ventilation in 60% of cases depended mainly on windows; 70% had also air conditioning, used especially during summer; only 35% of dental technicians worked in dental with laboratories air vacuum.Regarding light condition, the percentage of technicians who worked in good light was higher than of those working in poor light. Generally, the working space of technicians was considered wide. The condition of instruments/ equipment was good in case of 60% of technicians. Fire pumps available were in most dental laboratories, while only one private laboratory had warning alarm.

Regarding<u>infection</u> control <u>measures</u>,60% of the dental technicians reported that they are wearing coats during work, while 35% of them were keen of proper handling of sharps during work. None of the investigated laboratories had autoclave or dry heat oven for infection control. 65% of laboratories useddisinfection methods (bath immersion or spraying) for all that came from dental practice (impressions, metal frame or anything that got in touch with patient's moth). Paper masks (60%), protective glasses(40%), face shields (35%), and gloves (25%) were the infection control measures that had been used by the dental technicians in an descending order.None of the dental technicians had immunization against virus hepatitis B. No one was using hands disinfectant. Thehand washing was performed using the tap water and normal soap only.

The occupation related complaints were dermal reactions, usually located on hands & fingers including the nails and the nail borders (50%);musculoskeletal reactions in both neck and hands(65%); systemic reactions- headache&fatigue(75%);eye reactions involving running eyes(34%), problems in focusing or weakening of eve vision (65%); hearing problemsincreased noise sensitivity (20%);then respiratory tract reactions (45%), then neurological and vasomotor reactions

(30%), including reduced holding and failing contraction of the thumb. <u>Carpal</u> <u>tunnel syndrome(CTS)</u> was never found among the studied technicians.

A considerable number of dental technicians (90%) consider they have a<u>stressful job</u>. Among the attributed causes are deadlines, high case loads and high concentration, quite equally.

<u>The causes attributed for the</u> work related complaints:

Figure 1 shows that work load stress was the highest contributing cause of the systemic reactions for dental technicians.

Figure 2 shows that prolonged wrong postures &heavy work, followed by vibration of hand piece and then repeated grinding, sawing and wax work were the highest contributing factors for the musculoskeletal reactions for dental technicians.

Figure 3 shows that prolonged grinding & polishing and vibration of hand piece contribute equally to the neurological & vasomotor fingers reactions of dental technicians.

Figure4 shows that indoor climate, grinding dust and acrylic resin monomer contributequite equally to respiratory tract and mucosal reactions among dental technicians.

Figure 5 shows that MMA, ceramic and metallic processing,next to wet-work and plaster were the highest contributing causes of dermal reactions among dental technicians. No one of control group suffered from dermal reactions.



Figure 1. Causes attributed for systemic reactions of dental technicians



Figure 2. Causes attributed for muskuloskeletal problems in the neck & hand



Figure 3. Causes attributed for neurological & vasomotor finger's reaction



Figure 4. Causes attributed for mucosal and respiratory tract reactions among dental technicians



Figure 5. Causes attributed for dermal reactions among dental technicians

CONCLUSION

The present study was performed to investigate occupation related health complaints among dental laboratory technicians from Timisoara.The present profile of occupational health complaints is probably a characteristic of dental laboratory technicians themselves in Timisoara.

Dental laboratory technicians from Timisoara have occupational health complaints, attributed to different aspects of pollution in their

working environment. Systemic headache&fatigueand reactionsmusculoskeletal reactions are the most frequently related problems. Dermal reactions and weakening of eye vision should not be neglected. MMA is a serious respiratory and skin irritant. There is a positive relation between work-related health complaints and age/ years of practice. Infection control measures are ignored by many dental technicians. A great part of dental technicians work under hazardous

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environment, with poor ventilation. Preventive and /or therapeutic programs designed to reduce the occupational problems among dental technicians must be implemented. The dental laboratories must be designed and prepared according to the recommended safety measures.

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ASSESSMENT OF THE GOLDEN PROPORTIONS ON DIGITAL MOCK-UPS



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ABSTRACT

This study was conducted on a group of 31 patients, with ages between 18 and 33 years old, from which 18 were female and 13 were men. The patients were selected so they would have above average oral hygiene, no malpositions, no missing teeth, no fillings and no prosthetic restorations in the anterior maxilary region.

Each patient had his photography taken, from frontal view, with retractors in his mouth. Based on those photos, two digital simulations were realized for each patient, using a dedicated software (Adobe Photoshop CS5; Adobe Systems Inc., San Jose, California). Those simulations will be referred to as "digital mock-ups". In the digital mock-ups, we modified the proportions in which the frontal superior teeth were.

A team of 23 dentists who practice dentistry in Timisoara took part in the evaluating process: 6 orthodontists, 6 prosthetists and 11 dentists who practice general dentistry. The aim of this study was to assess the applicability of the Golden Proportions in the planning of esthetic fixed restorations in the maxillary anterior region. **Key words:** digital mock-up, Golden Proportions, maxillary anterior region, esthetics

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INTRODUCTION

One of the most well knowned definitions of the concept of beauty is based on the Golden Proportions, which mean that the ratio between a small and a large should be 1 to 1,618.

concept of the Golden The Proportions is widely documented in literature along time: Huntley (1970), Livio Maria (2002), Dunlap (1997), Le Architecture, Corbusier (1954) in LendaviErno (1971) in Music, D'Arcy Thompson (1952) in Biology and imortalised by Brown in 2003 in the "DaVinci Codes". Even Leonardo Da Vinci was fascinated with this concept and published a book on this matter "De DivinaProportione" called (The Devine Proportion) in 1509.

A pioneer in using the Golden Proportions in Dentistry is Dr. Edwin I. Levin, who all through his 50 years career documented and improved the concept. His first published work on this matter was an article in The *Journal of Prosthetic Dentistry*, in 1978.

The applicability of the Golden Proportions in Dentistry refers to the maxillary anterior region (1.4-2.4). Therefore, the projected width of the lateral incisor should be 61,8% from the projected width of the central incisor, and the projected width of the canine should be 61,8% from the projected width of thelateral incisor (fig.1). Also, the height of a central incisor (as measured from the highest point of the gingival level to the middle of the incisal edge) should be 61,8% from the projected width of bothcentral incisors (aswas demonstrated by Dr. Stephen Marquardt, oral surgeon, California) (fig.2).



The Golden Proportions are based on the Fibonacci number, also knowned as "Phi" (Phi=0,618). The Fibonacci number derives from the Fibonacci sequence: 0,1,1,3,5,8,13......144,233,377.... The sequence starts with the numbers 0 and 1 and every next number is obtained by adding the previous two numbers.

Mathematically, the numbers in the sequence are defined as follows: $F_0 = 0$ F1=1

 $F_x = F_{x-1} + F_{x-2}$ for $x \ge 2$

The golden ratio, or Phi, is the ratio between any two successive numbers in the sequence. To be noted that for the numbers at the beginning of the sequence, the ratio slightly differs from 1,618034..., but the bigger the pair of numbers, the closer the approximation:

 $\frac{F_{\rm x}}{F_{\rm x-1}} = 1,6180339887 \dots$ $\frac{F_{\rm x-1}}{F_{\rm x}} = 0,6180339887 \dots$

Α	В	A/B
2	3	1,5
3	5	1,6666
5	8	1,6
8	13	1,625
•••••	•••••	
144	233	1,618055

MATERIAL AND METHOD

A number of 31 patients participated in this study, with ages between 18 and 33 years old, from which 18 were women and 13 were men. They were selected so theywould haveabove average oral hygiene, no malpositions, no missing teeth, no fillings and no prosthetic restorations in the anterior maxillary region. The selection was made by the same dentist, who aimed to admit in the study patients with an attractive smile, from a specialized point of view.

Each patient was photographed from the front view, with retractors in the mouth. After that, based on those photos, two digital mock-ups were made for each patient using a dedicated software (Adobe Photoshop CS5; Adobe Systems Inc., San Jose, California). For both mock-ups, the teeth in the maxillary anterior region were cropped one by one and then resized. On one hand, we modified the ratio in which the height of one central incisor (as measured from the highest gingival point to the middle of the

233	377	1,618025

AIM AND OBJECTIVES

The main objective of this study was to assess the applicability of the Golden Proportions in the planning of esthetic fixed restorations in the maxillary anterior region. Knowing that everything around us comes to math and numbers eventually, we tried to determine the viability of such an equation, which would provide us with an accurate starting point in the planning of esthetic fixed restorations in the maxillary anterior region. This study is also a comparative one, due to the fact that we challenge the Golden Proportions against the results we obtained in the study "The Golden Proportion in the anterior maxillary region".

incisal edge) was with the width of both central incisors (as measured between parallels drawn through the two most distal proximal pointsof the two central incisors).On the other hand, we modified the mesial-distal ratios in which the teeth in the maxillary anterior region were to each other. In the first mock-up, we brought the ratios in the Golden Proportions, so the lateral incisor would be 61,8% from the central incisor and the canine would be 61.8% from the lateral incisor. In the second mock-up we modified the ratios according to the results we obtained in the study "The Golden Proportion in the anterior maxillary region", so the lateral incisor would be 67% from the central incisor and the canine would be 80% from the lateral incisor. It is important to mention that regarding the ratio between the height of one central incisor and the width of both central incisors, the Golden Proportion was proved to be valid in the study

mentioned above, therefore it was used in the making of both mock-ups.

The measurements were made in pixels, between parallels drawn through the contact point of the two central incisors and themost distal proximal points of the central incisors, lateral incisors and canines. The projected distance measured in pixels between the two parallels drawn through the most distal proximal points of the two canineswas defined as "T=100%". Having this distance defined, we were able to calculate the projected widths of the 6 maxillary anterior teeth, according to the two proportions in which they would have to be in the two digital mock-ups (Fig.3)(Fig.4).



Figure 3.



Figure 4.

Once the digital mock-ups were made, a PowerPoint presentation was created, which contained 31 slides, one for each patient. On each slide 3 photos were inserted: the unedited one and the twodigital mock-ups(fig.5). The photos were placed random on each slide, so we wouldn't create a pattern throughout the presentation.



Figure 5.

A team of 23 dentists who practice dentistry in Timisoara took part in the evaluating process: 6 orthodontists, 6 prosthetists and 11 dentists who practice general dentistry. They were all instructed to choose one picture from each slide, the picture that each one would find the most appropriate from an esthetic point of view. Every dentist recorded his choices in a table (fig6). In the end, the data was collected and centralized by summing the points each of the three types of photos obtained in all 23 evaluations.

Nr. slide	Photo1	Photo2	Photo3
1.	x		
2.			х
3.		x	
4.			х
31.	x		
	п.	<i>c</i>	

Figure 6.

RESULTS

From the three types of photos associated with each patient included in the study (the unedited one and the two digital mock-ups), mock-up 1 (the mock-up in which the 6 teeth in the maxillary anteriorregion were placedinthe golden ratio) was chosen in apercentageof 18,94%, obtaining a score of 135 points. The original photos were chosen in a percentage of 30,85%, with a score of 220 points. Mock-up 2 was chosen in a percentage of 50,21%, with a score of 358 points (fig7).

The orthodontists chose the original photos in a percentage of 31,72% (score – 59 points), mock-up 1 in a percentage of 23,65% (score – 44

points) and mock-up 2 in a percentage of 44,63% (score – 83 points). (fig8)

The prosthetists chose the original photos in a percentage of 33,33% (score - 62 points), mock-up 1 in a percentage of 14,51% (score - 27 mock-up points) and 2 in а percentageof 52,16% 97 (score _ points).(Fig.9)

The dentists who practice general dentistry chose the original photos in a percentage of 29,03% (score – 99 points), mock-up 1 in a percentage of 18,76% (score – 64 points) and mock-up 2 in a percentage of 52,21% (score – 178 points). (Fig.10)

			Mock-up 1	Mock-up 2	
TOTAL		photo			
	Pct	220	135	358	
	%	30,85	18,94	50,21	

Figure 7	7
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TOTAL						
Original photo Mock-up 1 Mock-up 2						
Pct	59	44	83			
%	31,72	23,65	44,63			
Figure 9						

Figure 8.

TOTAL						
Original photo Mock-up 1 Mock-up 2						
Pct	62	27	97			
%	33,33	14,51	52,16			
Figure 9.						

TOTAL							
	Original photo Mock-up 1 Mock-up 2						
Pct	99	64	178				
% 29,03 18,76 52,21							

Figure 10.

CONCLUSIONS

- The applicability of the Golden Proportions in the planning of esthetic fixed restorations in the maxillary anterior region did not prove to be valid by this study, at least not from the point of view of the 23 dentists that took part in the evaluating process
- The ratios used in the making of mock-up 2 could be considered as a starting point for planning esthetic fixed restorations in the maxillary anterior region, providing that

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ulterior individualization must be made

- The most common comment made by the dentists that took part in the evaluating process was that they considered a low degree of visibility of the canines to be unfavorable for great esthetics
- Most of the dentists that took part in the evaluating process considered that the central incisors are the dominant element that dictates the esthetics in the maxillary anterior region.

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CLINICAL APPLICATION OF CONEBEAM COMPUTER TOMOGRAPHY IMAGING IN MAXILLOFACIAL PRACTICE



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ABSTRACT

Introduction: The utility of cone beam computed tomography (CBCT) in oral and maxillofacial pathology has increased very rapidly in the last 10 years.

Even if in most cases, panoramic views are enough, when the dental pathology interferes with the neighboring cavities, CBCT becomes necessary.

The **objective** of this study is to assess the advantages of the cone beam CT compared with the two dimensionalimages.

Material and methods:10 cases withvarious maxillofacial pathologies were investigated using both CBCT and radiographic techniques. The diagnostic based on CBCT, as compared to the diagnosis based on panoramic radiograph, was evaluated.

Results: In the selected cases, cone beam CT images have a high diagnosis accuracy versus panoramic views, especially when the lesions extends into adjacent cavities.

In *conclusion,* is bone lesions detected on a digital orthopantomography are betteranalyzedusing CBCT. *Key words:* cone beam CT, orthopantomography, maxillary sinus

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INTRODUCTION

Cone beam computed (CBCT) has excellent tomography spatial and high contrast resolution and allows the production of maximum intensity projection and 3D volume rendered images[1]. The main advantages of CBCT over standard medical CT are the comparatively low doses of ionic radiation used (3-6 times), the extremely thin subslices in millimeter (0.1-0.2 mm) axial, coronal and sagittal planes with automatically additional generated

MATERIAL AND METHOD

10 patients presenting with different pathologyinthe maxillofacial territory were selected. All patients were initially investigated by digital orthopantomography (OPG). Due to the necessity of a complementary three dimensional investigation, cone beam CT images were obtained for each patient.

Radicular jaw cyst is the most common lesion of the jaw bone. The enlarging changes givefew slowly clinical symptoms delaying the diagnosis to the moment when the cyst's size is, in many cases, huge. Deformation of the alveolar process, alteration of the adjacent stuctures, displacement and tilting of the adjacent teeth happen in the period of increasing growth. The common image detected on the panoramic radiograph shows a relatively uniform radiolucent

surface and volume reconstructions as well as the high resolution bone details of the maxilla and mandible [2].

The most important feature of the use of the CBCT is represented by its high precision in detecting the relationship between the lesion and teeth, important neighboring anatomical structures, cortical expansion and erosions, the boundary of a lesion, the presence of single or multiple lesions [3].

lesion, round or oval, often surrounded by a thin compact lamella, with an apical location, rarely laterally of the root, or in relation with a non-vital tooth. Often, the maxillary odontogenic accompanied by bone disorders resorbtion, expand into he maxillary sinus or the nasal cavity. The bone lysis induced by the intralesional hydrostatic pressure happens in the minimal resistance direction. Once the osteoperiostal barrier is overcome, the rapid evolution takes place towards the neighboring nasal and sinus cavities, mandatory 3 making the D investigation.

On the cone beam CT images, the nasal and sinus invasion and thickening degree of the sinus membrane, as well as the cysts teeth implantation can be clearly evaluated [4,5].



Figure 1. Cropped panoramic CBCT view showing a well-defined radiolucency from the right upper first molar

A posible extension of a giant maxillary is towards maxillary sinus, but withoutinvading it in the early stages of evolution.In buccal direction, extensive evolution leads to cortical expansion and resorbtion, with further developing under mucosa.The evolution in apical direction istowards the maxillary sinus, keeping a thin cortical bone between the two neighboring cavities.

Figure 2. Cross sectional CBCT view shows the maxillary sinus extension of the radicular cyst

These features concerning the growth of the cysts are veryimportant for the surgical aproach.Involvement of the maxillary sinuscannot be determined on the 2D panoramic radiography. Detailed imagies can be obtained using the 3D cone beam CT, in order to establish the surgical steps in the preoperative stage.



Figure 3. Panoramic view shows a well-defined radiolucency circumscribed by a radiopaque line in the posterior right maxilla overlapping the maxillary sinus



Figure 4. Sagital CBCT view shows the radiolucency that doesn't invade the sinus cavity

In the lower jaw, radicular cysts producedecrease bone strength by adjacent bone lysis, root resorption of the involved tooth and displacement of theadjacent teeth and the mandibular canal.Cortical expansion may be seen with large lesions[4,5]. The utility of using cone beam CT imaging in casesof large mandibular cysts consists of better evaluation of the bone lysis, detailed mapping of the mandibular nerve and the morphology of the bony lesion (unilocular or multiloculated).



Figure 5. Cropped panoramic radiograph shows radiolucent lesion in lateral body of ramus of mandible with displacement of mandibular canal (outlined with red)

Odontogenic maxillary sinusitis accounts for approximately 10-12% of maxillary sinusitis cases.To establish the odontogenicnature of maxillary sinusitis, a clinical examination together with a 2D and 3D imaging techniques were used. [6]

CBCT scans provide images of the maxillary sinus mucosa changes[2,7].With a high degree of precision, the odontogenic sinusitis (accompanied by various degrees of mucosal thickening),caused by an infected sinusal tooth, an oro-antral fistula or a dental implant that

Figure 6. CBCT axial view shows cortical expansion and thinning of the buccal and lingual cortical plate

perforates the sinus membrane, can be clearly diagnosed using cone beam CT.

In unclear cases, where the sinus mucosal changes are noticed on the panoramic radiography can be then confirmed using a cone beam CT images.

The panoramic radiography presented below shows a diffuse opacity in the area of the right maxillary sinus. Cone beam CT shows the opacity of the entire right sinus after the second premolar extraction, clinically accompanied by the signs of an acute sinusitis.



Figure 7. OPG showing a discreet opacity on the area of the right maxillary sinus



Figure 8. A cross sectional CBCT view shows a fresh postextractionalsocket with the diffuse opacity of the right sinus



Figure 9. A panoramic CBCT view shows the opacity of the right sinus

A residual root pushed into the maxillary sinus during an extraction time can bediagnosed, at first, on a panoramic radiography.In this case, when a surgical approach is intended immediately after the extraction accident, three dimensional images are very helpful for precise assessment of the root location.



Figure 10. Digital orthopantomographshows the sinus root (green arrow)



Figure 11. CBCT shows a different position of the root at three hours after OPG examination

Dental imaging is an important tool that can be used in patient assessment for adequate implant treatment planning. In the effort to overcome the limitation of the 2D radiographs (image distortion,

magnification), 3D imaging becomes necessary when the implant insertion is done in a critical anatomical zone [8] (maxillary lateral region in the exampled case below).



Figure 12. Dental implant perforating the sinus membrane with consecutive sinusitis (cross sectional view from CBCT)

Mucous retention cysts of the maxillary sinus are an asymptomatic lesions incidentally found during the panoramic examinations. Although not suitable for evaluating maxillary sinus (along all extensions) because of its limitations, it is still used because of its availability, its low cost and ease of interpretations[9].On the panoramic radiography they are radiopaque, dome-shaped structures on the floor or on another wall of the maxillary sinus, with presenting a distinctly rounded edge. They are slow growing

lesions, that do not interfere with mucosal and cortical integrity. The images detected on the panoramic radiography have a clinical significance when they continue an evident periapical lesion of an infected tooth, interrupting the lamina dura contour. When, on the panoramic radiography, the image of the retention cyst is superimposed on the image of the radicular cyst, a three dimensional imaged investigation becomes necessary.



Figure 13. Orthopantomograph shows a radiolucency surrounding the apex of the first right upper molar overlapping on the well-defined dome shaped opacity on the right sinus floor



Figure 14. Cone beam CT shows the overlap between the radicular cyst at the palatal root of 1.6 and the mucous retention cyst

The sinus mucosal thickening of more than 2 mm(considered pathological) is a common radiograph finding when teeth are accompanied by periapical lesions. The degree and the type (plane or polypoid) of the mucosal thickening can be directly analyzed on the cone beam CT images. [10]

The follicular(dentigerous) cysts the second most common are odontogenic cyst occurring in the mandible and represent a frequent anatomopathologicaltype of the maxillary cysts, about 20% of the developmental cysts.Radiographically, a dentigerouscyst appears as a wellcircumscribed unilocular radiolucent lesion adjacent to the crown of an partially impacted or erupted tooth.Dentigerous cysts can vary in

size but have the potential to grow large enough to cause significant expansion of the jaw and displacement of adjacent teeth.Large lesions can develop undulating borders due to uneven expansion rates and may mimic ameloblastomas and keratocysticodontogenic tumors. A characteristic of the follicular cyst is that resorption of the root apex is uncommon.

In the case presented below, the digital orthopantomograph shows a discreet region of bone lysissurroundingboth the coronal and the radicular part of the partially included second premolar (the circumferential type of follicular cyst) [5,11]



Figure 15. Orthopantomograph showing a discreet radiolucency

The investigation that can diagnose with certainty this bony lesion is, in this case, cone beam CT. The coronal section taken with a cone beam CT shows a well-defined

Figure 16. Theretroalveolarthat sorrounds around the second right inferior premolarradiography shows closer the transulucency

radiolucencythat includes the second premolar crown. The cross-sectional mandibular CBCT shows the cortical expansion with the consecutive bone deformation (the single clinical sign).



Figure 17. The cross-sectional CBCT showing the cortical expansion of bone lysis

Figure 18. Coronal view with reconstruction

RESULTS AND DISCUSSIONS

The above presented casesemphasizethe importance of the three-dimensional patient investigation when the clinical examination together orthopantomograph with imaging, cannot establish a final diagnosis. Especially when it comes to bone lesions that exceed the maxillary jaws, the beam becomes cone CT necessary.On a cone beam CT, the extent of the injury into the neighboring anatomical cavities can be in details analyzed.

Maxillary sinus pathology is associated with dental periapical pathology in more than 50% of the cases[6,9].For this pathology, both panoramic radiography and CBCT are available required.The research indicates that 2D imaging techniques origin often hide the may of odontogenic maxillary sinusitis. This disadvantage is particularly evident in the maxillary molar region, stressing the need for 3D cross-sectional imaging [6].

Even if dental implant surgery is considered a routine procedure, there are some inherent risks associated with this type of intervention. The critical anatomical landmarks (maxillary sinus, mandibular canal), as well as the height, width, angulation of the bone must be accurate assessed prior surgery.

In his article, Tolstunov identified four functional implant zones (each with unique anatomy, blood supply, type ofresorbtion)[12]. Because of this specific features, CBCT should be considered an alternative imaging investigation when the

CONCLUSIONS

The use of cone beam CT images has a wide application in the various pathology of the oral and maxillofacial field. It helps clinicians to a better

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orthopantomography is not able to assess the dimensional presentation in complex cases[8].

Because of the limitations of the panoramic radiography (lack of fine details, distortion, artefacts) along with the increasing demand for proper surgical planning of an operation, three dimensional investigation become highly popular[1].

visualization and understanding of the pathology and has a huge role in the predictability and precision of thesurgery.

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EPIDEMIOLOGICAL SURVEY OF DENTAL FEAR AND ANXIETY IN ROMANIAN CHILDREN LIVING IN HUNGARY



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ABSTRACT

Aim: The aim of the epidemiological survey was to investigate anxiety and dental fear among children of the Romanian minority living in Hungary in order to compare with the already existing data from Hungary and Romania.

Methods: In this cross-sectional study 311 schoolchildren of Romanian minority living in Hungary were assessed (163 females, 148 males, aged 11-18 years). Questionnaires have been completed anonymously by children attending five schools in Bekes county, Hungary. The subjects' dental fear and anxiety was evaluated with Kleinknecht's DFS and Corah's DAS;; the anxiety level with Spielberger's STAI-S and STAI-T and their opinion about dentists with Getz's DBS. For statistical analysis t-test and Pearson's correlation were used by SPSS/PC statistics 17.0.

Results: The mean (±SD) scores of the surveyed subjects were high: DAS 11.8(±4.4), DFS

36.7(\pm 13.9), DBS 37.3(\pm 11.9), STAI-S 37.0(\pm 11.0) and STAI-T 38.8(\pm 9.5), respectively. Except for DBS, higher scores were found in females for every questionnaire, though the differences were statistically significant only in DAS and DFS (p≤0.05).

Conclusions: The obtained scores were higher than the international and some of the Hungarian ones, but lower in each case, than those found in the Hungarian minority living in Romania.

Key words: Romanian minority from Hungary, DAS, DFS, DBS, STAI-S, STAI-T

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The scientific analysis of dental fear and anxiety began with Corah's publication in 1969 [1]. Since then, the practical value and literature of the field has increased. Although in case of the younger population the topic has an even greater importance, the epidemiological data about children is much less and moreover, contradictory. For instance, analysing from the viewpoint of gender, some of the authors have found greater scores in girls [2], others could show this only in some age groups [3], whereas there are some, who did not find any differences between boys and girls [4]. Many researchers have found reversed correlation regarding age and dental fear [4, 5] and it has also been shown anxious mental that constitution accentuates the grade of dental fear [4, 6, 7].

The phenomenon of dental fear and anxiety has also raised the interest of some researchers from Romania, resulting in the validation of the two most commonly used self-assessment dental fear questionnaries MDAS (Modified Dental Anxiety Scale) and DFS (Dental Fear Survey) [8, 9] and using them on different populations, mainly adults [10]. We also found some data about the level of dental fear in children from Romania, however these studies have been performed with several different methodologies [11, 12].

Hungarian researchers began evaluating the level of dental fear and anxiety on children in their country in the last decade. A series of sudies have been performed using the same methodology [6,

13, 14, 15, 16, 17, 18]. In all these surveys the subjects were Hungarian as nationality and the conclusion was that they achieved greater scores compared to international data [6, 13]. Since then similar studies have been performed in Hungarian children living near the borders of Hungary: Romania and Slovakia. These studies revealed that the Hungarian minority living in Slovakia had better results than the Hungary, population of while Hungarian minority from Romania presented less favourable results [7, 19].

All these studies have lead to the following questions: Does dental fear depend on one's cultural belonging, in other words the way of perceiving life? Is dental fear related to the country where one lives in minority status? As we found no systematic epidemiologiacal evaluation of the children from Romania from the viewpoint of dental fear and anxiety, to answer these questions we initiated a succession of studies crossing the Romanian-Hungarian borders. According to our knowledge there is no study which would have had assessed the dental fear and anxiety of the Romanian children from Hungary. Therefore, the aim of the present survey was to fill this gap and also to make a connection between the long ago started systematic dental fear studies in Hungary and continue them Romania with further in epidemiological surveys performed with the same methods.

METHODS

The subjects of the cross-sectional study were Romanian children living in Hungary speaking Romanian and also Hungarian language. There are seven Romanian or bilingual schools in the entire country, all located in the southeastern part, near the Romanian border, in Bekes county. We managed to visit five from these schools in order to perform our study. In this questionnaire based survey 311 pupils were involved, 163 females and 148 males, aged 11–18 years, who can be seen as a representative sample for the Romanian community living in Hungary.

Respecting anonymity, the subjects participated voluntarily after the appropriate information about the study had been given and agreements of their parents had been obtained [20]. The study was approved by the Ethical Comity of Semmelweis University from Budapest (TUKEB 8.9/2008).

Dental fear was assessed using the Corah's Dental Anxiety Scale (DAS) [1] and Kleinknecht's Dental Fear Survey (DFS) [21, 22]. We opted for the Hungarian versions [14, 23] because these were used also in the previous

RESULTS

The mean (±S.D.) age of the surveyed subjects was 13.64 (±2.17) years. The main information about the subjects, gender, age and the scale scores, were included in Table I.

Table II presents the dental fear and anxiety scores of the investigated subjects according to gender and age, respectively. The mean values of the female subjects were significantly higher in case of DAS and DFS ($p \le 0.05$, independent t-test) than of males'. Taking into account the gender, in case of DBS, STAI-S and STAI-T we did not find any statistically significant differences. From the viewpoint of age in case of DAS (Figure 1) there is a peak at the 12-year-olds from where the scores gradually decreased below the level of the 11-year-olds. In case of DFS (Figure 1) the highest scores were observed in the 12 and 13-year-olds, the lowest in the 14-year-old group, while the others were mainly on the same level. The scores of DBS (Figure 1) resembled to the DFS with the studies in Hungarian population from Hungary and Romania as well [7, 24]. Anxiety level was assessed also by the Hungarian version of Spielberger's State and Trait Anxiety Inventory (STAI-S, STAI-T) [15, 24, 25] validated and also used in Hungarian population. The opinion of the children about dentists was assessed with the Hungarian version [16] of Getz's Dental Belief Scale (DBS).

All the questionnaires were completed in groups at school at one occasion, after lessons. For statistical analysis the SPSS/PC Statistics 17.0 software (SPSS, Inc. Chicago, IL) was used with the level of significance set at $p \le 0.05$.

exception that the group of the 14-yearolds was also situated around the average. STAI-S (Figure 2) also had a peak at the age of 12 years, from where it decreased linearly till the age of 18 years. In the same time STAI-T's (Figure 2) highest scores were at the age of 16 and 12, the lowest at 11 and 18, while the other four groups of age were on the same level. We have found statistically significant differences between the age groups in case of DFS, DBS and STAI-S (independent t test, p≤0.05) (see Table II).

Table III presents the Pearson's correlations of the dental fear and anxiety scales. There is a statistically significant positive correlation ($p \le 0.01$) between the values in each case. Moreover, the correlations between each other of the dental fear scales (DAS, DFS, DBS) and the anxiety scales (STAI-S and STAI-T) were stronger than the correlation of the two groups of scales.

		±	4.4	±13.9	±11.9	±11.0	±9.5
Ta the gen	able II. The sul der and age, re	ojects' dental : espectively (n	fea n=:	ar and anxiety 311)	y scores (mea	an values±S	D) according to
Group	n	DAS		DFS	DBS	STAI-S	STAI-T
Gender							
female	163	12.6±4.6		39.1±14.9	35.5±11.1	37.9±10.7	39.7±9.3
male	148	10.9±3.9		34.1±12.2	39.3±12.5	36.1±11.2	37.9±9.7
Age (years)							
11	53	11.2±4.9		34.0±12.9*	36.6±11.3	35.2±12.3	35.5±9.6
12	56	12.8±4.2		41.2±16.5*	40.8±13.2*	39.0±14.4	* 39.9±12.5
13	53	12.5±4.8		40.4±16.8*	41.1±8.9*	38.2±9.9	39.3±8.5
14	54	11.9±3.6		23.6±13.8*	37.3±11.4	36.6±9.8*	39±9.8
15	18	11.3±3.7		32.4±11.2*	37.2±12.8*	37.2±7.9*	39.1±8.9
16	33	11.3±4.0		35.2±10.4*	32.5±12.4	35.7±10.0	40.3±9.4
17	24	11.0±5.1		36.5±15.1*	33.4±11.7*	34.6±12.7	38.4±10.2
18	20	10.7±3.9		32.4±11.3*	31.9±11.7	34.4±9.1*	36.6±8.3
Total	311	11.8 ± 4.4		36.7±13.	37.3±11.9	37.0±11.0	38.8±9.5
* p≤0.05							

Table I. Summary of dental fear and anxiety scores (mean values±SD) of Romania children living in Hungary aged 11-18 years (n=311)

DFS

36.7

DBS

37.3

STAI-S

37.0

STAI-T

38.8

DBS

50

40

Nr. Of subjects (n) Female Male DAS

163

DAS

13

148

11.8

311

$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c} 40 \\ 30 \\ 36.6 \\ \hline 37.37.2 \\ 32.53 \\ 32.53 \\ 31.9 \\ \hline 32.53 \\ 32.53 \\ \hline 32.53 \\ 32.53 \\ \hline 32.5$
Figure 1. DAS, D	DFS and DBS scores for different age §	groups (n=311)

DFS

50

40



Figure 2. STAI-S and STAI-T scores for different groups of age (n=311)

Table III. Pea	arson-correlat	ions betweer	the scores c	of dental feat	and anxiety	(n=31.
	DAS	DFS	DBS	STAI-S	STAI-T	
DAS	1.00					
DFS	0.73**	1.00				
DBS	0.38**	0.32**	1.00			
STAI-S	0.42**	0.52**	0.36**	1.00		
STAI-T	0 31**	0.4 2 **	0 33**	0 67**	1.00	
**p≤0.01	().,)1		(),))	0.07		

TTT - D ւե 311)

DISCUSSIONS

Dental anxiety is a common phenomenon in children and adolescents. Whether or not children are referred by their dentist is partly dependent on the interaction between child, dentist and parent [26]. It has been long ago recognized that to be able to deal with a problem, first its cause has to be konwn. Moreover, the earlier the problem recognized, the better are the chances to deal with it. This observation is also valid in case of dental fear and anxiety. The epidemiological evaluation of а country's population from this point of view has a great importance. That is why the most commonly used selfassessment dental fear and also dental anxiety questionarries have been translated to a great number of languages all over the world. The evaluation of children confers the possibility for finding a solution and not letting the problem to aggravate. Overall the anxiety scores (STAI-S:37.0, STAI-T:38.8) of the assessed population

Romanian children living of in Hungary, on one hand were almost the same as the Hungarian children's scores in Hungary (aged 8-15 years: STAI-S:36.3, STAI-T: 38.8 [6]; aged 14-18 years: STAI-S>39.6, STAI-T 41.5 [16]), but on the other hand the scores obtained were lower than those found in Hungarian children living in Romania (aged 12-19 years: STAI-S 39.7, STAI-T 43.8 [7]). In case of a smaller group of orthodontic patients aged 9-18 years, Vaida et al. found higher scores for STAI-S (38.68) and lower for STAI-T (36,71) [12]. We can also see that our subjects' dental anxiety scores (DAS: 11.8) were higher than the Hungarian children's scores living in Hungary (aged 8-15 years: DAS: 10.7 [6], aged 14-18 years: DAS: 10.8 [17], Alberth's data for the 12to14-year-old children DAS: 10.3 [13]), but lower than the Hungarian children's scores living in Romania (aged 12-19 years: DAS:12.6 [7]). When validating the Romanian verison of the

Modified Dental Anxiety Scale, Mărginean and Filimon found a mean value of 9.30 on a young adult population aged 15-35 years [8]. This score is lower than the one found by us, however there is no information about the 15-18 years age group in this sample, so a concludent comparison cannot be made. In the same time Lazar et al. also used DAS for the evaluation of a somewhat bigger sample of children aged 14-18 years in Oradea, Romania, and stated that 68% of them accused low, 10% high and only 4% extremely high dental anxiety [10]. In case of Dental Fear Scale we found lower scores (DFS: 36.7), than those of the Hungarian children living either in Hungary (aged 8-15 years DFS:40.4 [6], aged 14-18 years DFS:40.6 [17]) or Romania (aged 12-19 years DFS:50.6 [7]). Mărginean and Filimon in Romania found 40.57 for DFS, but the age of the sample does not coincide with the one evaluated by us [9]. Although the DFS scores obtained in this survey were lower than those measured in the two countries, our DAS scores were situated closer to those measured in Romania. Making a comparison with the international data, where DAS was 8.6-9.3 [21, 27] and DFS 36.6-37.7 [27, 28], the scores obtained in this study were still high.

Our results revealed that, except for DBS, females showed higher scores than males in case of every scale. However, we found statistically significant differences only in case of DAS and DFS. DBS being higher in case of men is unusual [29], but the high DBS scores allover the sample correlate with the high dental fear scores.

Taking into account only the age in both cases, anxiety and dental fear scales, there was a peak around the age of 12–13 years from where the scores decreased gradually. This tendency is in accordance with the observations of other authors' [4, 5], who found inverse relationship between age and dental fear.

Positive correlation was found between anxiety and dental fear, similarly to the results in Hungary [18] and Romania [7]. The results of our consistent with study are the international results [4]. The lower correlation between the dental fear scales and the anxiety scales might suggest that the grade of dental fear is defined more by the dentist and his/her practice, than the psychosocial influences. This could be supported also by the fact that the DBS (37.3) scores were high along the whole sample.

CONCLUSIONS

The findings of this study suggest that dental fear and anxiety in Romanian children living as a minority in Hungary is comparable with the international results. Dental fear scores of the children surveyed by us belonging to the Romanian community living in Hungary have more favourable results in the analysed situations than the Hungarian children living in Romania as a minority. Comparing our subjects to their compatriots, we found less favourable scores only in case of DAS. Though, the overall comparison to the larger international situation showed also higher scores. The reasons behind these increased grades should be revealed. The high scores of the anxiety scales point to the role of the psychological characteristics. In the same time the details of DBS might show the differences in coping ability of the subjects. The differences might also come from the aspect of cultural belonging, as this influences one's emotional constitution and the way of perceiving life. In conclusion, no definite answer can be given concerning the possible relationship between dental fear, dental anxiety and minority status of children. It is

necessary to extend the study using representative samples of children living in Romania. To be able to draw more appropriate conclusions, further studies of the Romanian children are needed.

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- for articles: name of the authors and surname initials, title of the article in the original language, title of the journal according to the international abreviation system, year of issue, volume, number, pages;
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Citation of references inside the body of the paper will be put between brackets, Harward style (author, year) or Vancouver style (number in square brackets or superscript). Cited reference titles will be selected, maximum 6 for studies and case presentations and 12 for general reviews. Acceptance, rejection or the need of alterations in sent materials, or in inconography, will be comunicated to the authors in due time. For this, the authors will indicate the person and address for corespondence (phone number, e-mail address). Given the less pleasant experience of the editorial board with some articles being rejected because they did not meet publishing criteria, we decided to support those who intend to publish in this journal by detailing the way such a paper should be elaborated, as well as our requirements.

Except some particular aspects concerning this journal, the following details are general requirements asked or imposed by other journals as well. Conditions to be met in order to propose a paper for publishing. The main author has the responsability to make sure the article has been approved by all the other authors. The journal will have copyright for papers accepted for publishing. The editorial board reservs the right to change the style and dimensions of an article (major changes will be discussed with the main author) and to decide the date of issue.

2. FIRST PUBLICATION

The editorial board will not consider a paper already reported in a published general review or described in a paper proposed to or accepted by another journal. This does not exclude papers which have been rejected by other journals. Also, papers which have been presented at a scientific meeting will be accepted for discussion if they have not been entirely or partially published in a similar publication. "Multiple" publishing of the same study is seldom justified. One of the possible justifications is publishing in a second language but only if the following conditions are met:

- Editors of both journals involved are fully informed;
- Priority of the initial publication will be respected by a minimum publishing interval of two weeks;
- For the second publication, a shortened version will suffice;
- The second version strictly reflects data and interpretations in the first;
- A footnote may state: "This article is based upon a study initially published in [title of the journal]".

3. PATERNITY

Paternity must reflect the common decision of the coauthors. Each author must have participated enough to take public responsability for the content. A paper with collective paternity must have a key person responsable for the article.

4. COPYRIGHT

In order to reproduce materials from other sources, written agreement from the copyright owner must be obtained:

- photographer for unpublished photographs;
- hospital where the photographer (physician) is employed for unpublished photographs performed during the employment period;
- initial publisher for a table, picture or text which have previously been published elsewhere.

5. ETHICAL ASPECTS

Do not use name of patients, initials or hospital observation charts numbers. If a photograph of a body part which could allow direct or deductive recognition of the patient needs publishing, then the paper must be accompanied by the written consent of the patient and clinician, as well.

6. PRESENTING THE MANUSCRIPT

For the journal *"Medicine in evolution"*, the manuscript must be typed double spaced, on white A₄ paper – 210 x 297mm, on one side (2.5cm upper and lower borders, 3cm left and 2cm right border, respectively), in clear characters, no further corrections or addings. It is advisable that articles are presented on CD or other data transfer methods, in Word format, 12 Times New Roman fonts - using Romanian characters – respecting the same page order, accompanied by a printed version. Graphs – black and white or coloured – may be generated in MS Excel or MS Graph, inserted in the body of the paper or presented in a different file. Infected materials will not be used.

6.1. FIRST PAGE (TITLE PAGE)

Together with the title and names of the authors, the first page must include the affiliation, professional and university degree (if applicable), marked by asterisc for every author; it is advisable to give at least a phone and/or fax number or e-mail address of the first author who may be contacted by the editors for additional recommendations or explanations.

6.2. ABSTARCT OF THE PAPER

6.2.1 Recommendations for original studies

Original studies must include a structured abstarct of maximum 150 words, containing the following titles and informations:

- Aim and objectives;
- Material and methods;
- Results;
- Conclusions;
- Key words: give 3-5 key words;
- The abstract will be translated into an international circulation language.

6.3 CONTENT OF THE PAPER

6.3.1 For original articles

The text will usually be divided into sections:

- <u>Introduction</u> presentation of general aspects, in the context of the approached theme
- <u>Aim and objectives</u> Define the aim of the article. Briefly expose the rationale of the presented study or observation. Make strictly pertinent referals and do not exhaustively review the subject. Do not include data or conclusions from the paper.
- <u>Material and methods</u> Describe the selection of observations or subjects for the experiment (including controls). Identify methods, equipments (with the name and address of the manufacturer in brackets) and give sufficient details on procedures. Give references for the selected methods, including statistical methods; offer details and brief descriptions for previously published methods which are not well known; describe new or

substantially modified methods, justify their use and assess their limitations. Precisely identify all used drugs and chemicals, including generic names, dosage and administration ways. Describe statistical methods with sufficient details for reported results to be verified. Whenever possible, quantify discovered aspects and present them with appropriate measurement indicators for the uncertainty or error of measurement (such as confidence intervals).

- <u>Results</u> Present results in a logical succession as text, tables and illustrations. Emphasize or briefly describe only important observations.
- <u>Discussions</u> Underline new, important aspects of the study. Do not repeat in detail data which have been presented in previous sections. Include implications of revealed aspects and their limitations, including implications for future studies. Connect your observations to other relevant studies. Relate the results to the aim proposed for the study.
- <u>Conclusions</u> organize conclusions which emerge from the study. In the end state: a) contributions to be acknowledged but which do not justify paternity right; b) thanks for technical support; c) thanks for financial or material support.

6.3.2 Indications for case reports

Themes may be selected from all medical fields. Manuscripts which offer a special gain for daily activity will have priority. The title must be clearly, precisely stated. It may be completed by a subtitle. It is advisable to include in the key words of the title the main message, the special element which may be observed from the case evolution. The content of a case report must be divided into three parts:

- <u>Introduction</u> It must include a maximum of 15 typed rows (half page). Here, the main medical problem is summarized in order to place the case in a specific domain.
- <u>Case report</u> It contains essential specific information on the case.
- In order to make a logical, chronological and didactical case report the following 5 chapters are needed:
 - I. Anamnesis;
 - II. Clinical examination data;
 - III. Laboratory data;
 - IV. Additional paraclinical investigations;
 - V. Treatment and evolution.
- <u>Discussions</u> The reason for the case report must be stated. The report must be patient-centered. Occasional deviations from typical (characteristic) evolutions, nosologically important facts must be presented in such a manner to expose the clinical picture as completely as possible. The case report must not appear as an appendix of a general review. Dimensions of a case report: maximum 6-8 typed pages, 30 rows of 60 characters/page.

6.4. MEASUREMENT UNITS, SYMBOLS, ABREVIATIONS

All measurements must be expressed in International System (IS) units. Abreviations must be fully explained when first used.

6.5. TABLES

Tables are noted with Roman figures and they will have a brief and concise title, concordant with their content.

6.6. ILLUSTRATIONS

Number all illustrations in Arabic figures in a single succession. Apply a label on the back side of every illustration, containing its number and an arrow indicating the upper side. Coloured illustrations may be accepted but it is the choice of the editors, according to particular technical abilities of each journal issue, or it may involve a fee in special cases.

6.7. EXPLANATIONS FOR DRAWINGS AND GRAPHS

Explanation for drawings and graphs must be clear and in readable dimensions, considering the necessary publishing shrinkage.

6.8. PHOTOGRAPHS

Offer glossy, good quality photographs. Any annotation, inscription, etc. must contrast with the ground. Microphotographs must include a scale marker.

6.9. ILLUSTRATION LEGENDS

Include explanations for each used symbol, etc. Identify the printing method for microphotographs.

6.10. REFERENCES

A numbered list of references must be provided at the end of the paper. The list should be arranged in the order of citation in the text of the publication, assignment or essay, not in alphabetical order(according to the Vancouver rules). List only one reference per reference number. It is very important that you use the correct punctuation and that the order of details in the references is also correct.

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7. COPIES FOR PUBLISHING

In order to accelerate publishing, the main author will send a set of printed sheets presenting the final version of the paper, as it will appear in the journal. It is really helpful that texts to be also sent on electronic support, diacritic characters mandatory.

8. REJECTION OF PAPERS

If a paper does not meet publishing conditions, whatever these may be, the editors will notify the first author on this fact, without the obligation of returning the material. Original photographs or the whole material will be returned only if the author comes to the editor and takes them.

Papers submitted for publishing will be addressed to:

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