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Editura **EUROSTAMPA**

Tel./fax: 0256-204816

ISSN 1223 – 2076

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THE PATHOPHYSIOLOGY OF OSTEOPOROSIS – PREDISPOSING FACTORS IN FEMORAL PROXIMAL EPIPHYSIS FRACTURES

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ABSTRACT

The anatomoclinical study was conducted on patients belonging to three age groups and consisted in measuring the bone density of the femoral head, the femoral neck and the area of the greater trochanter.

The object of the study was to assess the degree in which a poor quality of the bone substance is correlated with age and, implicitly, with osteoporosis, making the areas of the femoral proximal epiphysis more susceptible to bone mass loss.

The upper femoral epiphysis was divided into three areas: the femoral head, the femoral neck, the greater trochanter. Research consisted in measuring bone density of the femoral proximal (upper) epiphysis, using a CT scan (unenhanced pelvic CT scan) expressed in Hounsfield Units (HU).

Ageing leads to a higher incidence of trochanteric fractures vs. femoral neck fractures. A female patient suffering from a trochanteric fracture is older and has a more severe osteoporosis than a female patient suffering from a femoral neck fracture. The anatomic characteristics of this region - the femoral proximal epiphysis - and the amount of cancellous bone which is more severely affected by osteoporosis are essential predisposing factors of the two major post-traumatic pathological entities in this area: femoral neck fractures and greater trochanteric fractures.

Key words: femoral head, femoral neck, greater trochanter, osteoporosis

INTRODUCTION

The incidence of hip fractures is continually growing, representing approximately 30 per cent of the fractures hospitalised in the ER. It is a public health problem occurring in elderly patients with associated disorders, and severely aggravates the functional impairment already caused by the fracture.

Femoral proximal epiphysis fractures can be divided into femoral neck fractures and trochanteric fractures. These two entities require totally different therapeutic approach; hence the necessity of a study that quantifies the degree in which bone substance quality may influence the occurrence of one or the other fracture patterns. Osteoporosis being the main underlying factor for femoral proximal epiphysis, the study focused on female patients who suffered from such fractures and on the impact the quality of bone structure has on triggering this pathology, everything correlated with the anatomic areas of the femoral proximal epiphysis.

The anatomoclinical study was conducted on patients belonging to three age groups and consisted in measuring the bone density of the femoral head, the femoral neck and the area of the greater trochanter.

MATERIAL AND METHODS

Femoral proximal epiphysis fractures represent a significant

percentage of the lower limb pathology. Besides post-traumatic fractures which may occur at any age, the fractures of elderly people, which are extremely common, raise major problems representing a challenge both for the patient and for the public health system.

Major progress has been made in the various methods of surgical treatment, arthroplasty being the therapeutic method of choice in femoral neck fractures, while dynamic implants (DHS, Gamma nail) represent the "golden standard" for trochanteric fractures.

The results of the surgical treatment are associated with a functional recuperation strategy adapted to each patient. When hospitalizing a patient with proximal femoral fracture one has to consider the social and family reintegration of the patient.

The accurate assessment of the various factors involved in the occurrence of these fractures requires extensive epidemiologic, clinic-statistical, anatomoclinical and anthropometric studies. There is a tight connection between osteoporosis-induced rarefying bone mass and the risk of fracture.

The first step in establishing an adequate approach and solution of this pathology is assessing the degree to which the quality of the bone substance of the femoral proximal epiphysis can influence fracture patterns.

Thus, the treatment of a patient with femoral proximal

epiphysis fracture is a pluridisciplinary process: the orthopaedic surgeon – for surgical healing, kinesiotherapy and balneology – for post-operative care, recuperation and reintegration, as well as all the physicians specialised in bone pathology and the calcium phosphorus metabolism.

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Femoral proximal epiphysis fractures can be divided into femoral neck fractures and trochanteric fractures. These two entities require totally different therapeutic approach; hence the necessity of a study that quantifies the degree in which bone substance quality may influence the occurrence of one or the other fracture patterns. Osteoporosis being the main underlying factor for femoral proximal epiphysis, the study focused on female patients who suffered from such fractures and on the impact the quality of bone structure has on triggering this pathology, everything correlated with the anatomic areas of the femoral proximal epiphysis.

A prospective study was conducted between February 2013 – September 2013, on three groups of 25 patients each, divided according to age-groups: < 40 year-old, between 40 – 60 year-old, and > 60 year-old.

Research consisted in measuring bone density of the femoral proximal (upper) epiphysis, using a CT scan (unenhanced pelvic CT scan) expressed in Hounsfield Units (HU).

The object of the study was to assess the degree in which a poor quality of the bone substance is correlated with age and, implicitly, with osteoporosis, making the areas of the femoral proximal epiphysis more susceptible to bone mass loss.

The upper femoral epiphysis was divided into three areas: the femoral head (1), the femoral neck (2), and the greater trochanter (3).

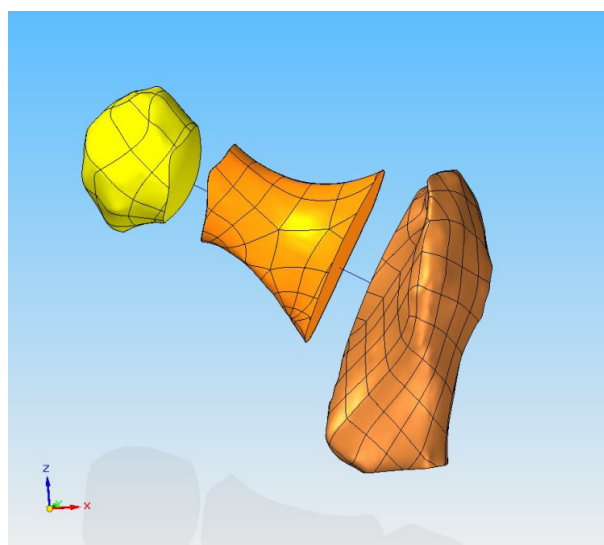
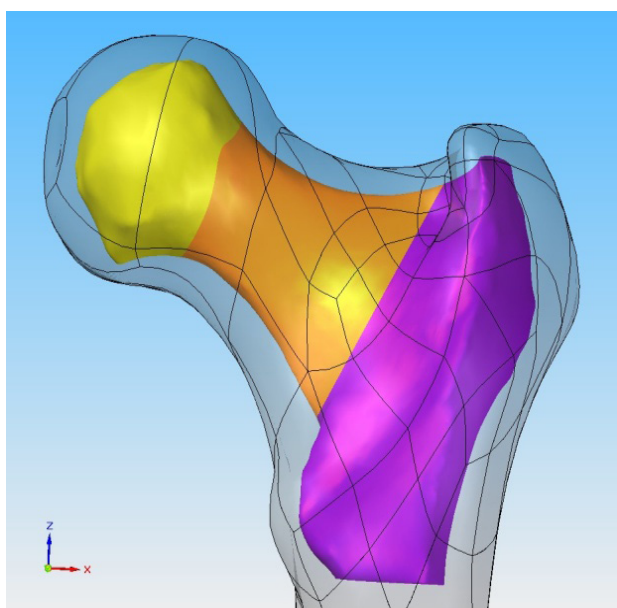


Fig.1. Bone density was measured on unenhanced pelvic CT scans for all the three areas.

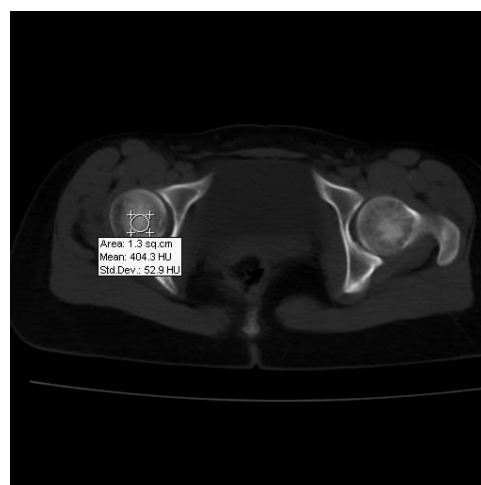


Fig. 2. Measuring bone density of the femoral head – 30-year-old female patient.

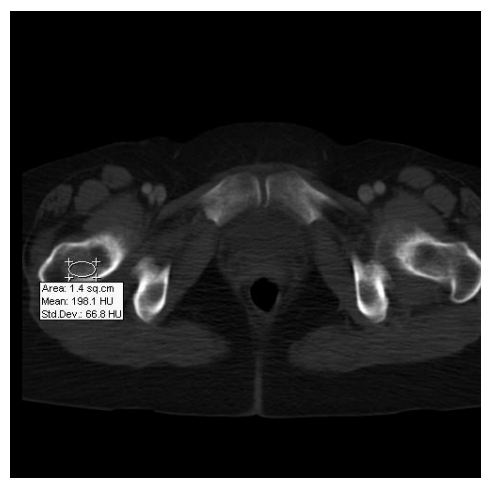


Fig. 3. Measuring bone density of the femoral neck – 72-year-old female patient.



Fig. 4. Measuring bone density of the greater trochanter – 27-year-old female patient.

The average of the measurements in the three areas/each study group were summarised in the table below (bone density was measured in Hounsfield units and converted in gr/cm^3).

Table I. Measured bone densities

	HU			gr/cm^3		
	area 1	area 2	area 3	area 1	area 2	area 3
<40	406.94	224.67	159.20	1.19488	0.83034	0.6994
40 - 60	373.40	194.24	128.38	1.1278	0.76948	0.63776
>60	335.98	160.95	103.85	1.05296	0.7029	0.5887

RESULTS AND DISCUSSION

The values show a decrease of bone density in the areas of the femoral neck and mainly that of the greater trochanter, due to the higher amount of cancellous bone in this area.

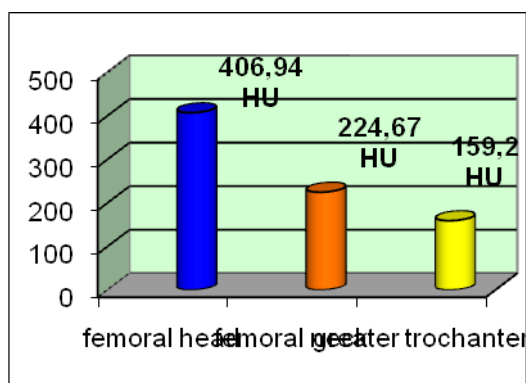


Fig. 5. The values of bone density measured in the study group <40 years.

The values show a decrease of bone density in the areas of the femoral neck and mainly that of the greater trochanter,

due to the higher amount of cancellous bone in this area. The decrease is more severe due to the bone mass loss induced by post-menopausal osteoporosis characteristic for this age-group.

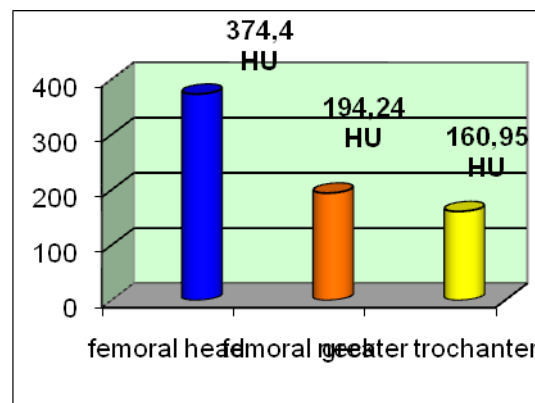


Fig. 6. The values of bone density measured in the study group 40 - 60 years

The loss of bone mass in the area of the greater trochanter is more severe due to more advanced osteoporosis (both senile osteoporosis and post-menopausal osteoporosis).

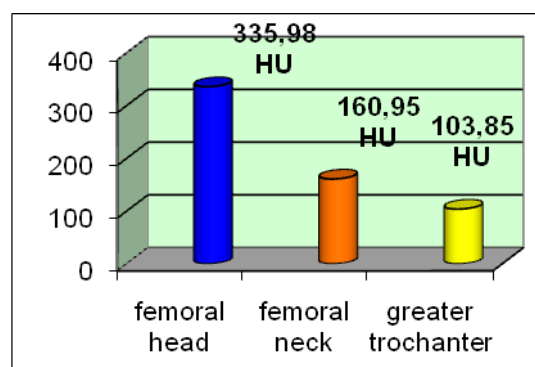


Fig. 7. The values of bone density measured in the study group >60 years

The results showed decrease of bone density associated with ageing in the region of femoral head.

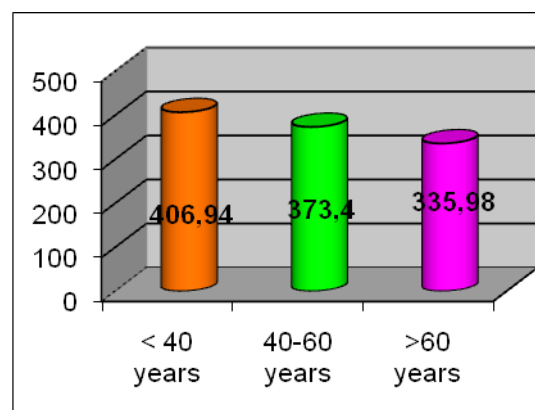


Fig. 8. The values of bone density in the femoral head area

The results showed decrease of bone density associated with ageing in the region of femoral neck.

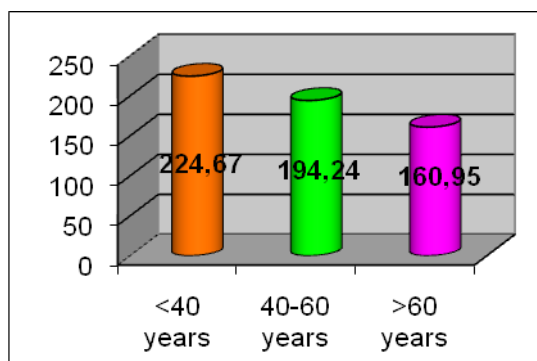


Fig. 9. The values of bone density in the femoral neck area

The results showed decrease of bone density associated with ageing in the region of greater trochanter.

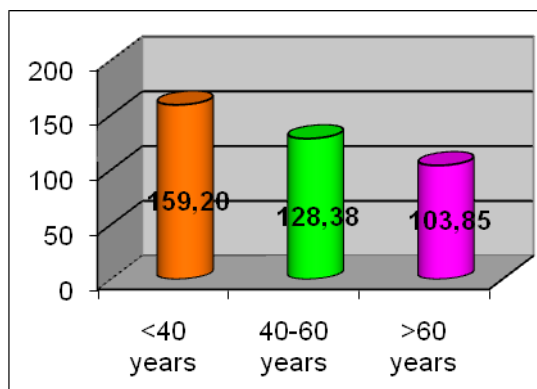


Fig. 10. The values of bone density in the area of the greater trochanter

The results of the investigations showed a decrease of bone density of the femoral proximal epiphysis associated with ageing.

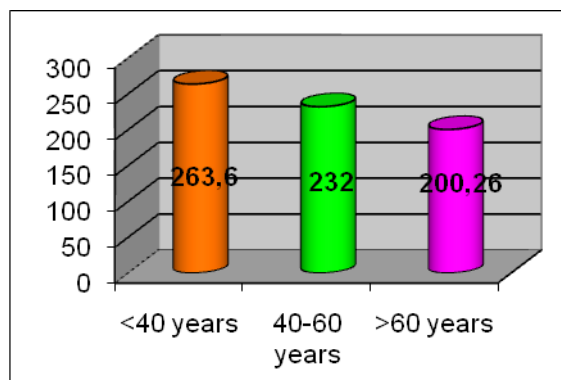


Fig. 11. Average bone density in the femoral proximal epiphysis

CONCLUSIONS

Measurements of the bone density in the three areas of the femoral proximal epiphysis – femoral head, femoral neck and

greater trochanter – reveal the following aspects:

- bone mass is physiologically lower in the trochanteric area due to the cancellous structure of the bone in this region;
- women aged between 40 and 60 years, therefore more susceptible to post-menopausal osteoporosis, show a decrease of bone density in the femoral neck, but mainly in the greater trochanter, due to the fact that this area consists predominantly of cancellous bone which is more severely affected by osteoporosis;
- in women over 60, the loss of bone mass in the greater trochanter is more severe due to the more advanced osteoporosis. Besides the progression of post-menopausal osteoporosis, senile osteoporosis is an additional factor;
- age-related loss of bone mass (and implicitly the progression of post-menopausal osteoporosis) is more severe in the greater trochanter which has a higher content of cancellous bone.

Consequently, ageing leads to a higher incidence of trochanteric fractures vs. femoral neck fractures. A female patient suffering from a trochanteric fracture is older and has a more severe osteoporosis than a female patient suffering from a femoral neck fracture. The anatomic characteristics of this region - the femoral proximal epiphysis - and the amount of cancellous bone which is more severely affected by osteoporosis, are essential predisposing factors of the two major post-traumatic pathological entities in this area: femoral neck fractures and greater trochanteric fractures.

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FIZIOPATOLOGIA OSTEOPOROZEI – FACTORI PREDISPOZANȚI ÎN FRACTURILE EPIFIZEI PROXIMALE A FEMURULUI

REZUMAT

S-a efectuat un studiu anatomico-clinic cuprinzând măsurarea densității osoase la nivelul capului femural, colului femural și regiunii masivului trohanterian, pe trei grupe de vârstă ale pacientelor. Odată cu înaintarea în vârstă stocul osos s-a deteriorat, iar susceptibilitatea unui anumit focar de fractură a afectat diferitele zone de fractură studiate.

Obiectivul studiului a fost de a determina măsura în care scăderea calității substanței osoase se corelează cu vârsta și implicit osteoporoza, porțiunile epifizei proximale a femurului mai susceptibile la pierderea de stoc osos.

Epifiza superioară a femurului a fost împărțită în trei porțiuni: cap femural, col femural, masiv trohanterian. Cercetarea s-a efectuat prin măsurarea densității osoase de la nivelul epifizei proximale (superioare) a femurului, realizată prin examinarea computer-tomografică (CT nativ de bazin) a celor trei loturi de paciente și exprimată în Unități Hounsfield (HU).

Odată cu înaintarea în vârstă, crește probabilitatea unei fracturi la nivelul regiunii trochanteriene în dauna uneia a colului femural. Pacienta cu fractură a masivului trohanterian este mai în vârstă și mai osteoporotică decât cea cu fractură a colului femural. Particularitățile anatomice ale acestei regiuni – epifiza proximală a femurului și proporția de țesut osos spongios mai susceptibilă la osteoporoză, vor deveni factori favorizanți esențiali în cele două mari entități patologice post-traumatice de la acest nivel: fracturile colului femural, respectiv fracturile masivului trohanterian.

Cuvinte cheie: cap femural, col femural, masiv trohanterian, osteoporoză

A REVIEW ON THE INFLUENCE OF MALOCCLUSION ON THE QUALITY OF LIFE

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ABSTRACT

Clinical significance of the oral health related quality of life is that dentists treat not oral disease but a human being who have different motivations and needs not only from the functionally point of view but also psychological. This concept aims to satisfy the treatment need not only normative but also experienced, therefore, the contemporary goal of the dental treatment plan is to develop a patient-centered plan, adapted to his oral health perception and motivation. Malocclusions are met nowadays with high frequency and this alters not only the functions of oral cavity but also the level self-esteem and the social interactions, all of these influencing the quality of life. Addressability to oral health services in order to correct the malocclusion is high and not only among children and teenagers, but also among adults. Depending on the severity of the malocclusion, clinicians can assess the orthodontic treatment need and, in addition, in countries where orthodontic treatment is offered through dental insurance, is a priority. For a successful approach of the orthodontic treatment plan, clinicians should set properly the orthodontic treatment need using appropriate instruments and adapt the treatment plan to each patient's psychological profile and demands and also demographic, educational and economic features.

Keywords: oral health, quality of life, malocclusion

INTRODUCTION

Quality of life is affected by any type of disease but oral diseases jeopardize not only the functional aspects but also the psychological and social aspects (1). As long as daily activities are altered because of the diseases in people's lives, research has been and will be done in order to prevent, minimize and correct their effects (1, 10).

World Health Organization defines quality of life as "individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns". The concept is multidimensional and it is influenced not only by the physical health but also by the psychological state, level of independence, social relationship, personal beliefs and their relationship to salient features of their environment (17).

Particularly, there is also the concept of oral health related quality of life which is, as well, multidimensional. Although, there hasn't been developed a definition of it, a report of the United States Surgeon General regarding oral health, provided a simple formulation: people's comfort when eating, sleeping and engaging in social interaction; self-esteem; and their satisfaction with respect to their oral health" (14).

Clinical significance of the oral health related quality of life is that dentists treat not oral disease but a human being who have

different motivations and needs not only from the functionally point of view but also psychological and concerns such as oral hygiene, dental check-ups and engaging in an dental insurance plan and paying the dental treatments might influence and also be influenced by the oral health related quality of life (1).

This concept, which aims to satisfy the treatment need not only normative but also experienced, started to develop in industrialized, well developed countries, where people were concerned about dental treatments not only to maintain the physical, functional health, but also for esthetic and self-esteem (14).

Thus, if the traditional goal of dental plan was the clinical achievement, the contemporary goal is to develop a patient-centered dental treatment plan, adapted to patient's oral health perception and motivation (10).

ORAL HEALTH

Malocclusions are met nowadays with high frequency and this alter not only the functions of oral cavity but also the level self-esteem and the social interactions, all of these influencing the quality of life (10).

Addressability to oral health services in order to correct the malocclusion is high and not only among children and teenagers, but also among adults (11). Depending on the severity of the malocclusion, clinicians can assess the orthodontic treatment

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need and, in addition, in countries where orthodontic treatment is offered through dental insurance, the priority (11).

Debates on these aspects existed due to the fact that malocclusions are considered not "disease" but "dental deviations". These deviations are compared to an arbitrary norm and orthodontic treatment aims not to "cure" but to "correct the deviations". This is the reason why the goals of the orthodontic treatment differs from the most of the dental treatments (that aim the regaining of the functions) because some of the malocclusion are asymptomatic, with only minor functional limitations, but with significant esthetic alteration. Thus, some patients seek orthodontic treatment mainly for the esthetic correction. In addition, patient claims and expectations differ: There are patients to whom a malocclusion is acceptable or indifferent and there are patients that complain about minor malocclusion (12).

To assess the severity of malocclusion, there are used different indices but these indices assess the normative treatment need, thus, from the clinician's perspective. This generates some discussions when they have to deal with patients that do not feel the treatment need although the orthodontic treatment need index indicates so, and vice versa. This is the reason why, nowadays, the trend in clinical practice is the approach of patients with malocclusion from both perspectives: clinical - functional and patient - esthetic, psychological, social (12).

To assess the impact of oral health status on quality of life, different instruments were developed.

Taking into consideration the World Health Organization recommendations, there was first developed the Oral Health Impact Profile - OHIP questionnaire. This had at first 49 questions about 7 aspects in life: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap (9).

More often, though, is used the short version of this questionnaire - OHIP14 which contains only 14 questions, 2 items per domain. Answers are organized as a frequency scale with 5 choices: 0 - never, 1 - hardly ever, 2 - occasionally, 3 - fairly often, 4 - very often/everyday. The scores varies between 0 and 56 (11, 3, 12, 10).

There are researchers that adapt or supplement this standard questionnaire. In United Kingdom it was applied the Oral Health Related Quality of Life - United Kingdom - OHQoL-UK that has 16 questions that refer not only to negative but only to positive aspects in life. The multiple choice answers are formulated as a scale of severity: 1 - very bad, 2 - bad, 3 - none, 4 - good, 5 - very good. The score varies between 16 and 80 (11).

In Brazil and Malaysia researchers applied the Oral Impacts on Daily Performance - ODIP questionnaire, assessing the impact of malocclusion on 9 daily activities: eating and enjoying food, speaking and pronouncing clearly, cleaning the mouth, smiling, laughing and showing teeth without embarrassment, maintaining emotional state without being irritable, performing common tasks, contact with people, playing sports, sleeping (8). Each performance is assigned two values: one for frequency of negative impact (0-3) and one for the severity of impact (0-3) (5).

In Saudi Arabia, Brazil, Belgium, Canada, there was used

the Child Perception Questionnaire - CPQ. This has 37 questions referred to the impact of malocclusion on 4 aspects: oral symptoms (6 items), functional limitation (9 items), emotional well-being (9 items) and social well-being (13 items). In Saudi Arabia the 13th question from the social well-being domain was eliminated because playing instrument is not a common activity among Arabic children, so the questionnaire applied there had 36 items. Answers were organized as a scale of frequency of the negative experience during the last 3 months: 0 - never, 1 - once-twice, 2 - sometimes, 3 - often, 4 - everyday, almost every day. The higher the score, the more affected the quality of life (7, 15, 8, 17).

In Belgium it was applied an additional questionnaire which assesses also the level of self-esteem: Self-Perception Profile. This questionnaire has 35 questions about subjects' perception on the following aspects in life: social skills, social acceptance, sports skills, physical appearance, behavioral manner, close friendship and sense of dignity (8). Self-esteem is defined as the perception of one's own ability to master or deal effectively with the environment and is affected by the reactions of others toward an individual. (8).

In Canada, quality of life was assessed in relation to material and social deprivation. Researchers used NZDep2006 Index of Deprivation. It evaluates 9 variables referring to social and material deprivation. Scores between 1 and 3 show a low level of deprivation. On the other hand, score between 8 and 10 shows a high level of deprivation (17).

Malocclusion is assessed using specific indices for orthodontic treatment need. Most used index is Index of Orthodontic Treatment Need - IOTN. It has two components: IOTN-DHC - Dental Health Component and IOTN-AC - Aesthetic Component.

IOTN-DHC - Dental Health Component evaluates 10 occlusal traits: overjet, underjet, deep bite, open bite, crossbite, crowding, impeded eruption, defects of cleft, lip and palate and other craniofacial anomaly, Class II and III buccal occlusions and hypodontia. Each parameter is given a value from 1 to 5 and the higher the score, the bigger the treatment need. Scores over 3 are considered as indicating a fair treatment need based on clinical signs (9, 8, 12, 10, 11).

IOTN-AC - Aesthetic Component have scores between 1 and 10, a higher score indicating a higher treatment need. Scores over 5 are considered as indicating a fair treatment need based on esthetic component (9, 8, 11).

DAI - Dental Aesthetic Index measures the orthodontic treatment need on the basis of social acceptability. It assesses 10 occlusal parameters such as overjet, underjet, missing teeth, diastema, anterior open bite, anterior crowding, anterior spacing, largest anterior irregularity (mandible and maxilla) and antero-posterior molar relationship. Each parameter is given a value depending on the severity and then the values of all 10 items are summed. It is added a constant value to the obtained sum and this represents the final score. It varies between 13 and 100. The higher the score, the higher the orthodontic treatment need. Based on the scores, malocclusion is classified in 4 categories: absent or minor: score 13-25, fair - score 26-31, severe - score

32-35 and handicap - score 36-100 (11, 4, 17, 16, 15).

ICON - Index of Complexity and Need assesses 5 components: esthetic, crowding/spacing, crossbite, open/deep bite, buccal antero-posterior relationship. Each component is given two values: one for the severity (from 0 to 5) and one for weight. These two values are multiplied and then the values obtained for all 5 components are added and this represents the final score. A higher score indicates a higher treatment need and complexity. To evaluate the 'outcome' component, then there must be compared the scores before and after the treatment (11, 12).

Traditionally, malocclusion is classified using the Angle system that take into consideration the relationship in the antero-posterior plan of the first molars. Thus, malocclusion are distributed in 3 categories: Class I - a normal molar relationship, Class II with lower molar distal than normal, while in anterior area there are 2 divisions: 1 - anterior upper teeth protruded, and 2 - anterior upper teeth retroclined and Class III - lower molar mesial than normal (5).

Extensive research has been done to evaluate the association between life quality and malocclusion.

A study conducted in Belgium in 2009 on a sample of 223 children 11-16 years old, revealed that the higher the orthodontic treatment need, the more affected life quality is (8). The most significant impact of malocclusion on life quality is the social and psychological aspect and children claim insignificantly oral symptoms or functional limitations (8). These conclusions were also found in another studies that took place in Brazil, one in 2012 on a sample of 519 children of 11-14 years of age (15) and another one in 2008 on 225 children, 12-15 years old (9). Also, the same results were obtained in a study developed between 2003 and 2006 in United Kingdom when were evaluated 273 patients whose age varied between 16 and 30 years. Another study conducted in New Zealand in 2012 that assessed 783 teenagers, showed results that emphasize these conclusions (17).

Another study that confirms the conclusions above, developed in Malaysia in 2013 on a sample of 325 subjects with ages between 15 and 25 years, also show that, beside that fact that patients with high normative orthodontic treatment need have more affected quality of life, the most important impact of malocclusion is on the emotional state. It affects all the patients, irrespective the severity of malocclusion, thus including those with minor deviations. On the other hand, patients feel they have a handicap in the presence of severe malocclusion reflected by a high orthodontic treatment need (12).

In addition, the study developed in 2008 in Brazil that included in the sample 220 teenagers (15-16 years old) used Angle Classification in these case for malocclusion assessment and it showed that quality of life was significantly more affected in patients with Class III and Class II division 1 (5).

Also in Brazil, but in 2003, another study evaluated 396 18 years old men and revealed that, moreover, malocclusion localized in maxillary anterior area affected the most the social well-being - smiling and laughing and showing the teeth were avoided around people. In addition, when in the anterior area malocclusion included overjet, the impact was also on the emo-

tional well-being and functions (there were found difficulties in biting the food). But, in contrast to the later study, mentioned before, life quality hasn't been altered in patients with malocclusion localized in molar area (16).

In South Arabia, in 2013, it was developed a study that included in the sample 278 subjects 11-14 years of age. The results found showed that only patients that were diagnosed with severe malocclusion, considered handicap, had the quality of life affected by malocclusion. In these cases, all of the components of quality of life were altered: not only the emotional state, social interaction but also there were functional limitations oral symptoms (7).

Another study, conducted in Egypt in 2007 that evaluated 366 subjects with ages between 21 and 25 years, also confirms the impact of malocclusion on the esthetic component of quality of life but it confirm the results regarding the functions. In this studies, the results found state that severity of malocclusion involve also functional limitations: pain (explained probably because of the temporomandibular joint alterations) and hampered mastication (10).

Children that have a higher level of self-esteem have also a higher quality of life. However, self-esteem does not decrease with the increase in the severity of malocclusion (8, 4).

Women seek orthodontic treatment more frequently than men. Also, impact of malocclusion in quality of life is bigger in women than men (12, 15, 17). Other authors, however, do not agree this (7).

Impact of malocclusion on quality of life diseases with age. Thus, teenagers are more affected than adults. It is considered that this can be explained by the fact that the longer people live with malocclusion, the more they get used to it and get aware that the limitations in their daily activities by the malocclusion are not that significant (12). Other authors, however, don't agree this (7).

The higher the educational level, the bigger the impact of malocclusion on quality of life. This might be explained by the fact that people with a higher educational status are also concerned about the self-esteem and self-awareness (12). Yet, other studies show that people from family with low income have a more altered quality of life because of malocclusion (12). Other authors concluded that the educational and economic aspects don't have a significant influence (9, 17).

The accuracy is better when the assessment of the association of malocclusion and quality of life is performed using, as instruments, OHQoL-UK compared to OHIP (for quality of life evaluation) and IOTN- DHC and ICON compared to IOTN-AC and DAJ (for malocclusion evaluation) (11).

Quality of live is significantly improved after orthodontic treatment (conclusion of a meta analysis that included 25 full-text articles, published in 2014) (3).

CONCLUSIONS

Malocclusions alter, for certain, the quality of life. And, while the severe malocclusion should be treated for the correction of both the functional and psychological issues, the orthodontic treatment for fair and even minor malocclusion aim the improvement in

the emotional and social status due to the fact that most of the patients have these components affected. For the approach of orthodontic treatment in this manner, clinicians should set properly the orthodontic treatment need using appropriate instruments and adapt the treatment plan to each patient's psychological profile and demands and also demographic, educational and economic features.

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REVIEW ASUPRA INFLUENȚEI MALOCLUZIILOR ASUPRA CALITĂȚII VIETII

REZUMAT

Semnificația clinică a conceptului de calitate a vieții asociată sănătății orale este aceea că medicii dentști tratează nu bolile orale, ci o ființă umană care are motivații și nevoi nu numai de ordin funcțional ci și psihologic. Acest concept urmărește satisfacerea nu doar a nevoilor de tratament normative, apreciate de medic, ci și pe cele resimțite de pacient. Astfel, actualmente medicii dentști ar trebui să elaboreze planul de tratament centrat pe pacient, deci adaptat percepției și motivației acestuia asupra sănătății orale. Malocluziile dentare sunt întâlnite actual cu o frecvență mare, iar această afecțiune orală are un impact nu doar asupra funcționalității la nivelul cavității bucale ci și asupra gradului de stime și a interacțiunii sociale, toate acestea fiind aspecte asociate calității vieții. Adresabilitatea către serviciile stomatologice pentru corectarea malocluziilor este una mare, și nu doar în rândul copiilor și adolescenților, ci și în cazul adulților. În funcție de severitatea acestor malocluzii se poate stabili nevoia de tratament ortodontic, iar în țările în care tratamentele ortodontice sunt oferite prin asigurări, se poate realiza prioritizarea corectării malocluziilor. Pentru abordarea de succes a planului de tratament, clinicienii trebuie să stabilească nevoia de tratament ortodontic pe baza unor instrumente adecvate și să adapteze planul de tratament în funcție de caracteristicile psihologice, dar și demografice, profesionale și economice ale pacientului.

Cuvinte cheie: sănătate orală, calitatea vieții, malocluzii

MOTIVATIONAL CHARACTERISTICS OF ORTHODONTIC PATIENTS

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ABSTRACT

Aim: Our study aimed to assess motivation factors of adherence to orthodontic treatment for children and adolescents from a private dental office in Bucharest. **Material and method:** Questionnaires for identifying specific items related to motivation for orthodontic treatment were distributed to 82 subjects aged 6-16 yrs. **Results:** For 83.7% of subjects the desire to straighten the teeth and improve the smile were the most frequently reported reasons, in 36.7% cases first decision to get treatment was own volition, for 63.3% it was someone else decision (38.8 % from the general dentist, 18.4% from parents and 6.1% from another known persons who had braces). The principal perceived benefits of the orthodontic treatment were improving facial appearance (77.8%), increased self-esteem (48.7%), and more self-reliant in social relationship (41.5%). 41.6% of subjects received negative commentaries from colleagues, neighborhood, and foreign people and 58.4% experienced teasing regarding their appearance in childhood. **Conclusions:** The results of present study emphasize the importance of assessing and understanding child patient motivation for orthodontic treatment to assess compliance to treatment and satisfaction results obtained after treatment.

Keywords: motivation, orthodontic treatment, adolescent

INTRODUCTION

To achieve a successful orthodontic treatment and to increase therapeutic compliance, it is important to understand the motivation of patient seeking this kind of dental treatment. The informed consent process should clearly identify the patients' motivations for treatment and if these cannot be satisfied as part of the treatment, this should be discussed in detail. By identifying a patient's motivation for treatment, these factors can enhance patient cooperation and compliance and reducing drop out.

Patient motivation for orthodontic therapy may be internal (when the patient perceives the treatment need and has its own desire to appeal to treatment) or external, that appeared following pressure from other people around them (2, 9).

From internal group factors, esthetic demands are the main motivation factor for seeking orthodontic treatment (3). For adolescent patients, the wish for a better dental appearance is the most important, followed by dentist's advice and by influence of significant others (external factors). A study from 2009 showed that 93.4% of the children estimated esthetic concerns as the most important reason and compared participants' motivation for treatment with their adherence to the treatment, these two factors being direct correlated (1).

From esthetic motivational factors, anticipation of improved esthetics was an important issue motivating factor (6, 7).

For adolescents, an important internal motivational factor is exploring the sense for their own identity, hoping that improving

appearance will enhance their self confidence and self image (8).

From external motivating factors category, previous studies conducted on adults by Kilpelainen et al (5) showed that another important factor in the motivation treatment was the recommendation of the general dentist. In addition, the detection of a malocclusion by a dentist could be an important motivational factor (10, 11). Some studies indicated that parents are responsible for 41% of initializing orthodontic treatment, and in a third of cases the dentist recommended orthodontic treatment (external influences). Adolescents were not always conscious of influences from exterior and believed that they had made self-determining decisions for treatment (4, 13).

Other external motivational factors as personal attack for peers, teasing and the influence of mass media should be taken into consideration, as well as internal factors (1).

Moreover, orthodontic treatment decision may be affected by adult patient's desire to enhance its dental and facial appearance, by socio-demographic factors related to patient (gender, age, living conditions, socioeconomic level) and also by other factors related to orthodontic treatment (time and personal values) (12).

MATERIAL AND METHODS

The objective of this study was to identify the patients' motives to start and adhere to an orthodontic treatment. Participants in this pilot study were 82 orthodontic patients of a private dental office in Bucharest, aged 6-16 years old (median age 13.25 years and a standard deviation of 7.05) and gender distribution is 37% boys

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and 63% girls. Prior to the study, were obtained official approval from dental office manager and informed consent from parents.

The questionnaire for assessing motivation for orthodontic treatment contains four questions established through semi-structured interview, for identifying specific items. The questionnaire contains closed-ended questions with dichotomous and multichotomous responses.

First question related to patient's reasons for seeking orthodontic treatment, the second question asked if it was the patient's own decision to start the treatment or external influences. The third question assessed the subjective benefits related to this type of treatment. The last question interrogated about previous negative comments about appearance from peers, relatives, teachers, etc.

RESULTS

Subjects answered at first question (Figure 1) that desire to straighten the teeth and improve the smile were the most frequently reported reasons (83.7% of subjects) for starting the orthodontic treatment. The responses for second question showed (Figure 2) that in 36.7% cases first decision to get treatment was own volition, for 63.3% it was someone else decision (38.8% from the general dentist, 18.4% from parents and 6.1% were influenced from another known persons who had braces).

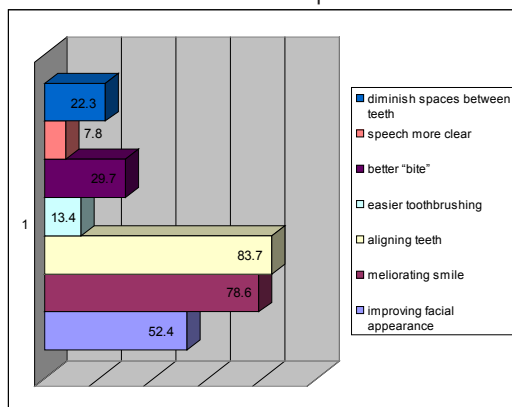


Fig.1. Percentage of answers regarding reasons for orthodontic treatment (%)

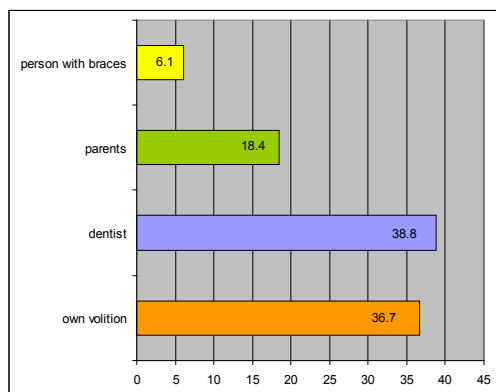


Fig.2. Percentage of answers regarding origin of treatment decision (%)

The results for third question (Figure 3) denoted that principal perceived benefits of the orthodontic treatment were estimated to be improved facial appearance (77.8%), increased self-esteem (48.7%), and more self-reliant in social relationship (41.5%). For fourth question, results pointed out that for 41.6% of subjects received negative commentaries from colleagues, neighborhood, and foreign people and for 58.4 having experienced teasing regarding their appearance in childhood (Figure 4).

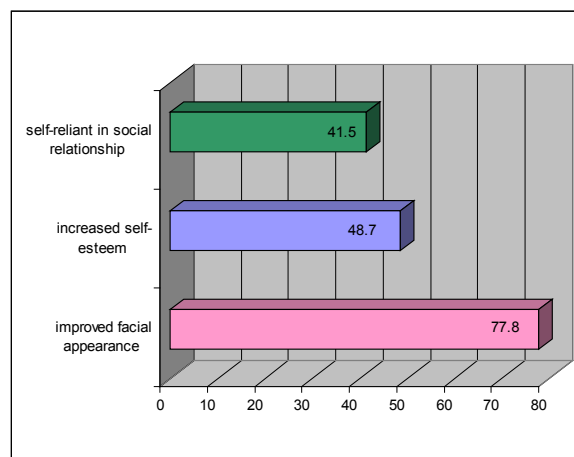


Fig. 3. Percentage of answers regarding perceived benefit of the orthodontic treatment

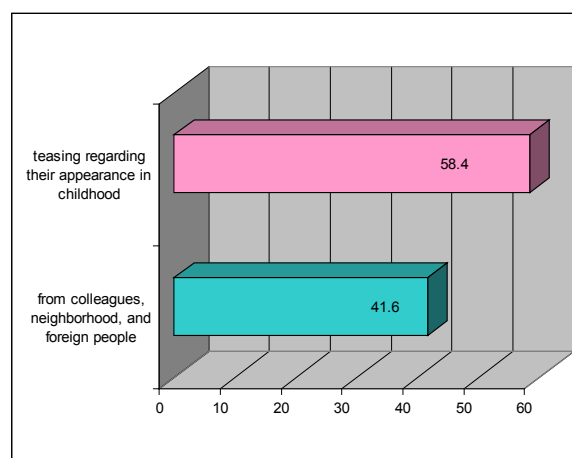


Fig. 4. Percentage of answers regarding negative commentaries (%)

CONCLUSIONS

The present study demonstrate that, for children and adolescent esthetic demands, like desire to straighten the teeth and improve the smile were the most frequently reported reasons for starting the orthodontic treatment, followed by improving oral functions, as occlusion, personal hygiene procedures, and speaking.

The majority (almost two third of subjects) had external motivation factors to adhere to treatment from which the dentist represent the most important decision factor to get treatment,

followed by parents and known persons under orthodontic treatment. The most commonly perceived benefits of treatment were estimated to be esthetic outcomes, expressed by improved facial appearance, psychological issues as increased self-esteem and social results, such as being more self-confident in relationships

The results of present study emphasize the importance of assessing and understanding child patient motivation for orthodontic treatment, the compliance to treatment and satisfaction with results obtained after treatment.

Various resources were used by the patients to gain more information on orthodontic treatment, most discussed it with their own dentist, thus highlighting the importance of the role of the general dental practitioner in educating their patients about orthodontic treatment.

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CARACTERISTICILE MOTIVAȚIONALE ALE PACIENȚILOR CU TRATAMENT ORTODONTIC

REZUMAT

Scop: Studiul urmărește evaluarea factorilor de motivație și a complianței la tratamentul ortodontic în rândul unui lot de pacienți copii și adolescenți dintr-un cabinet privat de medicină dentară din București. **Material și metodă:** Pentru identificarea elementelor specifice legate de motivația pentru tratamentul ortodontic au fost distribuite și completate chestionare la 82 de subiecți cu vârsta cuprinsă între 6 și 16 ani.

Rezultatele studiului arată că dorința de a-și îndrepta dinții și de a-și îmbunătăți zâmbetul au fost cele mai frecvent amintite motive (83,7% dintre subiecți), 36,7% din cazuri au apelat la tratamentul ortodontic din proprie inițiativă, pentru 63,3% dintre subiecți altcineva a luat decizia (38,8% - medicul dentist, părinții – 18,4% și 6,1% au fost influențați de alte persoane cunoscute care au purtat aparate ortodontice). Principalele beneficii ale tratamentului ortodontic percepute de copiii și adolescenții din studiu sunt: îmbunătățirea aspectului facial (77,8%), creșterea stimei de sine (48,7%) și îmbunătățirea relațiilor sociale (41,5%). 41,6% dintre subiecți au primit comentarii negative din partea colegilor, vecinilor și a persoanelor necunoscute și 58,4% au fost tachinați în copilărie în legătură cu aspectul fizionomic.

În **concluzie**, rezultatele studiului subliniază importanța evaluării și înțelegerii motivației pacientului copil și adolescent pentru tratamentul ortodontic în vederea stabilirii complianței la tratament și a nivelului de satisfacție în ceea ce privește rezultatele obținute după tratament.

Cuvinte cheie: motivație, tratament ortodontic, adolescent

TUMOR NECROSIS FACTOR EVALUATION FOR CASTING AND SELECTIVE LASER SINTERING CO-CR ALLOYS

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ABSTRACT

Materials for dental applications have to meet unique requirements, including suitable mechanical properties and acceptable biocompatibility, as they are to be placed in the oral environment with a variable pH. It is known that the technological process has an influence on the structure of the alloy, and the release of ions from dental prostheses is an indicator of the corrosion characteristics of dental alloys. Laser sintering is a promising technology that may enable the fabrication of dental devices overcoming some of the imperfections of casting. Systemic and local cytotoxicity, allergy, and carcinogenicity result from elements in the alloy being released into the mouth during corrosion. Tumor necrosis factor alpha (TNF- α) plays a central role in inflammation, immune system development, apoptosis, and lipid metabolism. The purpose of this paper is to evaluate the tumor necrosis factor (TNF α) corresponding to a cast and selective sintered dental Co-Cr alloys.

Key words: corrosion, laser sintered, dental alloy, tumor necrosis factor alpha

INTRODUCTION

There are certain requirements towards all the materials (implants or dental appliances) which are inserted in human body. The following problems are considered: biological safety tissue response, biofunctionality and corrosion resistance. The two significant features regarding the biocompatibility are the integrity and degradation of the material and the reaction of the host organism (toxic effects and allergic response) (1,2).

Systemic and local cytotoxicity, allergy, and carcinogenicity all result from elements in the alloy being released into the mouth during corrosion. Little evidence supports concerns of casting alloys causing systemic toxicity. The occurrence of local toxic effects (adjacent to the alloy) is not well documented, but is a higher risk, primarily because local tissues are exposed to much higher concentrations of released metal ions (3). Several elements such as nickel and cobalt have relatively high potential to cause allergy, but the true risk of using alloys containing these elements remains undefined (4-7). Prudence dictates that alloys containing these elements be avoided if possible. Several elements in casting alloys are known mutagens, and a few such as beryllium and cadmium are known carcinogens in different chemical forms. Despite these facts, carcinogenic effects from dental casting alloys have not been demonstrated.

Tumor necrosis factor alpha (TNF- α), also known as cachectin or TNFSF1A, is the prototypic ligand of the TNF superfamily. It is a pleiotropic molecule that plays a central role in inflammation,

immune system development, apoptosis, and lipid metabolism (8). TNF- α is also involved in a number of pathological conditions including asthma, Crohn's disease, rheumatoid arthritis, neuropathic pain, obesity, type 2 diabetes, septic shock, autoimmunity, and cancer. Human TNF- α is synthesized as a 26 kDa type II transmembrane protein that consists of a 35 amino acid (aa) cytoplasmic domain, a 21 aa transmembrane segment, and a 177 aa extracellular domain (ECD). Within the ECD, human TNF- α shares 97% aa sequence identity with rhesus monkey, and 71-92% aa identity with bovine, canine, cotton rat, equine, feline, mouse, porcine, and rat TNF- α . It is produced by a wide variety of immune, epithelial, endothelial, and tumor cells. TNF- α is assembled intracellularly to form a non-covalently linked homotrimer which is expressed on the cell surface. Cell surface TNF- α can both induce the lysis of tumor cells and virus infected cells, and generate its own downstream cell signaling following ligation by soluble TNF RI. Shedding of membrane bound TNF- α by TACE/ADAM17 releases the bioactive cytokine, a 55 kDa soluble trimer of the TNF- α extracellular domain.

The aim of this article is to evaluate the tumor necrosis factor (TNF α) corresponding to a cast and selective sintered dental Co-Cr alloys.

MATERIAL AND METHOD

The Quantikine Human TNF-alpha Immunoassay, which is a 3.5 or 4.5 hour solid phase ELISA designed to measure human

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TNF-alpha in serum, was used for this study. This assay employs the quantitative sandwich enzyme immunoassay technique. A monoclonal antibody specific for TNF- α has been pre-coated onto a micro plate. Standards and samples are pipetted into the wells and any TNF- α present is bound by the immobilized antibody. After washing away any unbound substances, an enzyme-linked polyclonal antibody specific for TNF- α is added to the wells. Following a wash to remove any unbound antibody-enzyme reagent, a substrate solution is added to the wells and color develops in proportion to the amount of TNF- α bound in the initial step. The color development is stopped and the intensity of the color is measured.

The collection of the serum was performed by using the separator tube (SST) and allows samples to clot for 30 minutes at room temperature before centrifugation for 15 minutes at 1000 x g. The serum was removed and used for the study. All reagents were brought to room temperature before use. Related to the wash buffer, if crystals have formed in the concentrate, warming to room temperature and mixing gently until the crystals have completely dissolved are recommended. 20 mL of wash buffer concentrate were diluted into deionized or distilled water to prepare 500 mL of wash buffer.

In order to obtain the substrate solution, the color reagents A and B were mixed together in equal volumes within 15 minutes of use being protected from light. 200 μ L of the resultant mixture is required per well.

The TNF- α Standard were reconstituting with deionized or distilled water. This reconstitution produces a stock solution of 10,000 pg/mL. The standards were allowed to sit for a minimum of 15 minutes with gentle agitation prior to making dilutions. 900 μ L of Calibrator Diluent RD6-35 (for serum/plasma samples) were pipetted into the 1000 pg/mL tube. 500 μ L of the appropriate Calibrator Diluent were pipetted into the remaining tubes. The stock solution was used to produce a dilution series. Each tube were mixed thoroughly before the next transfer. The 1000 pg/mL standard serves as the high standard. The appropriate Calibrator Diluent serves as the zero standards (0 pg/mL).

After the preparations of all the solution described before, the excess microplate strips were removed from the plate frame, return them to the foil pouch containing the desiccant pack, and reseal. 50 μ L of Assay Diluent RD1F were added to each well. Assay Diluent RD1F will have a precipitate present. Then 200 μ L of Standard solution was added per well. After that an incubation time of 2 hours at room temperature was performed. A plate layout is provided to record standards and samples assayed. Each well was aspirated and wash, repeating the process three times for a total of four washes. 200 μ L of TNF- α Conjugate was added to each well. Cover with a new adhesive strip. For serum samples an incubation of 2 hours was performed at room temperature. The aspiration and washing procedure is repeated. Then a 200 μ L of Substrate Solution was added to each well. The samples were incubating for 20 minutes at room temperature and protected from light. 50 μ L of Stop Solution was added to each well. The color in the wells was changed from blue to yellow. The optical density of each well was determined within 30 minutes,

using a microplate reader set to 450 nm.

RESULTS

The values observed for the two considered alloys were presented in the table below:

No.	TNF alpha for Cast Co-Cr pg/ml	TNF alpha for SLS Co-Cr pg/ml
1.	9.80	10.12
2.	8.71	9.21
3.	7.98	9.24
4.	11.24	12.47
5.	7.85	10.20
6.	9.45	10.87
7.	9.01	11.01
8.	9.63	10.98
9.	9.09	11.23
10.	9.89	10.89
11.	9.94	11.25
12.	9.87	11.89

In Figure 1 it can be observed the difference of TNF alpha evaluation between control group and the considered cast and SLS Co-Cr alloys.

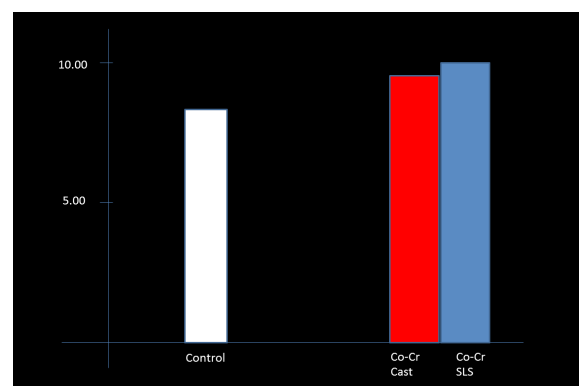


Fig. 1. The aspect of the mean results after the TNF alpha evaluation for the considered Cast and SLS Co-Cr alloy

The values of the TNF alpha obtained from the serum were slightly higher (between 9 and 11 pg/ml) than the normal values (2-5 pg/ml). However the increasing values are not comparable with the inflammatory situations in which 50-60pg/ml could be detected.

DISCUSSION

There is great concern that metal ions may impair the local and systemic immune responses of patients with cast metallic restorations. Therefore, interactive effects of metal ions with immunological parameters have been investigated *in vitro* and *in vivo*. The production of various immune mediators after treat-

ment with metallic materials has been studied in lymphocyte cell lines. The expression of the inflammatory mediator interleukin 2 (IL-2) and the immune effector, IgG, by T- and B-cells was determined after incubation with three copper-based casting alloys. The production of both immune mediators was altered by released cations (9). Lipopolysaccharide (LPS)-stimulated osteoblast-like cells revealed an increased production of IL-1 α and tumor necrosis factor- α (TNF- α) after incubation with Ti, Co, and Cr. In addition, synthesis of type I collagen was reduced (10).

Polymorphonuclear leukocytes (PMNs) are primarily involved in the host defense against bacteria, *e.g.*, by the production of reactive oxygen species (ROS). Thus, the expression of ROS was used as parameter for the determination of interactive effects between several metal ions and PMNs. While Mo, Al, and V enhanced ROS production, no such effect was observed with Cr, Co, Ni, and Ti (11). Release of several cytokines from unstimulated and stimulated peripheral blood mononuclear cells (PBMCs) as well as cell viability and DNA synthesis were investigated after incubation with Cr ions. This cation caused a dose-dependent reduction of cell viability, DNA synthesis, secretion of IL-6, and expression of soluble interleukin-2 receptor (sIL-2r). These findings suggest that chromium has the potential to suppress the immune system (12).

Ti wear particles did not significantly alter several investigated immunological parameters such as peripheral blood lymphocyte activation and IL-2 secretion (13). Similar data have been reported with murine macrophages which had been exposed to wear debris of a Co-Cr alloy (14). But IL-1 secretion from macrophages and bone-resorbing activity were significantly stimulated by fine Ti particles. In contrast, the respiratory burst and function of human PMNs were significantly inhibited by Co-base alloy particles of non-phagocytosable size (15).

The pro-inflammatory effects (IL-6 production) of numerous metals and one noble alloy were investigated in a three-dimensional co-culture model with human fibroblasts and keratinocytes. Increased IL-6 expression, suggestive of a pro-inflammatory potency, was detected with Cu, Zn, Co, Ni, and Pd at low or non-toxic concentrations (16).

Several metal ions (Ag, Au, Cu, Hg, Ni, Pd, Pt, Zn) altered the secretion of proteins from macrophages (3). Sub-toxic concentrations of a Ni solution also induced an increase of IL-1 α and TNF- α secretion from unstimulated and LPS-stimulated THP-1 monocytes (macrophages), whereas Ag and Cu enhanced IL-1 α expression only from LPS-stimulated cells (17).

Cell adhesion molecules (CAM) like E-selectin, intercellular adhesion molecule 1 (ICAM-1), *etc.*, are important for mediating cell-cell interactions of platelets and leukocytes with endothelial cells. Thus, it is of great interest to determine if metal ions can alter the production of CAM by endothelial cells. Very low, sub-toxic concentrations of Zn, Ni, and Co increased the expression of E-selectin, ICAM-1, and other CAM similar to that observed with inflammatory mediators. The authors concluded that clinically relevant very low concentrations of these metal ions, which may be released by corrosion, might participate in the pathogenesis of tissue inflammation (18). Contrary to previous

experiments, ICAM-1 expression of LPS-stimulated endothelial cells was reduced by sub-toxic Ni concentrations, but no effect was determined in the absence of LPS. At clinically relevant, cytotoxic concentrations, Ni stimulated ICAM-1 production. These results show that Ni might exhibit a dual action regarding ICAM-1 expression, which is modulated by microbial factors, like LPS. Solid specimens of a Ni-containing alloy caused a significant increase of IL-1 α secretion from THP-1 monocytes, confirming the pronounced inflammatory potency of Ni ions (4).

The significance of bacterial LPS stimulation on the inflammatory responses of various cell types following incubation with several metal ions is debated. After LPS stimulation, human monocytes/macrophages expressed significantly more cytokines following incubation with sub-toxic concentrations of three metal ions: IL-1 α (Ti, Cr, Co), TNF- α (Ti, Cr), and IL-6 (Ti). In addition, all cations that were used reduced the production of tumor growth factor- α 1 (TGF- α 1). In the absence of LPS, however, no stimulation of monocytic cytokine expression was observed.

The effects of noble alloys and Ni-containing base metal alloys on the levels of lymphocyte subpopulations after implantation were investigated *in vivo* in a murine model (19). No alteration in the proportion of the lymphocyte subpopulations was observed.

The concentrations of circulating T-lymphocytes and other parameters - such as hematocrit, total and differential leukocyte count, serum and salivary nickel concentrations, *etc.* - were determined over a six-month period after patients received fixed partial prostheses which had been made with a Ni-Cr alloy. No changes in salivary and serum Ni levels were found. Though the T-lymphocyte and monocyte populations did not change, the number of circulating eosinophils decreased and the neutrophil and basophil populations increased. Since basophils participate in hypersensitivity reactions, it was concluded that hypersensitivity caused by metal ions which are released from the Ni base alloy cannot be ruled out (20). On the other hand, T-lymphocyte proportions increased from 56% to 77% of all lymphocytes after removal of a Ni base alloy crown in a 20-year-old patient. This case report indicates that Ni may adversely influence the number of circulating T-lymphocytes (21).

There is evidence that metallic components derived from dental cast restorations can modulate the expression of various immunological factors and, therefore, may participate in the etiology of various intra-oral pathological conditions. The increased expression of cytokines after LPS stimulation of various cell types indicates that bacterial toxins and material-related factors, cation release due to corrosion, may produce synergistic or additive inflammatory effects in the pathogenesis of oral diseases, like oral mucositis, gingivitis/periodontitis, and alveolar bone resorption.

CONCLUSIONS

The results of our study reveal that the TNF- α related to the casting alloys and selective laser sintered samples of Co-Cr are similar. However more evaluation is necessary in order to draw a final conclusion.

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EVALUAREA FACTORULUI DE NECROZA TUMORALA PENTRU ALIAJELE DE CO-CR OBTINUTE PRIN TURNARE SI SINTERIZARE LASER

REZUMAT

Materialele care se utilizeaza in domeniul medicine dentare trebuie sa indeplineasca caracteristici corespunzatoare in ceea ce priveste proprietatile mecanice, dar si o biocompatibilitate acceptabila, ele fiind plasate in mediul bucal ce prezinta un pH variabil. Este bine cunoscut ca procesul tehnologic are o influenta majora asupra structurii aliajelor, iar eliberarea de ioni din protezele dentare este un indicator al caracteristicilor de coroziune al acestor aliaje dentare. Procedul tehnologic de sinterizare laser al aliajelor reprezinta o tehnologie promitatoare ce permite fabricarea unor restaurari dentare ce pot contracara anumite imperfectiuni ce pot apare in procesul traditional de turnare al aliajelor. Citotoxicitatea sistemica si locala, reactiile alergice si carcinogenitatea rezulta prin eliberarea in cavitatea bucala a anumitor elemente ca urmare a procesului de coroziune. Factorul de necroza tumorală α (TNF- α) joaca un rol central in inflamatie, dezvoltarea sistemului imun, apoptoza si metabolismul lipidic. Scopul acestui studiu a fost de a evalua comparativ factorul de necroza tumorală (TNF- α) ce corespunde unui aliaj din Co-Cr obtinut prin turnare si prin sinterizare laser.

Cuvinte cheie: coroziune, sinterizare laser, aliaj dentar, factor de necroza tumorală α

18-FDG-PET AND PET/CT FOR MINIMAL INVASIVE DIAGNOSIS OF HEAD AND NECK CANCER

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ABSTRACT

Aim: Our study aimed to establish the prognostic value of 18-FDG-PET by the standardized uptake values.

Materials and Methods: 18-FDG-PET is known to be useful in identifying unknown recurrent head and neck squamous cell carcinoma (HNSCC) in the post-treatment setting, second primary carcinomas or distant metastases and even primary head and neck squamous carcinoma.

Results and conclusions: PET presents a high negative predictive value for detecting recurrent HNSCC. There are some limitations for this diagnostic instrument regarding the identification of occult nodal metastases. Also false positive readings can be generated by the radiation effect, the muscle activity, infection and inflammation. Using new radioactive tracers, PET can be enabled in identifying sites of hypoxia, DNA replication and protein metabolism.

Keywords: squamous carcinoma, minimal invasive diagnosis, PET/CT.

INTRODUCTION

Positron emission tomography (PET) using the radiotracer [¹⁸F]-fluoro-2-deoxy-D-glucose represents a comprehensive imaging technique in the evaluation and staging of head and neck squamous cell carcinomas (HNSCC). A great number of malignant tumors, including squamous carcinomas, indicate an increase in the glucose metabolism when compared to normal tissues. A glucose analogue like 18-fluorodeoxyglucose (FDG) can be delivered intravenously, where glucose transporters preferentially transport it into squamous carcinomas. After undergoing phosphorylation by hexokinase, FDG becomes trapped in the cell, making it impossible to advance in the glycolysis pathway. Therefore PET can image cells with preferential uptake of FDG through the positrons emitted by ¹⁸F incorporated into the glucose analogue.

The salivary oncocytomas, thyroid Hurtle cell adenomas, salivary Warthin's tumors together with other benign tumors are known to accumulate FDG. It can also be found in the brain, salivary glands, lymphoid tissue, and active muscle; therefore FDG is not a specific marker for cancer (Figure 1).

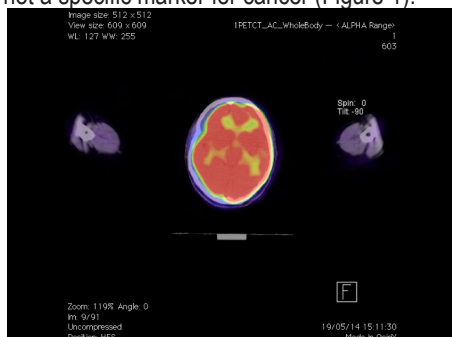


Fig. 1. 18-fluorodeoxyglucose increased uptake in the brain.

The kidney (Figure 2) and bladder (Figure 3) can also demonstrate activity on PET scan due to the excretion of ¹⁸F. False-positive findings can emerge also from increase FDG uptake in areas of infection, inflammation and trauma.

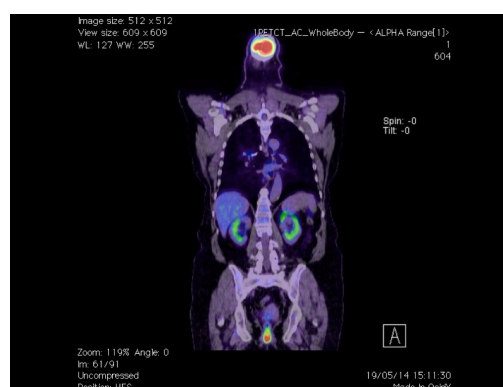


Fig.2. 18-fluorodeoxyglucose increased uptake in the kidneys.

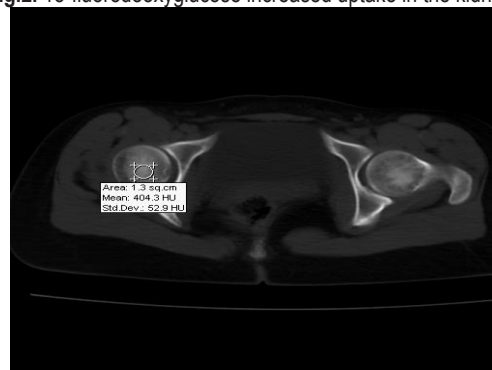


Fig. 3. 18-fluorodeoxyglucose increased uptake in the bladder.

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The standard procedure for PET scan includes introducing FDG intravenously and a waiting period for the FDG to be distributed systemically. During this interval the patient has to wait quietly because any muscular activity (e.g., talking) may lead to potentially false positive interpretation due to a possible increased FDG accumulation. Elevated serum glucose levels reduce the sensitivity of FDG uptake into tumor tissues there for patients who have eaten recently or with uncontrolled diabetes shouldn't undergo PET scanning.

FDG-PET scanning represents an important diagnosis and evaluation modality for a variety of scenarios in the HNSCC. In this manuscript we will assess the PET utility in identifying the recurrent disease in the post-treatment, the assessment of response following chemo-radiation therapy, the distant metastases and second primary tumors and the unknown primary tumor. We will also discuss the PET limitations for detecting occult nodal disease and the new developments in this imaging technique that may have a future impact on the HNSCC diagnosis and treatment.

MATERIALS AND METHODS

Detection of Recurrent Disease

Cancer treatment usually causes significant changes in the normal tissues including edema and fibrosis. Conventional cross sectional imaging can be ambiguous for possible residual or recurrent disease due to scar tissue or residual soft tissue thickening, obscuring the early detection of recurrent disease (Figure 4).

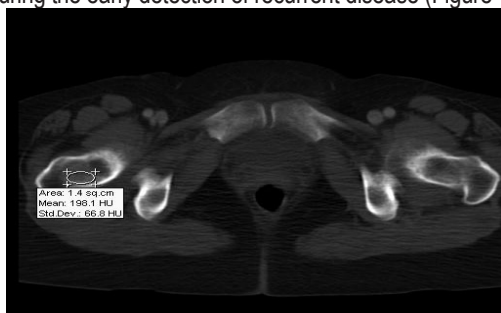


Fig. 4. Comparison of conventional CT and PET scans of the same patient. The FDG uptake in the PET image can easily indicate a possible recurrent disease.

The assessment of recurrent disease following HNSCC therapy has been one of the most widespread applications of FDG-PET (Figure 5).



Fig. 5. Comparison of conventional CT and PET scans of the same patient with a history of oral squamous cell carcinoma.

There are studies, which have demonstrated that PET has a high sensitivity for identifying recurrent carcinoma (84–100%) with moderate specificities (61 – 93%) (1-8). A review that examined 143 patients undergoing FDG-PET scans analyzed the performance at local, regional, and distant sites (8). Due to false positive readings PET's specificity was lower (79%) at local sites and higher at distant (95%) and regional (95%) sites. A SUV of 3.2 was identified as an optimal cutoff value for determining in this study. The importance of other clinical information to the overall PET interpretation was demonstrated by the sensitivity and specificity of the nuclear medicine physician which was superior to the SUV cutoff value. Another study reported that PET identified local recurrence in 37 of 75 patients with pharyngeal and laryngeal cancers (7). A negative FDG-PET correctly excluded recurrent disease in 24 patients, but overlooked it in 3 patients. A positive FDG-PET scan was less reliable showing 14 false-positive findings but correctly identifying 34 cases of recurrence. These studies suggest that a negative PET scan is able to exclude recurrent disease (Table I).

Table I. 18-FDG-PET detection of HNSCC

Study	Patient number	Overall sensitivity	Overall specificity	Negative predictive value
Wong et al.	143	96%	72%	96%
Terhaard et al.	75	97%	82%	89%

Other studies have attempted to establish an optimal time for the PET to be performed after the radiation therapy in order to obtain the highest accuracy. Lonneux et al. (3) showed that the accuracy of FDG-PET was the highest (94%) when the radiation therapy was completed more than 3 months prior to the PET scanning. Greven et al. (9) evaluated 45 patients before and after high- dose radiation therapy at the following intervals: 1, 4, 12, and 24 months. They discovered that PET scanning at 4 months post- radiation had a higher accuracy than at 1 month. FDG-PET scans performed at early intervals following therapy may lead to false results due to inflammatory effects from radiation or chemo-radiation therapy.

PET/CT for IMRT planning

Recent developments have been made for planning the intensity modulated radiation therapy (IMRT) by using PET/CT. In a study on 28 patients with HNSCC PET/CT was used to guide IMRT planning on. The results showed that 16 patients presented altered tumors staging, while with CT scan based staging 6 patients presented higher N stages and 12 patients presented higher T stages. Additionally with the CT the gross target volume (GTV) was larger in 9 cases, significantly different when compared to PET/CT GTV, which was larger in 5 cases.

Breen demonstrated that GTV assessment in 10 patients with HNSCC was not significantly different between PET/CT

and contrast CT scans, using 8 different observers. Breen also demonstrated a higher consistency for the CT derived volumes as compared to the PET/CT derived GTV's. These findings represent conflicting evidence regarding the utility of PET/CT in comparison with conventional contrast CT when considering GTV delineation and IMRT planning.

Distant metastases and second primary carcinomas

FDG-PET represents a great application as an initial staging because it can provide an overview of the distant metastases, nodal metastases, potential second primary carcinomas and even primary tumor (Figure 6).



Fig. 6. Whole body scans – relevant for identifying distant metastasis or second primary carcinomas.

Several small studies have assessed the potential of FDG-PET in identifying distant metastases. When reviewing these studies, a finding on FDG-PET suggesting second primary carcinoma or distant metastasis was assessed in 21% of patients. Following clinical follow up or biopsy, only 27% proved to be false positive sites of disease. A limitation of these studies is rarely reported false negative results together with the lack of controlled comparison between PET/CT and other initial staging techniques.

For patients with advanced HNSCC, using FDG-PET for identifying distant metastases has great importance in the initial staging. Alcohol or heavy tobacco consumption represents a higher risk for second primary carcinomas. Further analyses are necessary to determine the cost-effectiveness of routine FDG-PET imaging related to conventional cross sectional imaging.

The unknown primary carcinoma

The correct identification of occult primary sites is highly important because the treatment can then be specifically directed and individualized for the known site of origin, decreasing treatment-related morbidity. There are cases when a primary malignancy is not identified during long-term follow-up and diagnostic evaluation even with an accurate clinical examination, conventional cross-sectional imaging and endoscopy under anesthesia.

The use of FDG-PET in identifying unknown primary carcinomas was assessed in many small retrospective studies.

Unfortunately these studies present a lack of uniformity in the assessment modalities used in looking for the primary site and also in the inclusion criteria. Rusthoven et al. (10) performed an extensive review on 16 studies published between 1994 and 2003 referring to the FDG-PET capability of identifying unknown primary carcinomas. In all of these studies, 302 patients underwent physical examination together with CT or MRI, and most of them underwent also pan-endoscopy. The validation of the results was achieved by tissue biopsy, which remains the gold standard for primary tumor diagnosis. FDG-PET identified the primary tumor in 74 patients (24.5%). 16% of cases presented new regional metastases while new distant metastases were detected in 11% of cases. PET accuracy was of 79% for the primary tumor identification having a sensitivity of 88% and a specificity of 75%. When evaluating the performance by anatomic site, a lower specificity for tonsil malignancies and a lower sensitivity for base of tongue malignancies were observed.

In cases with an unknown primary carcinoma discovered by office examination, office laryngoscopy, and cross-sectional imaging (CT or MRI) is generally recommended that patients also undergo a PET/CT scan prior to biopsy in the operating room (Figure 7). It could be useful for intraoperative biopsies guiding through the sites with increased uptake on PET/CT. It can be suggestive for the location, depth, and aggressiveness. For up to 25% of patients, the PET/CT scan can help in establishing the correct primary site. A critical factor for the accurate identification of the unknown primary malignancy remains the clinical expertise of the.



Fig. 7. PET/CT scan of the lungs. The patient was recommended PET investigation after being clinically suspected of lung cancer. The PET scan revealed no malignancies in the lungs.

Occult nodal metastases

For previously untreated patient FDG-PET was not accurate in the detection of occult nodal disease. There are prospective clinical trials of patients with oral malignancies in which poor accuracy by PET was proven in detecting occult nodal metastases (11-13). These lesions were identified and ultimately removed by supraomohyoid neck dissection. In all studies sentinel lymph

node mapping proved to be much more accurate than PET/CT in identifying occult nodal metastases. In a recent prospective clinical trial, 31 patients with oral malignancies and clinically negative necks were submitted to preoperative PET/CT investigation prior to 36 neck dissections (14). PET/CT presented a specificity of 95% and a sensitivity of just 67%. It was considered that false negative results were likely related either to the proximity to the primary tumor obscuring its detection or to the presence of microscopic metastases not detected by PET/CT. Due to the limited sensitivity of PET/CT, it is not recommended for the identification of occult lymph node metastases.

RESULTS AND DISCUSSIONS

The invasive common therapy for HNSCC usually results in a significant alteration of social and biologic functions (eating, breathing, speaking etc). Therefore structural integrity of these structures is essential for the wellbeing of the patient. In order to preserve the functionality of these organs chemoradiotherapy (CRT) is being introduced as a definite therapy in the treatment scheme (15-19). A disadvantage for this type of approach would be the distortion of the anatomy in the affected area due to the radiation effects. Early detection of an occult tumor can become challenging in this situation therefore thorough examinations must be carried out for these patients. The therapeutic paradigm has shifted in these cases toward "function-preserving" CRT. Therefore, a PET-based diagnostic method is desirable for post-CRT monitoring of HNSCC.

There are some studies in the literature, which describe the FDG-PET utility in detecting unknown primary tumors. Usually they are limited in size and report varying results. A recent meta-analysis covered all the literature in this topic in order to guide clinical treatment by using FDG-PET (20). They investigated 589 patients and they obtained an accuracy of 81.5 with a specificity of 82.1% and a sensitivity of 80.6%. These results suggest that ¹⁸F-FDG PET can bring important benefits to the oncologic patients and are in accordance also with another study (21) on 302 patients that reported a sensitivity of 88.3%. The detection rate for primary tumors is higher (33.5%) when compared with the results in Fogarty et al. study (22.5%) (22). The 82.1% specificity was higher than in Neider et al. review (62%) (23).

False-positive results can appear due to physiologic uptake in the mastication muscles, lymph nodes and tonsils. FDG accumulation can sometimes occur in patients with benign tumors of the salivary glands (24,25), granulomatous disease or sarcoidosis. Recent mucosal biopsies can generate tissue repair reaction, which can increase the FDG uptake (26). There can exist other causes for false-negative results like a disruption in signal-to-noise ratio due to an increase background uptake (eg. in the brain) (27). Kole et al. have also demonstrated that small tumors (below FDG PET resolution) may lead to false-negative results. The high sensitivity of FDG-PET can be associated with the great number of true-negative results. There is a study (28) in which it is indicated that the failure to detect a primary tumor can be attributed to immune-mediated destruction of the lesion

or to spontaneous regression. The high tumor uptake having a low background uptake in the nodal areas enables PET to better detect nodal disease as compared to primary HNSCC. Lesions up to 1 cm can be detected by PET/CT if they have good uptake of FDG (29).

An intra-observer variability in PET results can be observed even with highly experienced nuclear medicine radiologist (30). The identification of a primary tumor is depended on the experience of the personnel that conducts the clinical, radiologic and endoscopic examinations. Instead of indicating PET investigation for unknown primary tumor detection in all clinical situations, it would be recommendable to ensure that the initial diagnostic procedure was done correctly and by experienced personnel.

False-positive results can be reduced by PET scanning in order to obtain physiologic imaging and by CT imaging for anatomic imaging. The CT can enhance the assessment of tumors anatomic distortion at sites with increased FDG uptake.

PET/CT compared to FDG-PET or CT was found to be superior in the detection of head and neck malignant disease (31). In a large study (32) it was demonstrated that combined PET/CT resulted in accurate staging in 10 of the 12 patients with CUP, whereas MRI resulted in accurate staging in 8 of these 12 patients. The anatomic data obtained using PET/CT enhances the accuracy of FDG-PET-directed biopsies (33).

There are studies (20,34) that confirm a percentage of approximately 60% of squamous cell carcinoma for occult primary tumors in head and neck pathology. 30% are adenocarcinomas and the rest are tumors from the mucosa and skin, the thyroid gland and poorly differentiated carcinoma. Usually when the metastases are from a SCC a primary tumor is found in the head and neck area. A small number of adenocarcinoma metastases can originate in the salivary glands, nasal cavity, and the paranasal sinuses (35).

According to Ossama H et al (20) among head and neck primary carcinomas, tumors of the tonsils (21.6%), and the base of the tongue (13.8%), were the most prevalent. Mendenhall et al. (36) reported similar results for tumors of the tonsils that accounted for 43% and for tumors of the base of the tongue that accounted for 39% of all primary tumors.

Prognostic Value of PET scanning

There is evidence that the standardized uptake value (SUV) measured by FDG-PET for HNSCC may have prognostic value. The SUV level of PET scans identifying recurrent disease was strongly correlated with both overall survival and relapse-free (8). Patients with SUV's more than 6 had a 2-year relapse-free survival of only 10%, while patients with SUV's less than 2 had a 2-year relapse-free survival of 85%.

In a review on 54 patients it was demonstrated that the pre-treatment SUV for patients who underwent FDG-PET prior to treatment of HNSCC was predictive of both disease-free and local recurrence-free survival (37). In another study on 47 patients undergoing radiation or chemo-radiation therapy for head and neck cancer, FDG-PET was performed before and up to 3 weeks after the therapy was initiated (38). PET was analyzed

using measurements of tumor metabolic rate (MR) and SUV derived from blood sampling of FDG and glucose. They found that high MR from the post-treatment PET showed overall 5-year survival rates of 72% and for low MR the survival rate was 35%. Therefore, measures related to FDG metabolism obtained using PET may have prognostic value for patients.

New Radiotracers for PET

PET represents a technique that can identify positron emission from a variety of radioactive isotopes including carbon-11, oxygen-15, and nitrogen-13, additional to fluorine-18. Some tracers have shown high promise in selectively localizing malignant tumors (39). A carbon-labeled amino acid (11C-methionine) can be used as a surrogate marker for protein metabolism, having a highly specific potential of localizing tumors. 18-Fluorothymidine (FLT) is phosphorylated by thymidine kinase able to image DNA synthesis. FLT is generally correlated to tumor proliferation demonstrating encouraging early results.

Resistance to radiation therapy and tumor progression is related to hypoxia, which is commonly present in malignant tumors. Hypoxic imaging with PET can be performed with ¹⁸F-misonidazole (FMISO). It selectively accumulates in hypoxic conditions presenting minimal uptake in sites with normal oxygenation. Early developments have suggested that FMISO can be very useful in imaging head and neck malignancies, having prognostic value for cases following radiation therapy (40). All new tracers present early promise for future application, even so clinical trials and additional investigation are absolutely necessary for validating their utility in head and neck cancer diagnosis.

CONCLUSION

FDG-PET represents a highly accepted technique in evaluating HNSCC. However it cannot be considered a substitute for careful clinical and endoscopic examination. PET/CT is an extremely useful tool for detecting recurrent HNSCC. In these cases, PET is moderately specific but highly sensitive. Negative predictive values are high, considered reassuring for both clinician and patient. Positive predictive values are lower due to false positive readings in infections, inflammations, biopsy or post-treatment areas. An interval of 3 months or greater following completion of radiation is recommended for PET scanning. A controversial application for PET/CT remains the intensity modulated radiation therapy planning. In approximately 20% of cases it can be used in identifying sites of possible second primary carcinomas or distant metastases. PET is not recommended in the detection of occult nodal metastases. Recently discovered radioactive tracers can be useful in identifying, on a PET/CT scan, sites of hypoxia, protein metabolism, DNA replication, and other processes related to malignancy.

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DIAGNOSTIC MINIM INVAZIV AL CANCERULUI DE LA NIVELUL CAPULUI SI GATULUI UTILIZAND 18-FDG-PET SI PET/CT

REZUMAT

Scop: Studiul nostru isi propune stabilirea valorii prognostice a 18-FDG-PET prin standardizarea valorilor de absorbtie.

Materiale si Metode: 18-FDG-PET este cunoscut a fii util in identificarea situatiilor necunoscute recurente de carcinom scuamos celular de la nivelul capului si gatului (HNSCC) post-tratament, carcinomului primar secundar, metastazelor la distanta sau chiar carcinom scuamos primar al capului si gatului.

Rezultate si concluzii: PET prezinta valoare predictiva crescuta negativa pentru detectarea HNSCC recurent. Exista unele limitari ale acestui instrument diagnostic in ceea ce priveste identificarea nodulilor metastatici oculti. De asemenea interpretari fals pozitive pot fi generate datorita efectului radiatiilor, a activitatii musculare, a infectiilor si a inflamatiilor. Utilizand noi indicatori radioactivi, se poate facilita identificarea prin PET a zonelor hipoxice, a replicariilor AND sau a metabolismului proteic.

Cuvinte cheie: carcinoma scuamos, diagnostic minim-invaziv, PET/CT.

THE INCIDENCE OF OBSTRUCTIVE NASAL PATHOLOGY AMONG THE PATIENTS WITH SLEEP APNEA SYNDROME

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ABSTRACT

Obstructive sleep apnea is a sleep related disorder common among middle-aged and elderly people, most of them being unaware of their condition. Symptoms of obstructive sleep apnea include loud snoring, daytime sleepiness and personality changes. Treatments include lifestyle changes such as losing weight (excess fat around the neck increases airway collapse) and smoking cessation.

Materials and methods: A number of 159 patients from the Institute of Phono-audiology and Functional Surgery “Prof. Dr. D. Hociota” Bucharest were enrolled in this study between January 1st 2010 and December 31st 2013. ENT diagnosis was established performing anterior rhinoscopy, video-endoscopy, allergic tests and CT scans.

Results: The majority of cases associated nasal deviated septum and rhinitis. Most of the patients were male smokers and the most common associated pathology was arterial hypertension.

Key words: sleep apnea, deviated septum, sinusitis, polypsis

INTRODUCTION

Obstructive sleep apnea is a sleep-related breathing disorder that is particularly common among middle-aged and elderly people. Most of them are unaware that they have the condition and it is usually characterized by the occurrence of numerous brief (ten seconds or so) breathing interruptions during sleep. These episodes occur when relaxation of the upper airway muscles decreases airflow, which lowers the level of oxygen in the blood, leading to hypoxia and reoxygenation and from these to significant endocrine and metabolic disturbance which are direct responsible for the appearance of hypertension, metabolic syndrome and cardiovascular risk. Symptoms of obstructive sleep apnea include loud snoring, daytime sleepiness and personality changes (4,5,8). Treatments include lifestyle changes such as losing weight (excess fat around the neck increases airway collapse) and smoking cessation (6). Mild to moderate obstructive sleep apnea can also be treated using a mandibular advancement device (MAD), a “splint” that fits inside the mouth and pushes the jaw and tongue forward to increase the space at the back of the throat and reduce airway narrowing. For severe sleep apnea, doctors recommend continuous positive airway pressure (CPAP), in which a machine blows pressurized air into the airway through a facemask to keep it open.

Allergic rhinitis is a major chronic respiratory disease due to its prevalence, its impact on quality of life, performance and productivity at work, its cost to society and its relationship to asthma. It consists of an IgE-mediated inflammation of the nasal mucosa alone or associated with asthma (1).

Chronic rhinosinusitis (CRS) is one of the most common chronic medical conditions, with a significant impact on patient quality of life. CRS is broadly classified into two groups: CRS with nasal polyposis and CRS without NP. Chronic rhinosinusitis

(CRS) is a clinical syndrome characterized by mucosal inflammation of the nose and paranasal sinuses. It has been suggested that CRS occurs as the result of an inappropriate or exaggerated response to external environmental triggers (2,3).

It is known that patients with chronic sinusitis have reduced sleep quality, although the underlying etiology or pathophysiology has received little attention. There are probably a multitude of factors involved in the mechanism of sleep impairment in CRS among them being nasal obstruction, efferent and/or afferent neural signaling, or brain-immune signaling via immune mediators such as interleukin-1 (IL-1) and tumor necrosis factor (TNF). Accumulating evidence is elucidating the sophisticated and intertwined communication between the central nervous system (CNS) and the immune system (1,9).

The obstructive ENT pathology of the upper respiratory tract has an important correlation with the obstructive sleep apnea syndrome and the further study wants to point out this fact.

MATERIALS AND METHODS

A number of 159 patients from the Institute of Phono-audiology and Functional Surgery “Prof. Dr. D. Hociota” Bucharest were enrolled in this study between January 1st 2010 and December 31st 2013. In order to establish the ENT diagnosis we performed anterior rhinoscopy, video-endoscopy, allergic tests and CT scans. The patients were divided in groups according to gender, hygienic and dietary factors and associated pathology. The results were analyzed using Microsoft office excel 2010.

RESULTS

Of the 159 patients in the study a total of 81% were male and

19% were female. This is consistent with the literature data and shows a predominance of males.

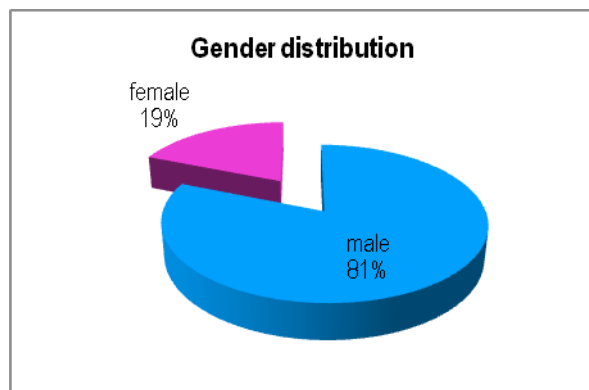


Fig.1. Gender distribution

Regarding the age distribution the majority of cases (84) were between 36-45 years old. Our data is consistent with international literature and is highlighting an increase of the pathology in the middle aged of population.

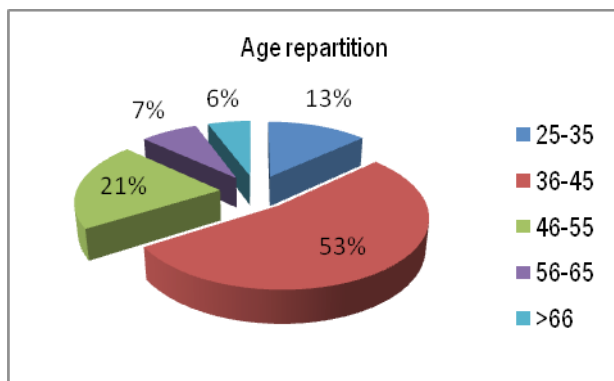


Fig.2. Age repartition

Hygienic-dietary factors are very important in the appearance of the nasal obstructive syndrome. In our group a number of 115 patients were smokers and 56 worked in a polluted environment.

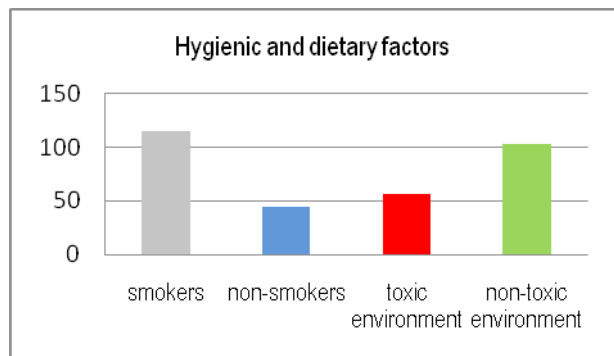


Fig.3. Hygienic and dietary factors

ENT clinical examination is very important for the systematic investigation of all areas of mucosa and submucosa of the supe-

rior aero-digestive tract and also for the clinical diagnosis of the nasal obstructive syndrome. This way we can have a complete diagnosis that includes nasal septum deviations, chronic rhinitis, chronic sinusitis, polyposis or adenoiditis.

ENT examination was completed in all patients with rigid or flexible endoscopy of the nasal region, the nasopharynx, oropharynx, larynx and tongue base and multiple allergic tests.

Besides the ENT clinical and endoscopic examination we performed a complete clinical examination to evaluate the general condition and function of various organs and systems including the liver, spleen, digestive and respiratory systems.

The main ENT pathology seen with the group of patients studied was:

- Nasal deviated septum and chronic rhinitis (in 73 patients)
- Nasal deviated septum, chronic rhinitis and chronic sinusitis - in 35 patients
- Nasal deviated septum, polyposis and chronic sinusitis - in 25 patients
- Allergic rhinitis - in 13 patients
- Adenoiditis - in 3 patients.

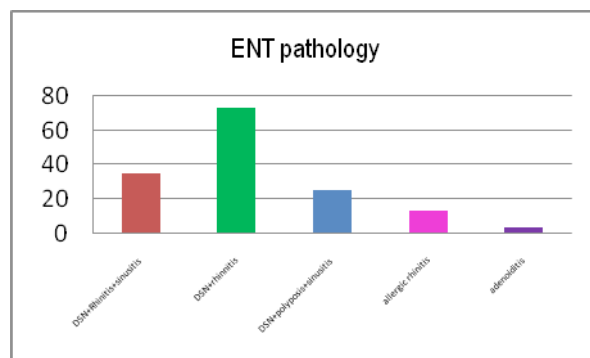


Fig.4. ENT pathology

It is known that low levels of oxygen in the blood leading to hypoxia and re-oxygenation and from these to significant endocrine and metabolic disturbance are direct responsible for the appearance of hypertension, metabolic syndrome and cardiovascular risk. In our group of patients 41 were known with different types of allergies, 23 were known with arterial hypertension and 8 with type 2 diabetes.

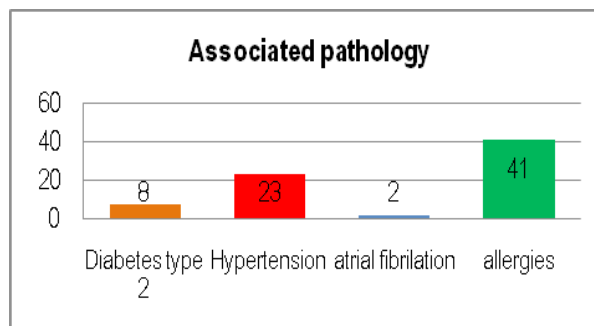


Fig.5. Associated pathology

DISCUSSION

Sleep apnea is a chapter of pathology of major importance due to its implications of the quality of life, this patients being known for falling asleep during day activities and lack of concentration due to cerebral hypoxia. Several factors must be solved so that the patients would have a better quality of life. The main factor is losing weight and smoking cessation. In some patients removing the upper respiratory tract obstacle can be of help. The ENT associated pathology can be treated medical or surgical. Among medical treatments are nasal drops, anti-inflammatory and anti-allergic drugs and sometimes antibiotics.

When there are no contraindications for surgery we can perform different procedures for removing the obstacle (septoplasty, turbinectomy, FESS, adenoidectomy) (7,8,10). Therapeutic strategies must be based on a accurate diagnosis pointed out by the ENT, allergist and the pulmonology specialists.

Once the diagnosis of sleep apnea has been properly made the management of the disease requires interdisciplinary collaboration to initiate the appropriate treatment. A nutritionist is very important to ensure an adequate nutritional status and help the patient lose weight and maintain it. We may also need a psychologist and the family support for the smoking cessation.

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INCIDENTA PATOLOGIEI OBSTRUCTIVE NAZALE IN RANDUL POPULATIEI CU SINDROM DE APNEE IN SOMN

REZUMAT

Sindromul de apnee in somn reprezinta o tulburare comuna la pacientii de varsta medie si varstnici, majoritatea neconstientizand patologia de care sufera. Simptomatologia include sfarait, oboseala in timpul zilei si schimbari de personalitate. Tratamentul include schimbari in stilul de viata al pacientului cum ar fi slabitul (excesul de grasime din jurul gatului ingusteaza caile aeriene) si renuntatul la fumat. Material si metoda: Un numar de 159 de pacienti din Institutul de fono-audiologie si chirurgie functionala "Prof. Dr. D. Hociota" Bucuresti a fost studiat intre 1 ianuarie 2010 si 31 decembrie 2013. Diagnosticul ORL a fost stabilit in urma efectuarii de rinoscopii anterioare, video-fibroscopii, teste alergice, examen CT. Rezultate: Majoritatea cazurilor asociau deviatie de sept nazal si rinita. Cei mai multi pacienti au fost de sex masculin, fumatori, si cea mai comuna patologie asociata a fost hipertensiunea arteriala.

Cuvinte cheie: sindrom de apnee in somn, deviatie sept nazal, sinuzita, polipoza

EFFECTIVENESS ASSESSMENT CRITERIA FOR CT DIAGNOSIS IN MEDIASTINAL LYMPHATIC EXTENSION OF THE LUNG CANCER

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ABSTRACT

Lung cancer, through the characteristics of lymphatic dissemination by different areas, and in strict accordance with the cell typology of and evolutionary stage, is one of the most common causes of mediastinal lymph nodes.

The article aims to outline the radio imaging exploration in the diagnosis of mediastinal lymphatic extension of broncho pulmonary cancer, highlighting the clinic and morphological and anatomical interrelationships that emphasizes the importance of detection in staging and post therapeutic evaluation of the neoplastic broncho pulmonary pathology of the drained territory of the mediastinal lymph nodes

Broncho-pulmonary neoplasm is the leading cause of cancer death throughout the world (17% of male cancers and 12% of female cancer deaths). As a result, the medical management has been rigorously quantified in terms of clinical-histological characteristics and the invasive tumour stage, the degree of mediastinal lymph node extension and the presence of distant metastases determined with the TNM staging system that is recognised globally

The x-ray examination reveals only pathological mediastinal lymph nodes that cause changes of mediastinal margins and the pleural reflection lines.

Also if the lymph nodes are hidden behind other tumour masses existing in the mediastinum, they cannot be discovered at the x-ray examination, which offers little information about the mediastinal structure: vessels, pericardium, pleura, and thoracic wall.

Due to the possibility to reveal all groups of pathological mediastinal lymph nodes, computed tomography is the first choice examination for the diagnosis of mediastinaladenopathies.

Besides the traditional, cytological and histopathological methods that enable the identification of pulmonary neuroendocrine carcinoma, its malignancy degree and stage, the immunohistochemical methods are very valuable for the assessment of the evolution capacity of pulmonary neoplasia. The lung can be subjected to a large variety of complementary investigations.

Keywords: mediastinal lymphadenopathy, broncho-pulmonary neoplasm, pulmonary neuroendocrine tumours, radio-imaging examinations

INTRODUCTION

The article aims to outline the radio imaging exploration in the diagnosis of mediastinal lymphatic extension of broncho pulmonary cancer, highlighting the clinic and morphological and anatomical interrelationships that emphasizes the importance of detection in staging and post therapeutic evaluation of the neoplastic broncho pulmonary pathology of the drained territory of the mediastinal lymph nodes.

MATERIALS AND METHODS

There were subjected to statistical analysis 134 retrospective cases of lung cancer with mediastinal lymph extension examined by chest CT in CT Laboratory of Military Hospital Timisoara during January 2004-December 2006. They were investigated clinic and biologic, bronchoscopic and histopathologic in order to identify the diagnosis, status, appropriate therapeutic method, and in some cases post therapeutical evaluation.

Each case was analyzed from the clinical biological data,

epidemiological and histopathologic bronchoscopic. They were combined with the results of radiographic examination and CT. It was also a review of radiographs in the images assessment, in order to detect morphological alterations of mediastinal lymph nodes.

Radiographic examination

Radiographic examination was the first choice in all studied cases, being performed by SIEMENS SIREGRAPH CF, in at least two incidents: anteriorly and lesion profile, supplemented whenever it was necessary to oblique incidence, tough-ray radiographies or even mediastinal plane CT scans.

Diagnosis criteria

Normal mediastinal lymph nodes are not outstanding in classical radiology because they are too small or masked by the mediastinum. With their involvement in various morbid processes by increasing the sizes or changing the structure and consistency, mediastinal lymph nodes are visible to normal radiology, radiological aspects determining characteristic for each lymph

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nodes affected group (1,2).

CT examination

CT examinations were performed using a PICKER IQ PRE-MIER apparatus; the sequential thoracic examining images were obtained in multiple windows density, in order to detect mediastinal lymph nodes morphological alterations.

Mediastinal lymph nodes location using CT examination

"American Thoracic Society" Classification regarding the mediastinal lymph nodes quantifies best radio anatomical the mediastinal lymph node group's topography. This is, therefore, by far the most widely used in practical imaging (3). According to this classification groups nodes are divided into two categories: parietal and visceral (4).

I. Parietal lymphatic groups

Internal mammary group

It is located on the side of the sternum, posterior to the anterior thoracic wall, along the internal mammary vessels. Normally they are not revealed. Pathologically, they are affected by metastases from breast carcinoma or much more rarely in a mediastinal lymphoma.

Diaphragmatic group

Classic, are described three groups:

- pre-pericardic, located between xiphoid appendage and sternum;
- para-cardiac, on the lateral side of the heart, along the phrenic nerves;
- retro-crural, behind diaphragmatic insertions.

They drain lymph from the pericardium, pleura, thoracic-abdominal wall and diaphragm. They are related to peritoneal cavity and anterior segment of the liver. Efferent path links them with the internal mammary and anterior mediastinal lymph nodes. Normally they are not revealed. Pathologically, they are affected in mediastinal lymphoma, metastases from breast cancer and cancer of the mediastinal pleura, and in ovarian cancer, after metastatic involvement of peritoneum.

Posterior group

Is located paravertebral, normally not highlighted. They are interested in lymphoma and inflammatory and neoplastic pathology of posterior mediastinum.

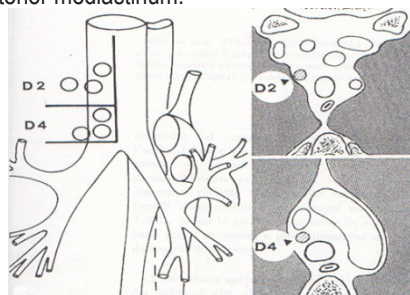


Fig. 1. CT sites of right paratracheal lymph nodes group. Right N paratracheal group (D2, D4)

II. Visceral lymphatic groups

They comprised of two groups of nodes, located to the right side of the midline around trachea, from the entrance in the thorax to the superior border of the azygos vein arch. The cleavage plane between the superior group (D2) and lower group (D4) passes through the point where the brachiocephalic trunk crosses the anterior surface of trachea. Normal is highlighted 1-3 a number of superior and 2-4 inferior ganglia. Pathologically, are the most affected, in the inflammatory and tumor pathology.

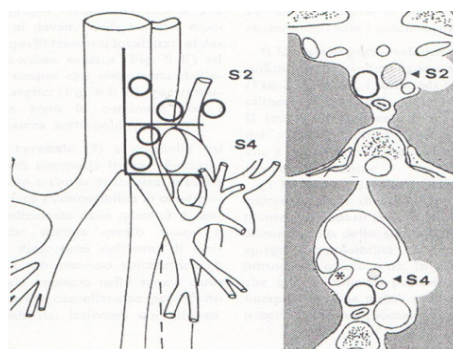


Fig. 2. CT sites of left paratracheal lymph nodes group. Left paratracheal group (S2, S4)

They are disposed left paratracheal, medial of the epy aortic vessels, forming two groups, the delimitation plane between the superior group (S2) and the inferior group (S4) is consisting of the superior border of the arc aortic. Ganglia from the inferior left para tracheal group are different from the ones from the aortic pulmonary group by location medially from the arterial ligament. Normally, they are highlighted, but the number and volume are smaller than the right group. Pathologically, are also the most common group affected nodes.

Aortic pulmonary group (5)

This is located outside the arterial ligament, occupying the sucutaneous space between the aortic arch and the left pulmonary artery, being located to outline their external border. Normal numbers is 2-5 and no more than 10, with a diameter of 4-8 mm. Pathologically they are affected in lymphoma and metastasis from lung cancer.

Anterior mediastinal group (6)

They are disposed retro-sternal, before the aorta, being classically described in three groups:

- the right, in front of the superior vena cava;
- transversal, in front of the left brachio-cephalic;
- the left, outside of the epi-aortic vessels.

Usually they are highlighted as 1-6 under nodes of 8 mm diameter. Pathologically are affected in lymphoma, sarcoidosis and bronchial cancer metastasis.

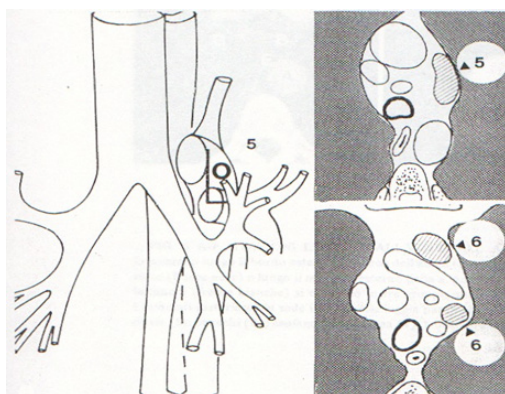


Fig.3. CT sites of the ganglionic groups from the aortic pulmonary window and anterior mediastinal group.

Subcarinal group (7)

They are located between the bifurcation of the trachea and the left atrium. Usually are 1-3 nodes below 15 mm diameter. Pathologically are affected in lung disease, lymphoma and metastasis of bronchial cancer. Paraesophageal group (8) is composed of ganglia arranged around the oesophagus. Usually they are not highlighted; it is difficult to distinguish from the wall of the oesophagus. Pathologically are affected in metastasis of oesophageal cancer and lung cancer located in the lower lobes and dome

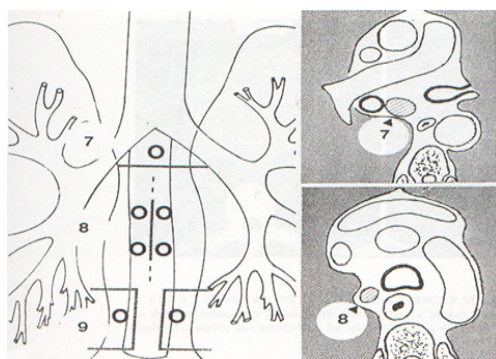


Fig.4. CT sites of subcarinal ganglionic groups and paraesophageal

Pulmonary ligament group (9)

They comprise ganglia contained between the two pleural layers. Usually are not highlighted. Pathologically are affected metastases from lung cancer and lymphoma.

Right tracheobronchial group (D10)

They are medially disposed by superior lobar bronchus origin, above right pulmonary artery. Normal is highlighted in number and small volume. Pathologically, are constantly affected during episodes of pulmonary infections.

Left traheo-bronchial group (S10)

Usually is easy to be identified. Pathologically, lymph nodes give compression to carina and superior lobar bronchus in front of main bronchus.

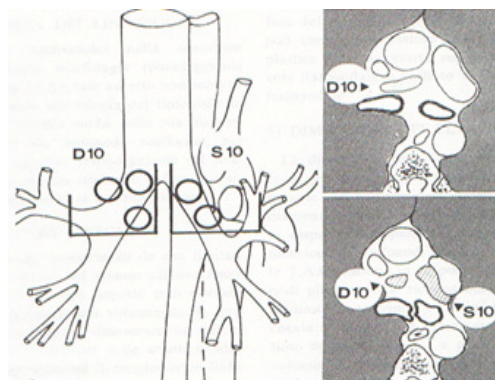


Fig.5. CT sites of bilateral tracheal bronchial groups

Intrapulmonary group (11)

They are all the ganglia disposed around the bronchial branches, inferiorly to the main bronchi. They are located at hilum.

All these mediastinal lymph groups get a code number (5):

- 1- supraclavicular - scalmi
- 2D, 2S - para trachealis superior, right and left
- 3 - pre and retro -tracheal
- 4D, 4S - paratrahealis inferior, right and left.
- 5 - aortic-pulmonary
- 6 - anterior mediastinal
- 7 - subcarinal
- 8 - para-oesophageal
- 9 - pulmonary ligament
- 10D, 10S - broncho tracheal, right and left
- 11D, 11S - intrapulmonary, right and left
- 12 - lobar
- 13 - segmentary
- 14 - diaphragmatic

CT positive diagnosis criteria

Mediastinal lymphadenopathy is a structure CT detectable, located in the mediastinum that has the following semiological characteristics: form, shape, size, density +/- calcification, iodophilia, relationship with the interstitium (6).

I. Shape

In an axial CT section, mediastinal lymph nodes may appear as round when the section plane is perpendicular to the longest axis of the lymph or may be oval when the section plane is parallel to it.

II. Outline

A net, regular outline of a lymph node shows an integrated capsule, an adenopathy having this nature can have a compressive effect on adjacent structures. A diffuse irregular outline signifies overcoming the capsule by a malignant process, revealing the existence of infiltration of adjacent structures through: a tumoural process, an inflammatory process, mediastinal reaction to a pathologic ganglion, being impossible the differentiation by the

computer tomography (7).

III. Sizes

Sizes are the semiotic major, determinant element of computer tomographic diagnosis of metastatic mediastinal lymph-nodes affected. It has been taken into account the transverse diameter of the scanned lymph node, limit which separates malignant from benign, stretching the limit of visibility more than 2 cm, according to the literature. Thus, about 25-30% of nodes 1-2 cm in size is malignant, while ganglia greater than 2 cm turn out to be malignant in 75% of cases (8). Generally, the use of a smaller diameter as the limit of malignancy means the greater the sensitivity of the diagnosis and less computer tomography of malignant lymph nodes specificity (9).

According to dimensional criteria, mediastinal lymph node groups are divided into two categories (9):

Ganglia which normally highlights to computer tomography:

- Internal mammary
- Diaphragmatic
- Posterior
- Para-oesophageal
- of pulmonary ligament;

Any visible node is likely to be pathologic.

Groups nodes highlighted in normal CT scan:

- para, pre and retro-tracheal
- subcarinal
- Aortic pulmonary
- Anterior mediastinal;

Any node with transverse diameter greater than 10 mm is considered pathological unless:

- more than 7 mm for the left superior group and right para tracheal group;
- more than 10 - 11 mm for subcarinal and right tracheo bronchial groups.

That is true, with the amendment that a normal sized ganglion may be the site of a malignancy, confirming the decisive role of cytology and histopathology for definite affirmation of malignancy (10).

IV. Density

Normal or pathological lymph nodes are subdivided according to their densitometric structure into several categories (9):

1. ganglia with homogeneous density between 30 and 60 UH.
2. ganglia with central hypo density may occur under the following conditions:
 - normally, due to adipose central involution, where the density equals mediastinal loose tissue;
 - in tuberculosis, due to caseous necrosis, when the density is slightly superior to fluid;
 - in lymphoma, after radio and chemo therapy due to necrosis.

V. The presence or absence of calcification

They can occur at the lympho-ganglionic level in the following conditions (11):

- after a non specific infection or radiotherapy;
- in tuberculosis when fully calcified ganglion may produce artefacts that appears to scan;
- marginal calcifications occur in silicosis;
- in sarcoidosis, the lymph node appears calcified in 'eggshell'.

CT scanning detects mainly the existence of small calcifications, proving most often a benign etiologic, but they do not exclude malignancy when parenchyma component prevails (9).

VI. Iodophilia

Normally the lymph node density increases slightly after administration of contrast agent, attesting a slightly iodophilia.

Depending on contrast dose, lymph nodes may present the following aspects:

- central hypo density with marginal hyper dense ring, found it in normal cases, in tuberculosis, in post radio and chemo-therapy lymphoma, as well in metastases of testicular cancer or bronchial adenocarcinoma;
- important hyper density, after contrast agent administration, certifying the existence of an inflammatory or tumoural hyper vascularisation, being found in: Castleman's disease; angioimmunoblastic lymphadenopathy; metastases from: melanoma, hipernefoma, thyroid cancer, sarcoma, carcinoid tumour.

VII. Relationship with interstitium

New semiotic element, based on radio-anatomic appearance of hylum lymph nodes, in relation to the bronchi and vessels at interstitial site, their exploration is detected by spiral CT examination. Normal hylum lymph nodes located in the interstitial space between the bronchi and pulmonary vessels, often difficult to differentiate from it, causes some straight or concave borders of the interstitial space to the lung parenchyma. The interstitium containing metastatic ganglia has convex borders toward the inflammatory reaction caused by carcinomatous lymphangitis (12).

CT diagnosis of extension

Mediastinal lymphatic extension of the broncho alveolar cancer benefits of CT scanning both the semiotic elements that may indicate the location of primary tumour and highlighting the lymph nodes whose topography and features may be criteria for resection or not, according to TNM staging (13):

Ganglionar metastatic sites of the lung cancer:

- N1 – lymph nodes in 10D and 10S homolateral
- N2 – lymph nodes in 7
- N3 – lymph nodes in 10D and 10S controlateral, revealing an inoperable lung cancer in stage IIIB (14).

CT exploring has been required scanning with the patient in blocked deep inspiration, using a mediastinal window width of 300-500 UH and centre between 0-60 UH. Mediastinal

lymphadenopathy when is highlighted, lead to detailed study of its contiguous thin sections of 3 mm, rigorously semiological analyzing the specific CT elements: form, shape, size, density, presence or absence of calcifications and iodophilia.

A total of 7 patients with lung cancer were hilar region spiral CT investigated, using a SIEMENS SOMATOM PLUS 4 with an apnea after deep inspiration technique, with sections of 3 mm thickness and progression 3 mm / s of examination table, resulting in a pitch of 1: 1. Mediastinal lymphadenopathies diagnosis benefited by acquiring the spiral data to identify their relationship with the interstitium, new semiotic element, based on radio-anatomic appearance of hylum lymph nodes, related to bronchi and vessels at interstitial level. They have been detected the interstitium marginal characteristics toward lung parenchyma, considering as normal hylum lymph nodes which determine straight or concave borders and pathologic which due to an inflammatory reaction caused by carcinomatous lymphangitis have determined an interstitium with convex edges (12).

Table I. Mediastinal lympho-ganglionic staging of bronchopulmonary cancer, according to N criterion from TNM classification

N Stag- ing	Lymph ganglion extension
N0	no lymph nodes
N1	peri bronchial and/or hylum metastases in the same side ganglia or direct intrapulmonary metastasis through the primary tumour extension
N2	mediastinal and/or subcarinal in the same side metastases
N3	mediastinal and/or subcarinal contra lateral metastases

RESULTS AND DISCUSSION

Diagnosis, staging and posttherapeutic imaging assessment of mediastinal lymphatic extension of lung cancer has established lymph nodes presence in 134 cases. In 88 of the cases of lung cancer have been examined for diagnosis and staging, have been isolated lymph nodes as N1 stage quantization established in 31 cases, 34 cases in N2 staging and N3 in 23 cases. Postoperative imaging evaluation, revealed mediastinal lymph nodes in 17 cases of resected bronchopulmonary neoplasms, which was an important argument for associating radio and chemotherapy.

Assessment of studied cases according to the ganglia sites

Statistical analysis of the sites of the 134 cases of lung cancer with detected mediastinal lymph nodes shows in each studied case, the predominant involvement of drained lymphoganglionar group, specific to area the morbid entity. The examinations for evaluation post radio and chemotherapy, detection of mediastinal lymph nodes in 29 cases required continuation or restart, respectively. The large number of subcarinal lymph nodes occurring in 17% of cases studied, are due to damage to the lymphatic site both in right lung cancer and in the left and also for the 39% of cases in stage N2.

N staging results of the 88 cases of lung cancer

Assessment using postoperative chest CT scan, revealed mediastinal lymph nodes in 17 (13%) cases of broncho-pulmonary resected neoplasms, which was an important argument for the association of radio and chemotherapy. The examinations for post radio- and chemotherapy assessment, detection of mediastinal lymph nodes in 29 (22%) cases required the continuation or their restarting, respectively.

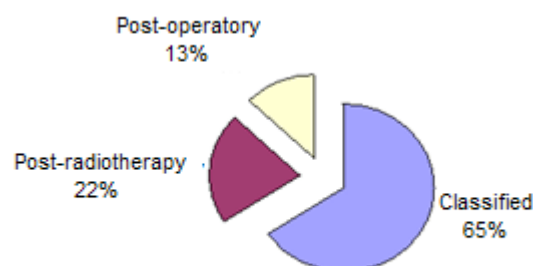


Fig.6. N staging results of the 88 cases of lung cancer

Relationship with interstitium

Spiral CT examination performed at the hilum regions belonging to a number of 7 patients with lung cancer imaging investigated, for staging and accurate assessment of further therapeutic conduct, managed to identify lymph nodes CT examination previously unknown.

New semiotic element, based on radio-anatomic appearance of hilum lymph nodes is in relation to the bronchi and vessels at interstitial site, detected their by spiral CT examination.

Normal hylum lymph nodes, located in the interstitial space between the bronchi and pulmonary vessels, often difficult to differentiate from it, causes some straight or concave sides of the interstitial space toward the lung parenchyma.

This diagnostic exploration was based on identifying a specific relationship of hilum interstitial lymph nodes with interstitium in case of their neoplastic infiltration; it appeared outlined with convex edges toward lung parenchyma due to the inflammatory reaction caused by carcinomatous lymphangitis.

Thus, hilum lymph nodes are belonging to right 10 and group left10 group, respectively, led to the formation of convex edges toward the parenchyma, highlighting this type of relationship with the interstitial space being a full specified diagnostic criterion, in the cases spiral CT explored.

CONCLUSIONS

The skills of diagnosis, staging, quantification and therapeutic tracking, thoracic CT scan is the examination strictly necessary for lung cancer mediastinal lymph nodes extension assessment. Highlighting the interstitial relationship is a diagnosis criterion of maximum specificity for malignant hilum lymph nodes highlighted using the spiral CT, which has become a standard method of investigation, with comparative radio imaging interferences.

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EVALUAREA EFICIENȚEI CRITERIILOR DE DIAGNOSTIC COMPUTER TOMOGRAFIC ÎN DIAGNOSTICAREA EXTENSIEI LIMFOGANGLIONARE MEDIASTINALE A CANCERULUI BRONHOPULMONAR

REZUMAT

Cancerul bronho-pulmonar, prin caracteristicile specifice de diseminare pe cale limfatică în funcție de teritorializare și în strictă concordanță cu tipologia celulară și stadiul evolutiv, este una dintre cele mai frecvente cauze de adenopatii mediastinale. Lucrarea își propune să evidențieze valoarea explorărilor radio-imagistice în diagnosticarea extensiei limfoganglionare mediastinale a cancerului bronho-pulmonar, cu relevarea unor interrelații clinico-morfologice și anatomice ce subliniază importanța detectării acestora, în stadializarea și evaluarea postterapeutică a patologiei neoplazice bronho-pulmonare din teritoriul drenat de limfoganglionii mediastinali.

Materiale și metode: Au fost supuse analizei statistice retrospective 134 cazuri de cancer bronho-pulmonar cu extensie limfatică mediastinală examinate prin computer tomografie toracică în Laboratorul CT al Spitalului Militar Timișoara, investigate clinico-biologic, bronhoscopic și histopatologic în vederea stabilirii diagnosticului, stadiului, conduitei terapeutice adecvate și în unele cazuri pentru evaluare postterapeutică. Fiecare caz a fost analizat pornind de la datele clinico-biologice, epidemiologice, bronhoscopice și histopatologice din fișa de solicitare, care au fost coroborate cu rezultatele examinării radiografice și CT, procedându-se la o reexaminare a radiogramelor din dosarele de evaluare a pacienților și a imaginilor obținute prin scanare, în mai multe ferestre de densitate, pentru a decela alterările morfologice ale ganglionilor limfatici mediastinali. **Rezultate:** Prin abilitățile de diagnostic, stadializare, cuantificare și urmărire terapeutică, scanarea CT toracică este examinarea strict necesară pentru evaluarea extensiei limfatice mediastinale a cancerului bronho-pulmonar. **Concluzii:** Evidențierea relației cu interstițiul constituie un criteriu de diagnostic de maximă specificitate pentru evidențierea adenopatiilor hilare neoplazice prin computer tomografie spirală, aceasta devenind o metodă standard de investigație, cu interpolări comparative în radioimagică.

Cuvinte cheie: limfadenopatie mediastinală, neoplasm bronhopulmonar, tumori pulmonare neuroendocrine, explorări radio-imagistice.