Morphological Nasal Changes Associated with Rapid Maxillary Expansion

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ABSTRACT

The aim of this study was to evaluate the morphological nasal changes associated with rapid maxillary expansion (RME) which is used in the treatment of skeletal maxillary narrowness. The study was performed with 20 patients 12 girls and 8 boys between the ages of 10 and 15 (13.4±0.99) and compared with a control group consisting of 16 subjects 10 girls and 6 boys between the ages of 10 and 15 (13.2±1.18). Lateral and anteroposterior radiographs were taken before RME (T1), after RME (T2), and after retention (T3). Greater alar cartilage width, nasal cavity width, vertical and sagittal movement of the tip of nose, SNA° and nasolabial angle measurements were evaluated to understand the morphological and positional changes of the nose associated with RME. The results showed that the greater alar cartilage width returned to its original position, the nasal cavity width increased, and the tip of the nose moved downward and minimally forward; as well, SNA° returned to its original value and a small increase occurred in the nasolabial angle due to RME. Soft tissue changes may be considered clinically non-significant compared with the controls. RME did not affect the patients' frontal nasal appearance and mid-face soft tissue profile.

Key words: Rapid maxillary expansion, nasal morphology, soft tissue

Hızlı Üste Çene Genişletilmesinde Morfolojik Burun Değişiklikleri

ÖZET

Bu çalışmanın amacı; maksiler kemik darlıklarının tedavisinde kullanılan hızlı üst çene genişletmesi (RME) işlemi sonucu oluşan morfolojik burun değişikliklerinin değerlendirilmesidir. Çalışmada 12'si bayan ve 8'i erkek olmak üzere yaşları 10 ile 15 (13.4±0.99) arasında değişen 20 hastanın bulguları, 10'u bayan ve 6'sı erkek olmak üzere yaşları 10 ile 15 (13.25±1.18) arasında değişen 16 kişilik kontrol grubu ile karşılaştırılmıştır. Lateral ve anteroposterior grafiler RME öncesi (T1), RME sonrası (T2) ve retansiyon sonrası (T3) çekilmiştir. RME ile ilişkili olarak burunda oluşan morfolojik ve pozisyonel değişikliklerin anlaşılabilmesi için major alar kartilaj genişliği, nazal boşluk genişliği, burun ucunun vertikal ve sagital hareketleri, SNA° ve nazolabial açı ölçümleri değerlendirilmiştir. Sonuçlar göstermiştir ki; major alar kartilaj orijinal genişliğine dönmekte, nazal boşluk genişliği artmakta ve burun ucu aşağıya ve hafifçe öne doğru hareket etmektedir. Ayrıca SNA° orijinal değerine dönerken, nazolabial açıda RME ile ilişkili olarak küçük bir artış olmaktadır. Yumuşak doku değişiklikleri kontrol grubu ile kıyaslandığında anlamsız olarak düşünülebilir. RME hastaların frontal nazal görünüşünü ve orta yüz yumuşak doku profilini etkilememektedir.

Anahtar kelimeler: Hızlı üst çene genişletme, nazal morfoloji, yumuşak doku

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INTRODUCTION

Rapid maxillary expansion (RME) is one of the most impressive orthopedic procedures that corrects maxillary arch constrictions, increases arch perimeter to reduce crowding, and corrects disharmonies in the transversal plane between the maxillary and mandibular arches (1-6). The basis for the rapid expansion procedure is to produce immediate midpalatal suture separation by disruption of the sutural connective tissue with rapid palatal expanders, which creates large forces at the sutural site in a short period (6, 7). Although RME is performed for orthodontic indications, the main outcomes of this procedure are orthopedic effects on the orofacial system and soft tissue. Karaman et al. (8) analyzed soft tissue changes after RME using lateral cephalograms. They concluded that the tip of the nose followed the hard tissue and moved forward and downward. Possible changes in soft tissue morphology of the nose with RME were first investigated by Berger et al. (9, 10). They photographically monitored 20 subjects treated with RME and 24 subjects with surgically assisted RME (SARME) to correct a unilateral or bilateral cross-bite. Their study revealed that soft tissue nasal width increased by 2 mm during treatment, and that this increase remained stable at 1 year post treatment. Although, previous studies demonstrated a significant increase in nasal cavity width (2, 4-6) and decrease in nasal resistance after RME (11-14), a wider nose may be undesirable for patients. Proffit (15) notes that RME should not be used in preschool children because of the risk of producing undesirable changes in the nose at that age. Johnson et al. (16) focused on the transversal morphological changes and used a digital caliper to measure the transversal dimensional changes of the nose after RME and after retention. They found less than 1.5 mm changes at the alar base and greater alar cartilage (GAC) widths. They concluded that this increase is clinically non-significant when compared with the controls. Finally, Adams et al. (17) evaluated soft tissue changes using Cone Beam Computerized Tomography (CBCT) images immediately after RME. Their results revealed that similar changes to the soft tissues occur after RME.

The aim of this study is to evaluate the morphological changes in the shape of the nose after RME and retention in transversal, sagittal and vertical planes.

MATERIALS AND METHODS

Rapid Maxillary Expansion and Control Sample

The RME sample consisted of 20 patients -12 girls and 8 boys- between the ages of 10 and 15 (13.4 \pm 0.99 mean), presenting posterior cross-bite of skeletal origin. The acrylic bonded RME appliance, which covers the posterior teeth, was used as an expansion appliance in all patients. The RME appliance was cemented in all subjects with the use of glass ionomer cement (Ketac-Cem, Espe Dental AG, Seefeld, Germany). The appliance was activated one-quarter turn once a day during the expansion period until the desired suture opening was achieved. The average amount of screw expansion was 8 mm. After removal, the appliance used in active treatment was cleaned and the screw was fixed with a 0.014-inch ligature wire and reused as a removable retention appliance for 6 months. The average duration of the RME procedure was 7.1 months.

The control group consist of 16 patients -10 girls and 6 boys- between the ages of 10 and 15 (13.25 ± 1.18) , with maxillary narrowness, who were waiting for treatment. Table 1 shows the distribution of age and gender along with average expansion periods, as well as average retention periods of subjects.

All patients were treated at Faculty of Dentistry, Department of Orthodontics. Exclusion criteria were: having a history of nasal trauma, surgery, or rhinoplasty, craniofacial anomaly (including but not limited to cleft lip and/or cleft palate), and RME treatment previously. The purpose of the study and the procedure were explained to the participants and their informed consents for the experiment were obtained. This study was approved by the local research ethics committee.

Nasal Width Measurements

Lateral cephalometric and posteroanterior cephalometric radiographs were taken from the study patients at three separate time points: T1, prior to placement of the RME appliance; T2, after completion of active expansion; and T3, after retention. The same radiographs were taken at two time points for the control subjects: T1, the first time point: the second (T3) was taken 7 months after T1. The intermediate radiographs (T2) were not taken for the control sample because of ethical reasons. Small lead markers were placed at the widest points of GAC with a resin-based adhesive (Figure 1). The GAC width was obtained by measuring the distance between

	Number of subjects (n)		Mean	age	Mean expansion	Mean retention	
	RME	Control	RME	Control	duration / m	duration / m	
Girls	12	10	13.40 ± 0.99	13.25 ± 1.18	1.1	6	
Boys	8	6					
Total	20	16					

Table 1. Distribution of sex, age, expansion, and retention time for the groups

hemoglobin A1c (HbA1c) (%), high density lipoprotein cholesterol (HDL-C; mg/dL)-cholesterol, low density lipoprotein-cholesterol (LDL-C; mg/dL), aspartate aminotransferase (AST; mg/dL), alanine aminotransferase (ALT; mg/dL), blood urea nitrogen (BUN; mg/dL) triglyceridetrigl (TG) epicardial adipose tissue (EAT) body mass index (BMI)

the radiopaque points of the lead markers on the posteroanterior radiographs. Also, the skeletal nasal cavity width was measured from posteroanterior radiographs in order to correlate the skeletal and soft tissue changes (Figure 2). A perpendicular line to the Sella-Nasion (SN) line was drawn at the Nasion (N) to evaluate the sagittal and vertical soft tissue changes at the tip of the nose. The measurements are shown in Figure 3. The SNA° and nasolabial angles were also measured from the lateral cephalograms.

Statistical Analyses

All measurements were performed by the same observer (BZ), thus eliminating the interobserver error factor. Twenty lateral radiographs were randomly chosen to calculate the error of the method. Measurements were repeated after a 2-week interval, without knowledge of the first measurements and the error of the method was calculated using Dahlberg's (18) formula. The SPSS software package (Release 14.0, SPSS Inc. Chicago, IL, USA) was used to analyze the results. A Mann-Whitney U test was performed to compare parameters of the groups according to time intervals. A nonparametric paired Friedman test was performed to compare intra-group differences of parameters according to time intervals for the RME group. Finally, a Wilcoxon signed rank test was performed for the control group. The level of significance was set at p< 0.05.

RESULTS

The measurement errors were calculated to vary from 0.282° to 0.488° and 0.181 mm to 0.244 mm indicating no statistically significant differences between repeated measurements. Descriptive statistics including means and standard deviations for the groups are presented in Table 2 and 3.

Greater Alar Cartilage Width Changes

GAC width measurements showed a significant increase from T1 to T2 (1.45 mm) (p< 0.05), and a non-significant decrease from T2 to T3 (1.2 mm). The total increase from T1 to T3 was 0.25 mm for the RME group (p> 0.05) and 0.16 mm for the control group (p> 0.05) (Table 3). These results demonstrated that the GAC width returned to its original position after RME.

Nasal Cavity Width Changes

Nasal cavity width increased significantly from T1 to T2 (2.6 mm) (p< 0.05), and increased non-significantly from T2 to T3 (0.025 mm) (p> 0.05). The total increase from T1 to T3 was 2.65 mm for the RME group (p< 0.05). The small increase for the control group from T1 to T3 was non-significant (0.281 mm) (p> 0.05) (Table 3). These results demonstrated that the nasal cavity width increases due to RME.

Table 2. Comparison of starting forms (T1)

Parameters	RMI	E	Cor	ntrol				
	х	SD	х	SD	р			
GAC width	31.77	2.66	31.59	2.06	NS			
Nasal cavity width	29.02	3.45	29.71	2.16	NS			
Sagittal distance	22.55	3.58	23.40	4.78	NS			
Vertical distance	52.10	4.45	52.06	4.03	NS			
SNA°	77.65°	3.69	76.68°	4.32	NS			
NL°	105.35°	9.21	105.81°	6.28	NS			

NS, Not significant P>0.05

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Paramete	r	τ1	RME T2	T 2		Control	T 2	RME	Control			
	T 4 T 2	X 74 72	SD	<u>х</u>	SD	x	SD	x	SD	x	SD	T1-T2
GAC Widt	11-13 h	31.77	2.66	33.22	2.45	32.02	4.01	31.59	2.06	31.75	2.07	*
- Nasal Cav	- rity Width *	29.02	3.45	31.62	3.41	31.65	3.67	29.71	2.16	30	2.02	*
- Sagittal D)istance *	22.55	3.58	23.3	3.55	23.6	3.64	23.4	4.78	23.93	5.03	-
Vertical D)istance *	52.1	4.45	52.9	4.08	53.52	3.96	52.06	4.03	52.65	4.01	-
SNA °	77.65	3.69	78.92	3.28	78.40	3.35	76.68	4.32	77.09	4.35	*	-
- NL° *	- 105.35 *	9.21	-	-	108.12	9.78	105.81	6.28	107.12	5.86	-	-

Table 3. Comparison of changes for RME and control groups

*P< 0.05, a Friedman test, b Wilcoxon signed rank

Vertical Movement of the Tip of the Nose

The tip of the nose moved downward statistically nonsignificantly from T1 to T2 and from T2 to T3 (0.8 mm and 0.625 mm, respectively) (p> 0.05); however, the total downward movement from T1 to T3 was statistically significant (1.425 mm) for the RME group (p< 0.05). For the control group, the increase from T1 to T3 was nonsignificant (0.594 mm) (p> 0.05) (Table 3). These results demonstrated that the tip of the nose moves downward due to RME.

Sagittal Movement of the Tip of the Nose

The tip of the nose moved forward statistically non-significantly from T1 to T2 and from T2 to T3 (0.75 mm and 0.3 mm, respectively) (p> 0.05), and the increase from T1 to T3 was statistically significant (1.05 mm) (p< 0.05) for the RME group. For the control group, the increase from T1 to T3 was non-significant (0.531 mm) (p> 0.05) (Table 3). These results demonstrated that the tip of the nose moves forward due to RME.



Figure 1. Placement of the lead markers with a resinbased adhesive



Figure 2. Posteroanterior cephalometric analysis: 1. Distance between lead markers; 2. Nasal cavity width



Figure 3. Lateral cephalometric analysis: 1. Vertical reference plane; 2. Distance to measure vertical movement of the tip of the nose; 3. Distance to measure sagittal movement of the tip of the nose; 4. SNA°; 5. Nasolabial angle

Changes at SNA°

SNA measurements showed a significant increase from T1 to T2 (1.275°) (p< 0.05), and a non-significant decrease from T2 to T3 (0.525°). The total increase from T1 to T3 was 0.75° for the RME group (p> 0.05) and 0.403° for the control group (p> 0.05) (Table 3). These results demonstrate that the SNA° returned to its original position after RME.

Changes in the Nasolabial Angle

The nasolabial angle increased significantly for both the RME and control groups from T1 to T3 (2.275° and 1.313° respectively) (p< 0.05) (Table 3).

DISCUSSION

The traditional explanation for the influence of RME on the nasal cavity is based on the separation of the nasal cavity's lateral walls. The width of the nasal cavity increases about 2.1-4.5 mm after RME (6, 16, 19, 20). Our study shows that the nasal cavity width increases after RME and that the results are stable after retention. Cameron and colleagues (21) reported that this increase was stable 8 years after RME. Although this positive effect of RME due to enlargement of the nasal cavity's lateral walls (which increases the nasal volume, decreases nasal resistance and facilitates breathing) is pleasing, the possible negative changes of the shape of the nose may be guestionable. Berger et al. (9) photographically monitored 20 subjects treated with RME and 24 subjects with SARME to correct a unilateral or bilateral cross-bite. Their study revealed that soft tissue nasal width increased by 2 mm during treatment, and this increase remained stable at 1 year post treatment. Their results are inconsistent with our results. Our findings show that after increased width due to RME, the nose returns to its initial size after retention when compared with the controls (Table 3). Johnson et al. (16) evaluated soft tissue nasal width changes in their study. They measured the alar base and GAC width before and after RME and after retention. Although, they found an increase of nose width after retention, they concluded these changes were clinically non-significant. They used digital calipers to measure the distances; however, it is difficult to measure the alar cartilage width with digital calipers because of the elastic characteristics of soft tissue which moves easily when the alar cartilage is touched softly. Adams et al. (17) evaluated the soft tissue changes immediately following the active phase of expansion using CBCT. They noted a 1.79 mm increase of the nose width, which is consistent with our results. However they did not evaluated the changes after retention.

Berger et al. (10) then correlated the nasal soft tissue changes with changes in skeletal nasal width in 24 patients via posteroanterior cephalograms. Their results showed that the changes in soft tissue and skeletal nasal widths were correlated in a 1:1 ratio. Our findings are not consistent with a 1:1 ratio of increased nasal width to skeletal increases. This contradiction may be due to the lack of control group in the Berger study samples. Previous studies showed that after expansion, the maxilla moves downward and forward (5, 6, 20). Kilic et al. (22) evaluated the prominence of the nose after retention and found no difference after RME. Adams et al. (17) noticed that the tip of the nose moved 1.63 mm forward immediately after RME, in their CBCT study. In our study, we found that the tip of the nose moves 0.8 mm and 1.05 mm in the forward direction after RME and after retention, respectively (Table 3). Previous studies did not focus on the vertical movement of the nose. We found that downward movement after the retention was 1.425 mm. The forward and downward movement of the tip of the nose was found to be statistically significant, however; this movement may be considered clinically non-significant when compared with the controls after a 7 - month time period.

Previous studies demonstrated an increase of the SNA° due to the forward movement of the A point (8, 20). Haas (5) reported a decrease of the SNA° after 4 months of retention. Our findings are concordant with the previous studies; the SNA° increased after RME and tended to return to its original angle after retention (Table 3). Haas (5) explains this decrease as re-establishing the former proximity of the related bones.

Karaman et al. (8) concluded that the nasolabial angle increases non-significantly after RME. In our study, the increase of the nasolabial angle for the RME group was significant (Table 3). Interestingly, similar increase was found for the control group, which may be due to growing. Kiliç et al. (22) focused on the changes seen with Holdaway soft-tissue measurements rather than nasolabial angle changes. They concluded that due to the concerted forward movement of the nose, maxilla and upper lip together, the nasolabial angle did not change significantly. Schulz et al. (23) concluded that the changes in the RME group could be considered clinically significant if they were equal to or greater than 2 mm or 2° , due to the small sample size. The changes in our study are within the limits of these boundaries and our results may be considered as clinically non-significant. Gender is an important factor due to pubertal maturity of the subjects. Given that girls complete puberty earlier than boys, this may affect resistance to the forces of expansion. Johnson and colleagues (16) found different results for males and females when compared with controls. The gender differences between the RME and the control group were found to be non-significant in our study (Table 1) (P > 0.05).

Age is another factor that may be carefully considered during the selection of the subjects in RME studies. Proffit (15) notes that RME should not be used in preschool children because of the risk of producing undesirable changes in the nose at that age. On the other hand, Tai et al. (24) recommends slow expansion by using Schwarz appliances so as not to change the facial appearance of 7-8 year old children. In our study, the mean age was 13.40 and 13.25 for the RME and control groups, respectively, and the difference between groups was non-significant (Table 1) (P > 0.05).

Several studies have evaluated the effects of RME on the

nasomaxillary complex, performed with two-dimensional radiographs with frontal and lateral cephalograms. Due to the limitations of two-dimensional imaging in assessing 3D structures and their movements, CT images (which allow visual registration in all 3 dimensions without magnification or distortion) were advised. Lagravere et al. (25) hold that comparing computed tomography images may be the gold standard for evaluating soft tissue changes. However, more radiation dose of computed tomography than conventional radiographs should not be ignored. Further studies using CBCT are recommended for the better understanding of the soft tissue changes after RME.

In conclusion, both nasal skeletal cavity and alar widths increased significantly during expansion; however, the alar base width returned to its normal values during the retention period. The tip of the nose moved downward and forward; however, this movement may be considered clinically non-significant when compared with the control group. The SNA° returned to its original value, too. The nasolabial angle increased a small amount; however, a similar increase was found in the control group. RME did not affect the patients' frontal nasal appearance and mid-face soft tissue profile.

REFERENCES

- 1. Angell EH. Treatment of irregularities of the permanent or adult teeth. Dent Cosmos 1860; 1: 540-4.
- 2. Haas AJ. Rapid expansion of the maxillary dental arch and nasal cavity by opening the midpalatal suture. Angle Orthod 1961; 31:73-90.
- 3. Bishara SE, Staley RN. Maxillary expansion: clinical implications. Am J Orthod Dentofacial Orthop 1987; 91: 3-14.
- 4. Haas AJ. The treatment of maxillary deficiency by opening the midpalatal suture. Angle Orthod 1965; 35: 200-17.
- 5. Haas AJ. Longterm post treatment evaluation of rapid palatal expansion. Angle Orthod 1980; 50: 189-217.
- Wertz RA. Skeletal and dental changes accompanying rapid midpalatal suture opening. Am J Orthod 1970; 58: 41-66.
- Isaacson RJ, Wood JL, Ingram AH. Forces produced by rapid maxillary expansion. I and II. Angle Orthod 1964; 34: 256-70.
- Karaman AI, Basciftci FA, Gelgör I, Demir A. Examination of soft tissue changes after rapid maxillary expansion. World J Orthod 2002; 3: 217-22
- Berger JL, Pangrazio-Kulbersh V, Thomas BW, Kaczynski R. Photographic analysis of facial changes associated with maxillary expansion. Am J Orthod Dentofacial Orthop 1999; 116: 563-71.

- Berger JL, Pangrazio-Kulbersh V, Borgula T, Kaczynski R. Stability of orthopedic and surgically assisted rapid palatal expansion over time. Am J Orthod Dentofacial Orthop 1998;114: 638-45.
- 11. Hershey HG, Steward BL, Warren DW. Changes in nasal airway resistance associated with rapid maxillary expansion. Am J Orthod 1976; 69: 274-84.
- 12. Linder-Aronson S, Aschan G. Nasal resistance to breathing and palatal height before and after expansion of the median palatal suture. Odontol Revy 1963;14: 254-70.
- Doruk C, Sökücü O, Sezer H, Canbay E. Evaluation of nasal air- way resistance during rapid maxillary expansion using acoustic rhinometry. Eur J Orthod 2004; 26: 397-401
- Doruk C, Sökücü O, Bicakci A, Yilmaz U, Tas F. Comparison of nasal volume changes during rapid maxillary expansion using acoustic rhinometry and computed tomography. Eur J Orthod 2007; 29: 251-5.
- Proffit WR, White RP, Sarver D M (eds). Contemporary treatment of dentofacial deformity. St Louis: C V Mosby; 2003. p. 515
- Johnson BM, McNamara JA, Bandeen RL, Baccetti T. Changes in soft tissue nasal widths associated with rapid maxillary expansion in prepubertal and postpubertal subjects. Angle Orthod 2010; 80: 995-1001.
- Adams D, Araujo E, Behrents R, Kim K. Evaluation of immediate Soft Tissue Effects of Rapid Maxillary Expansion using Three Dimentional Imaging. Master Thesis, Saint Luis University. 2009.
- Dahlberg G. Statistical Methods for Medical and Biological Students. London, UK: George Unwin Ltd; 1940: 122-32.
- da Silva Filho OG, Montes LA, Torelly LF. Rapid maxillary expansion in the deciduous and mixed dentition evaluated through posteroanterior cephalometric analysis. Am J Orthod Dentofacial Orthop 1995; 107: 268-75.
- Doruk C, Bicakci AA, Basciftci FA, Babacan H, Agar U. A comparison of the effects of rapid maxillary expansion and fan-type rapid maxillary expansion on dentofacial structures. Angle Orthod 2004; 74:184-94.
- Cameron CG, Franchi L, Baccetti T, McNamara JA Jr. Longterm effects of rapid maxillary expansion: a posteroanterior cephalometric evaluation. Am J Orthod Dentofacial Orthop 2002; 121: 129-35.
- 22. Kılıç N, Kiki A, Oktay H, Erdem A. Effects of rapid maxillary expansion on Holdaway soft tissue measurements. Eur J Orthod 2008; 30: 239-43.
- Schulz SO, McNamara JA Jr, Baccetti T, Franchi L.Treatment effects of bonded RME and vertical-pull chincup followed by fixed appliance in patients with increased vertical dimension. Am J Orthod Dentofacial Orthop 2005; 128: 326-36.
- Tai K, Park JH, Mishima K, Shin JW. 3-Dimensional conebeam computed tomography analysis of transverse changes with Schwarz appliances on both jaws. Angle Orthod 2011; 81: 670-7.
- 25. Lagravère MO, Hansen L, Harzer W, Major PW. Plane orientation for standardization in 3-dimentional cephalo-

metric analysis with computerized tomography imaging. Am J Orthod Dentofacial Orthop 2006; 129: 601-4.

- Lehman SJ, Massaro JM, Schlett CL et al. Periaortic fat, cardiovascular disease risk factors, and aortic calcification: the Framingham Heart Study. Atherosclerosis. 2010; 210:656-61.
- 27. Sacks HS, Fain JN. Human epicardial adipose tissue: a review. Am Heart J 2007; 153:907-17.
- Iacobellis G, Corradi D, Sharma AM. Epicardial adipose tissue: anatomic, biomolecular and clinical relationships with the heart. Nat Clin Pract Cardiovasc Med 2005; 2:536-43.
- 29. Ho E, Shimada Y. Formation of the epicardium studied with the scanning electron microscope. Dev Biol 1978; 66: 579-85.
- Cheng K-H, Chu C-S, Lee K-T et al. Adipocytokines and proinflammatory mediators from abdominal and epicardial adipose tissue in patients with coronary artery disease. Int J Obes 2005 2008; 32:268-74.
- 31. Iacobellis G, Willens HJ, Barbaro G et al. Threshold values of high-risk echocardiographic epicardial fat thickness. Obes Silver Spring Md 2008; 16:887-92.
- Iacobellis G, Assael F, Ribaudo MC et al Epicardial fat from echocardiography: a new method for visceral adipose tissue prediction. Obes Res 2003; 11:304-10.
- Chaldakov GN, Stankulov IS, Aloe L. Subepicardial adipose tissue in human coronary atherosclerosis: another neglected phenomenon. Atherosclerosis 2001; 154:237-8.
- Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004; 364:937-52.
- Iacobellis G, Ribaudo MC, Assael F, et al. Echocardiographic epicardial adipose tissue is related to anthropometric and clinical parameters of metabolic syndrome: a new indicator of cardiovascular risk. J Clin Endocrinol Metab 2003; 88:5163-8.
- 36. Natale F, Tedesco MA, Mocerino R, et al. Visceral adiposity and arterial stiffness: echocardiographic epicardial fat thickness reflects, better than waist circumference, carotid arterial stiffness in a large population of hypertensives. Eur J Echocardiogr J Work Group Echocardiogr Eur Soc Cardiol 2009; 10:549-5.
- 37. Ahn S-G, Lim H-S, Joe D-Y, et al. Relationship of epicardial adipose tissue by echocardiography to coronary artery disease. Heart Br Card Soc 2008; 94-7.
- Eroglu S, Sade LE, Yildirir A, et al. Epicardial adipose tissue thickness by echocardiography is a marker for the presence and severity of coronary artery disease. Nutr Metab Cardiovasc Dis Nmcd 2009; 19:211-7.
- Mansour AA, Ajeel NA. Atherosclerotic cardiovascular disease among patients with type 2 diabetes in Basrah. World J Diabetes. 2013 Jun 15;4(3):82-7.
- 40. Taleb N, Salti H, Al-Mokaddam M et al Prevalence and determinants of albuminuria in a cohort of diabetic patients in Lebanon. Ann Saudi Med 2008; 28: 420-5.

- 41. Jurado J, Ybarra J, Solanas P et al. Prevalence of cardiovascular disease and risk factors in a type 2 diabetic population of the North Catalonia diabetes study. J Am Acad Nurse Pract 2009; 21: 140-8.
- Greif M, Becker A, von Ziegler F, et al. Pericardial adipose tissue determined by dual source CT is a risk factor for coronary atherosclerosis. Arterioscler Thromb Vasc Biol 2009; 29:781-6.
- 43. Iacobellis G, Leonetti F. Epicardial adipose tissue and insulin resistance in obese subjects. J Clin Endocrinol Metab 2005; 90:6300-2.
- 44. Iacobellis G, Willens HJ. Echocardiographic epicardial fat: a review of research and clinical applications. J Am Soc Echocardiogr Off Publ Am Soc Echocardiogr 2009; 22:1311-9
- Jeong J-W, Jeong MH, Yun KH, et al. Echocardiographic epicardial fat thickness and coronary artery disease. Circ J Off J Jpn Circ Soc 2007; 71:536-9.
- 46. Kim HM, Kim KJ, Lee HJ et al Epicardial adipose tissue thickness is an indicator for coronary artery stenosis in asymptomatic type 2 diabetic patients: its assessment by

cardiac magnetic resonance. Cardiovasc Diabetol. 2012 Jul 18;11:83.

- 47. Wang CP, Hsu HL, Hung WC et al. Increased epicardial adipose tissue (EAT) volume in type 2 diabetes mellitus and association with metabolic syndrome and severity of coronary atherosclerosis. Clin Endocrinol (Oxf). 2009 Jun;70(6):876-82
- Cetin M, Cakici M, Polat M et al. Relation of epicardial fat thickness with carotid intima-media thickness in patients with type 2 diabetes mellitus. Int J Endocrinol. 2013;2013:769175.
- Flüchter S, Haghi D, Dinter D, et al. Volumetric assessment of epicardial adipose tissue with cardiovascular magnetic resonance imaging. Obes Silver Spring Md 2007; 15:870-8.