Clinico-radiological correlates of achalasia

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ABSTRACT

Objectives: To study the clinical and radiographic characteristics of achalasia in a cohort Jordanian patients and to investigate the presence of any clinico-radiological relationships.

Methods: Thirty-five cases of recently diagnosed untreated achalasia patients were studied at Jordan University Hospital, Amman, Jordan during the period of January 1999 to December 2002. Measurements of maximum esophageal and gastroesophageal (GE) junction diameters, as radiographic features, were obtained from films. The clinical features included age; gender; nature; frequency and duration of typical and atypical symptoms; total number of symptoms; calculated typical symptoms score; and diagnostic delay. Pearson correlation coefficients were calculated between radiographic and clinical features, and among the radiographic features themselves. Using Spearman's correlation coefficients, the later analysis was repeated for patients with diagnostic delay of 2 years or less and patients with more than 2 years. All results were evaluated based on the 0.05 level of significance.

Results: There were 35 consecutive achalasia patients enrolled in this study (20 females and 15 males) with a mean age of 42.3 ± 15.6 years and diagnostic delay of 29 ± 26 months. On average, each patient has presented 2 typical symptoms and 2 atypical symptoms. The mean typical symptoms score was almost 3 out of the full score of 6. The mean GE junction diameter was 2.4 mms and maximum esophageal diameter was 29 mms. Maximum esophageal diameter was significantly correlated with the number of typical, atypical and total symptoms as well as with the typical symptom score and diagnostic delay. Negative correlation was found between GE junction diameter and maximum esophageal diameter; but only statistically significant for patients with diagnostic delay of more than 2 years.

Conclusion: Statistically significant relationship exists between maximum esophageal diameter and all clinical variables. Negative correlation exists between maximum esophageal diameter and GE junction diameter; however, only significant for patients with a diagnostic delay more than 2 years. The possibility of achalasia is high in patients with longer diagnostic delay who demonstrate negative relationship between maximum esophageal diameter and GE junction diameter.

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Achalasia is a rare primary esophageal motor disorder of unknown etiology characterized manometrically by insufficient lower esophageal sphincter (LES) relaxation and loss of esophageal peristalsis, and radiographically by aperistalsis, esophageal dilation, minimal LES opening with a "bird beak" appearance, and poor emptying of barium.[1] First recognized more than 300 years ago when initially labeled cardiospasm. In 1937, Lendrum[2] proposed that the functional esophageal obstruction in this syndrome resulted from incomplete relaxation of the LES and renamed the disease achalasia (failure to relax).[2,3] The disorder is caused by degeneration or dysfunction of the inhibitory innervation of the esophageal smooth muscle resulting in incomplete relaxation of the lower sphincter and absent peristalsis in the esophageal body.[4-7] The diagnosis should be suspected in anyone complaining of dysphagia for solids and liquids with regurgitation of food and

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saliva. The clinical suspicion should be confirmed by barium esophagogram (barium swallow) showing smooth tapering of the lower esophagus leading to the closed LES, resembling a "bird's beak". Esophageal manometry establishes the diagnosis showing esophageal aperistalsis and insufficient LES relaxation. All patients should undergo upper endoscopy to exclude pseudoachalasia arising from a tumor at the gastroesophageal (GE) junction.[1] The disease affects both sexes equally, onset is usually in the third to fifth decades with wide variation in duration of symptoms before diagnosis and unclear relationship between clinical symptoms and radiographic findings.[8] The aims of this study were 2-fold: to study the clinical and radiographic characteristics of achalasia in a cohort of Jordanian patients and to investigate the presence of any clinico-radiological relationships.

Methods. Thirty-five cases of recently diagnosed untreated achalasics were prospectively and jointly evaluated at the time of diagnosis by the Radiology Department and the Gastrointestinal Unit at Jordan University Hospital, Amman, Jordan. The evaluation took place during the period of January 1999 to December 2002 where all patients underwent upper endoscopy to eliminate the possibility of pseudoachalasia. Single-contrast barium swallow with fluoroscopy and measurement of maximum esophageal diameter and GE junction diameter were performed and recorded into a structured questionnaire (***Appendix 1**) for all patients by 2 consultant radiologists throughout the study period. The clinical part of the questionnaire was also recorded for all patients by one senior gastroenterologist.

Measurements of maximum esophageal diameter and GE junction diameter were obtained from films and then standardized for magnification by measuring height of a thoracic vertebral body and relating them to an average expected measurement of 20 mms.[9,10] The clinical part has included age; gender; nature; frequency and duration of presenting typical and atypical symptoms and total number of symptoms along with the calculated typical symptoms score (TSS). As illustrated in ***Appendix 1**, 3 typical symptoms were included: dysphagia, chest pain and regurgitation. The frequency of each symptom was recorded as "absent" (score 0), "sometimes present" (score 1) or "present daily" (score 2). The TSS for each patient was calculated as the sum of the 3 typical symptoms' scores. Thus, the minimum typical symptoms score for each patient was zero while the maximum was 6. On the other hand, the "presence" or "absence" of each of the following 15 atypical symptoms was recorded: heartburn; weight loss; slow eating; halitosis; drinking carbonated beverages while eating; sitting up-straight with meals; raising arms over head with meals; arching of shoulders and neck during meals; standing or walking around with meals; presence of oral debris at night; sleeping up-right in a chair; nocturnal cough; history of bronchitis; bronchial or aspiration pneumonia; history of asthma and airway compromise or stridor. The duration in months for each typical and atypical symptom was also recorded for all patients. The last row of ***Appendix 1** shows age at first (initial) symptoms and age at manometric and/or radiological diagnosis. Diagnostic delay was calculated as the difference between the 2.

Pearson correlation coefficients were calculated between maximum esophageal diameter and GE junction diameter as radiographic features on one hand, and number of typical, atypical total symptoms, typical symptoms score, and diagnostic delay as clinical features, on the other hand. The aim was to investigate the presence of any relationship between radiographic and clinical features. Also, the Pearson's correlation coefficient was calculated between maximum esophageal diameter and GE junction diameter to investigate the presence of a relationship between the 2 radiographic features themselves. Using Spearman's correlation coefficients, the later analysis was repeated twice; one for patients with diagnostic delay of 2 years or less (group I) and another for patients with more than 2 years (group II). Due to the small sample sizes, Spearman's correlations were utilized; all results were evaluated based on the 0.05 level of significance.

Results. As stated above, 35 consecutive achalasia patients were enrolled in this study; 20 females and 15 males. The mean age was 42.3 $\pm$ 15.6 years (range 12-74 years) and male to female ratio was 3:4, mean age for males was 41.3 while for females 43 years. Mean diagnostic delay was 29 $\pm$ 26 months (range 3-120 months). Twenty-one patients (group I) had a diagnostic delay $\leq$2 years, while 14 patients (group II) had a diagnostic delay >2 years.

Table 1 shows the means, standard deviations and sample sizes for all clinical and radiographic variables. On average, each patient has presented nearly 2 typical symptoms and a slightly more than 2 atypical symptoms; namely a total of nearly 4 symptoms. The mean typical symptoms score was almost 3 out of the full score of 6. The mean diagnostic delay was 28.9 months with a reasonably high variation as indicated by the standard deviation (26 months). The mean GE junction diameter was 2.4 mms which is close to severely narrowed. The mean maximum esophageal diameter was 29.35 mms which is considered within the normal limit according to Blam et al[11] and D'Alteroche et al.[12]

*The full text including Appendix 1 is available in PDF format on Saudi Medical Journal website (www.smj.org.sa)

Table 2 shows the Pearson's correlation coefficient and associated *p* values between radiographic and clinical variables. The maximum esophageal diameter as a radiographic variable has correlated significantly ($p<0.05$) with all clinical variables (number of typical, atypical and total symptoms; typical symptoms score and diagnostic delay). In particular, maximum esophageal diameter had a strong correlation with the typical symptoms score ($p=0.001$). The GE junction diameter did not reveal any significant correlation with any of the clinical variables. But, it seems that the longer the diagnostic delay the narrower GE junction diameter; however, this relationship was not significant ($p=0.123$).

As shown at the end of **Table 2**, there was a negative correlation between the 2 radiographic variables (maximum esophageal diameter and GE junction diameter); but did not reach the significance level of 0.05. However, it was noticed that the relationship between maximum esophageal diameter and GE junction diameter seems to depend on the diagnostic delay. To verify this observation, the 35 patients were divided into 2 groups; group I with diagnostic delay ≤2 years (21 patients) and group II with >2 years (14 patients). Spearman's correlation coefficients between the 2 radiographic variables were calculated for the 2 groups separately. Statistically significant correlation was found in group II (Spearman's correlation –0.54 and $p=0.045$); but not in group I (Spearman's correlation 0.003 and $p=0.991$). Thus, it is evident that there is a strong and negative correlation between maximum esophageal and GE junction diameter but only for patients with longer diagnostic delay (in this case longer than 2 years).

Discussion.

This study has analyzed the clinical and radiological correlates of 35 recently diagnosed, untreated achalasia patients in Jordan. Most patients were referred to our specialized (tertiary) gastroenterology unit from different parts of the country; thus could be looked at as a pilot study investigating the profile of clinico-radiological correlates of achalasia in Jordan. In addition, since there were no studies conducted in the Arab World on this subject before (at least to our knowledge), the profile might also be extended to represent other Arab countries. A first novel finding in this study is the presence of a statistically significant correlation between maximum esophageal diameter and all clinical variables (number of typical, atypical and total symptoms; typical symptoms score and diagnostic delay). In a 2002 study, Blam et al[11] has concluded that there is no statistically significant relationship between total radiographic score on one hand and total number of symptoms and typical symptoms score on the other hand. Our result seems to contradict Blam et al[11] study; however, this contradiction can be attributed to several reasons; mainly related to the radiographic aspect of their assessment. First, and most importantly, the total radiographic score used by Blam et al[11] was a subjective score calculated from 4 different components; GE junction diameter, maximum esophageal diameter, retained debris and configuration of the esophagus. Each component was assigned a score of 0, 1, 2 or 3 based on severity, and the total radiographic score was the sum of the 4 components. Unfortunately, the total

Table 1 - Means, standard deviations and sample sizes for clinical and radiographic variables.

Clinical and radiographic variables	Mean	Standard deviation	N of patients
Number of typical symptoms	1.97	0.79	35
Number of atypical symptoms	2.20	1.35	35
Number of total symptoms	4.17	1.76	35
Typical symptoms score	2.94	0.91	35
Diagnostic delay	28.91	26.16	35
Gastroesophageal junction diameter	2.37	0.90	35
Maximim esophageal diameter	29.35	8.50	35

Table 2 - Pearson's correlation coefficient and (*p* values) between radiographic and clinical variables.

Clinical variable	Radiographic variables	
	Gastroesophageal junction diameter	Maximum esophageal diameter
Number of typical symptoms	0.06 (0.710)	0.34 (0.045)*
Number of atypical symptoms	-0.145 (0.407)	0.343 (0.043)*
Number of total symptoms	-0.082 (0.641)	0.415 (0.013)*
Typical symptoms score	0.142 (0.417)	0.545 (0.001)*
Diagnostic delay	-0.265 (0.123)	0.398 (0.018)*
Gastroesophageal junction diameter	-	-0.274 (0.112)
Maximum esophageal diameter	-0.274 (0.112)	-

*Result is significant at the 0.05 level.

radiographic score did mask the variations of the individual components. Also, GE junction diameter and maximum esophageal diameter represent continuous variables measured in mms and could have been used as they are; namely without assigning scores to them. Furthermore, retained debris and configuration of the esophagus were subjective (not measurable) variables, and were combined with the aforementioned continuous variables. Thus, the analysis made by Blam et al[11] was not adequate to reveal which one of the 4 radiographic components could have a significant correlation with the clinical parameters. Second, most of the barium esophagograms (barium swallows) in Blam et al[11] study were performed by different radiologists in the referring community hospitals then acquired later for retrospective evaluation by one of the authors. In our study, all barium esophagograms with measurement of maximum esophageal diameter and GE junction diameter were performed, evaluated and recorded prospectively by 2 radiologists throughout the study period. Third, most of the evaluated barium esophagograms in Blam et al[11] study were either double contrast or water soluble swallows in contrast to our standardized single contrast swallows used for all patients, which is the standard assessment method for achalasia. Fourth, 68% of Blam et al[11] patients had undergone one or more achalasia directed treatments by the time of barium esophagogram and the rest (32%) had their assessed barium esophagogram immediately after pneumatic dilation or surgery which would naturally affect the GE junction diameter. This more likely explains why the mean GE junction diameter in their study was only mildly narrowed (6.5 mms); while in our untreated patients, the mean GE junction diameter was severely narrowed (2.4 mms). Fifth, on the clinical side, almost half of the patients in Blam et al[11] study were evaluated retrospectively over the phone by one author, while the rest were evaluated prospectively by a different author. In our study, all patients were evaluated prospectively by a single author. It should be noted that a statistically significant relationship had been established before between maximum esophageal diameter and duration of disease (diagnostic delay).[12]

A second novel finding is the presence of a significant negative correlation between maximum esophageal diameter and GE junction diameter only for patients with a diagnostic delay more than 2 years; a relation which (to our knowledge) had never been investigated before. The implication here is that the radiologist should always consider the diagnostic delay (duration of symptoms) when assessing the possibility of achalasia. As the diagnosis appears to be probable in a patient presented with achalasia-related symptoms for a longer period (more than 2 years) who demonstrated negative relationship between maximum esophageal diameter and GE junction diameter. This is particularly true when endoscopy had eliminated the possibility of pseudoachalasia.

A third novel feature in this study is that all patients included were never undergone any kind of achalasia directed treatment. The mean maximum esophageal diameter in this study was nearly 30 mms while in previous studies it was between 40-45 mms.[11,12] This difference could be attributed to 2 reasons. First, the duration of symptoms (diagnostic delay) in the previous studies, with exception of Howard et al[13] was 4-6 years; while in this study, it was nearly 2.5 years (close to Howard et al[13] study). Second, in the previous studies many patients (particularly in Blam et al[11] study) already had one or more achalasia directed treatments before radiographic assessment; while in this study, all patients were untreated at the time of assessment. The implication is that achalasia directed treatments would interfere with the proper assessment of the clinico-radiological relationship.

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Appendix 1
Illustration of the structured questionnaire filled out for each patient

Patient Name: _____ Hospital. No._____ Age_____ Gender_____

Maximal Esophageal Diameter _____mm

Gastroesophageal Junction Diameter _____mm

Other Findings:

Typical Symptoms & Score

Dysphagia: Absent (0) Sometimes Present (1) Present Daily (2) Duration_____
Chest Pain: Absent (0) Sometimes Present (1) Present Daily (2) Duration_____
Regurgitation: Absent (0) Sometimes Present (1) Present Daily (2) Duration_____

Calculated Typical Symptoms Score_____

Atypical Symptoms

	Yes	No	Duration
1. Heartburn			
2. Weight loss			
3. Slow eating			
4. Halitosis			
5. Drinking carbonated beverages while eating			
6. Sitting up-straight with meals			
7. Raising arms over head with meals			
8. Arching of shoulders and neck during meals			
9. Standing or walking around with meals			
10. Presence of oral debris at night			
11. Sleeping up-right in a chair			
12. Nocturnal cough			
13. History of bronchitis, bronchial or aspiration pneumonia			
14. History of asthma			
15. Airway compromise or stridor			

Total Number of Symptoms: _____

Age at First (Initial) Symptom _____years Age at Diagnosis _____years

Diagnostic Delay _____months