Chulalongkorn Medical Journal

Volume 58
Issue 2 *March 2014*

Article 2

3-1-2014

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Sangsasri V, Sirisalipoch S, Gonlachanvit S, Chaiwatanarat T. Accuracy of esophageal scintigraphy for evaluation of esophageal motility disorders. Chula Med J 2014 Mar – Apr;58(2): 113 - 23

Background : *Esophageal scintigraphy is a non-invasive tool for detection of esophageal functional abnormality. But the lack of standardized procedure results in a wide range of reported sensitivity and specificity. Concerning the method of data acquisition, some studies found from their data that several swallowing provide a better result than single swallowing technique.*

Objective : *To compare the accuracy of single swallowing and multiple swallowing methods in detection of esophageal functional abnormality using manometry as gold standard.*

Methods and Materials : *Thirty-six patients who were clinically suspected of esophageal motility abnormality were examined using six consecutive swallows of the radiolabeled liquid and semisolid bolus. Six parameters were calculated for each swallowing technique. The first was used to calculate single swallowing parameters. Averages of six swallowing parameters were used as multiple-swallowing parameters. All patients were investigated with manometry for their final diagnosis.*

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Results : *Twenty-eight patients had abnormal manometry results. Multiple liquid swallows provided the best diagnostic accuracy; all parameters, except mean time, had area under ROC curves of more than 0.85. The mean transit time of 8.8 sec. and emptying of 82% using multiple liquid swallows resulted in the best sensitivity (96%). The semisolid swallowing gave variable results; 2 parameters were better for multiple-swallowing technique, the other 4 parameters were better for single-swallowing technique.*

Conclusion : *Multiple liquid swallowing technique provides best diagnostic accuracy in detection of esophageal functional abnormality. The results of semisolid swallowing varied, probably because it was difficult to standardize the consistency of semisolid bolus.*

Keywords : *Esophageal scintigraphy, liquid bolus, semisolid bolus, single swallowing, multiple-swallowing, esophageal manometry.*

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Received for publication. August 16, 2013.

วนา แสงสระศรี, ศศิธร ศิริสาลิโภชน์, สุเทพ กลชาญวิทย์, ธวัชชัย ชัยวัฒนรัตน์. ความถูกต้องในการประเมินความผิดปกติของการเคลื่อนไหวของหลอดอาหารด้วยภาพถ่ายทางเวชศาสตร์นิวเคลียร์ จุฬาลงกรณ์เวชสาร 2557 มี.ค – เม.ย; 58(2): 113 – 23

เหตุผลของการทำวิจัย : *Esophageal scintigraphy เป็นการตรวจทางเวชศาสตร์นิวเคลียร์ที่ใช้ประเมินความผิดปกติของการทำงานของหลอดอาหาร แต่การขาดมาตรฐานในวิธีการตรวจทำให้มีการรายงานผลความไวและความจำเพาะแตกต่างกันเป็นอย่างมาก ในแง่ของการเก็บข้อมูลภาพถ่ายนั้นบางการศึกษาพบว่าการตรวจโดยให้ผู้ป่วยกลืนหลาย ๆ ครั้งจะให้ผลการวินิจฉัยที่ดีกว่าการกลืนเพียงครั้งเดียว*

วัตถุประสงค์ : *เพื่อเปรียบเทียบความถูกต้องของการตรวจแบบกลืนครั้งเดียวและหลายครั้งในการประเมินความผิดปกติของการทำงานของหลอดอาหาร โดยใช้ผลการตรวจ manometry เป็นการวินิจฉัยอ้างอิง*

วัสดุและวิธีการ : *ผู้ป่วย 36 รายที่สงสัยว่าจะมีความผิดปกติของการทำงานของหลอดอาหาร ได้รับการตรวจโดยการกลืนอาหารทั้งที่เป็นของเหลวและกึ่งเหลวเป็นจำนวนอย่างละ 6 ครั้ง จากนั้นจึงคำนวณค่าที่แสดงถึงการทำงานของหลอดอาหารต่าง ๆ กัน 6 ค่า โดยค่าสำหรับการกลืนครั้งเดียวคำนวณจากการกลืนครั้งแรก ส่วนค่าจากการกลืนหลายครั้งคำนวณจากการหาค่าเฉลี่ยของการกลืน ทั้ง 6 ครั้ง ผู้ป่วยทุกคนจะได้รับการตรวจด้วย manometry เพื่อได้ผลการวินิจฉัยอ้างอิง*

ผลการศึกษา : *ผู้ป่วย 28 รายได้รับการวินิจฉัยว่าผิดปกติจากการตรวจ manometry การตรวจ Esophageal scintigraphy ด้วยการกลืนอาหารเหลวแบบหลายครั้งให้ผลการตรวจที่ถูกต้องที่สุดสำหรับทุกค่าที่แสดงถึงการทำงานของหลอดอาหาร ยกเว้น mean time โดยมีพื้นที่ใต้กราฟ ROC มากกว่า 0.85 โดยที่ค่า mean transit time 8.8 วินาทีและ emptying ร้อยละ 82 ให้ค่าความไวสูงที่สุด (ร้อยละ 96) สำหรับการกลืนอาหารกึ่งเหลวให้ผลการตรวจที่ไม่แน่นอน มี 2 ค่าจากการกลืนหลายครั้งให้ผลการตรวจดีกว่าแต่อีก 4 ค่าจากการกลืนครั้งเดียวให้ผลการตรวจดีกว่า*

สรุป : *การตรวจด้วยการกลืนอาหารเหลวแบบหลายครั้งให้ผลถูกต้องที่สุดในการตรวจพบความผิดปกติของการทำงานของหลอดอาหาร ผลการตรวจด้วยอาหารกึ่งเหลวให้ผลไม่แน่นอนทั้งนี้อาจเนื่องจากการควบคุมความหนืดของอาหารให้ได้มาตรฐานทำได้ยาก*

คำสำคัญ : *Esophageal scintigraphy, อาหารเหลว, อาหารกึ่งเหลว, การกลืนครั้งเดียว, การกลืนหลายครั้ง, Esophageal manometry.*

Esophageal scintigraphy is a non-invasive tool for esophageal function study. It is generally accepted as an effective method for detection of esophageal functional abnormality.[1-3] However, the reported sensitivity and specificity vary widely from 44% to 100% and 47% to 96%, respectively. [2, 4-11] More likely, this was caused by differences in the studies' methodology such as differences in population, types of meal, method of data acquisition, image analysis and thresholds of interpretation. It is clearly seen that the main problem is the lack of standardization of the imaging method. An important difference is the method of data acquisition. Many studies found data acquisition through single-swallowing method did not provide a good result because there are variations in each swallow in the same patient. [12-13] A study using an average of the parameters acquired by several swallows provides a better result. [14] However, practically the technique may be difficult in patients who already have a problem of difficulty in swallowing. So the real need of multiple-swallowing technique has to be addressed.

This study is aimed to compare the accuracy of single-swallowing and multiple-swallowing methods in detection of esophageal functional abnormality using esophageal manometry as the gold standard.

Materials and Methods

Thirty-six patients who were clinically suspected of having esophageal motility abnormality and visited the gastrointestinal motility clinic at King Chulalongkorn Memorial Hospital were recruited. All patients were investigated with esophageal manometry for their final diagnosis. The study protocol has been approved by the Ethics Committees of the Faculty of Medicine, Chulalongkorn University.

Esophageal scintigraphy procedure consists of 2 steps, namely: first, 6 swallows of liquid bolus; and second 6 swallows of semisolid bolus. Before investigation, the subject was advised to keep NPO for at least 6 hours. Ten milliliters of pure water was used as a liquid bolus. Twenty grams of infant powder formula (Nestle Cerelac™) mixed with 40 milliliters of pure water, divided into 6 boluses of 10 milliliters each, was used as semisolid boluses. Each bolus, both liquid and semisolid, was mixed with 0.2 mCi Tc-99m Phytate as an imaging agent.

The dynamic data (240 frames, 0.25 sec/frame, byte mode, 64 $\times$ 64 matrix) was acquired in each swallow in supine position using gamma camera equipped with low energy collimator. The subject was asked to swallow each bolus only once, followed by one dry swallow 30 seconds later. Six swallows of both liquid and semisolid boluses were repeated in each subject using the same swallowing technique.

Data analysis was performed by drawing the region of interest covering the whole esophagus from below the oropharynx to above the stomach using sum of all frames as a guided-image. Time-activity curve was created for each set of 12-data sets of each patient. Three-point smoothing was applied to all curves. Time-activity curves were used to calculate the following 6 quantitative parameters:

1. Tmax: time from starting of a swallowing to time at maximal activity.
2. Transit time: time from the starting of a swallowing to time when activity fell to 10% or less of the maximal activity. This parameter represents 90% emptying time.

3. Mean time = Σ[cts(t) × t] / Σcts(t). Where cts(t) is the activity at time "t". This parameter represents center of gravity of the time-activity curve.
4. Mean transit time = Σcts(t) / cts(max). This parameter represents mean duration of stay of the activity.
5. Esophageal emptying (Tmax+10sec) = cts (max+10sec)/cts(max) × 100: Emptying, in percent of the maximal activity, at 10 seconds from time of maximal activity.
6. Esophageal emptying (12sec) = cts(12sec)/ cts(max) × 100: Emptying, in percent of the maximal activity, at 12 seconds from the starting of a swallow.

Parameters of single swallowing were calculated from the first swallowing data sets. Parameters of multiple-swallowing technique were the average of each parameter calculated from each of 6-data set boluses. Sensitivity and specificity in detection of esophageal motility abnormality of each parameter were calculated using the result of esophageal manometry as the final diagnosis, either normal or abnormal. Receiver operator characteristic (ROC) curve for each parameter was created and the cutoff value of each parameter was selected.

Results

There were 36 patients: 13 males and 23 females, recruited in the study. Their ages were 28 - 80 years old. Twenty-eight patients, 10 males and 18 females, had abnormal esophageal manometry results. And 8 patients, 3 males and 5 females, had normal esophageal manometry results.

Figures 1 - 6 show ROC curve of each parameter in the diagnosis of esophageal motility abnormality. Each figure consists of 4 curves for single liquid swallowing, multiple liquid swallowing, single semisolid swallowing and multiple semisolid swallowing respectively. Table 1 shows area under each of the 4 ROC curves of each parameter.

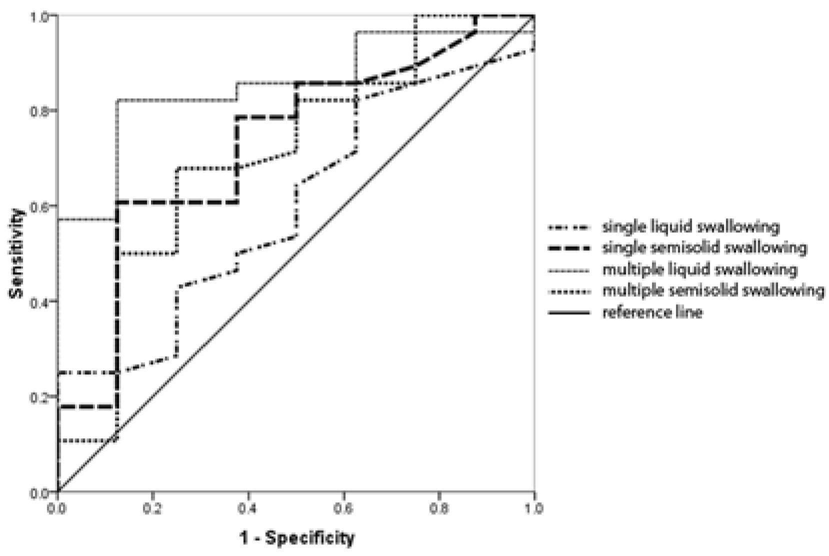

Figure 1. ROC curve of Tmax of 4 different swallowing techniques

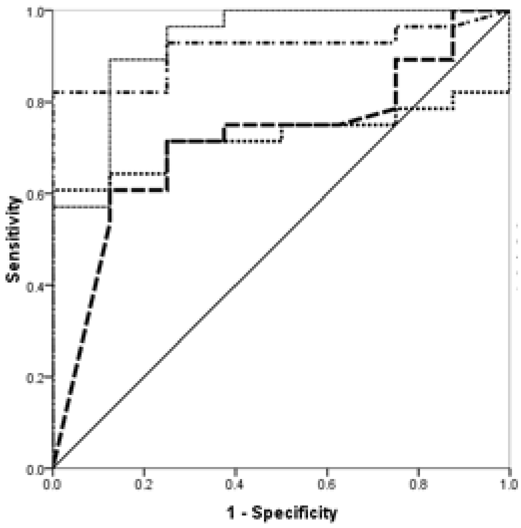

Figure 2. ROC curve of transit time of 4 different swallowing techniques (legend is the same as in Fig. 1)

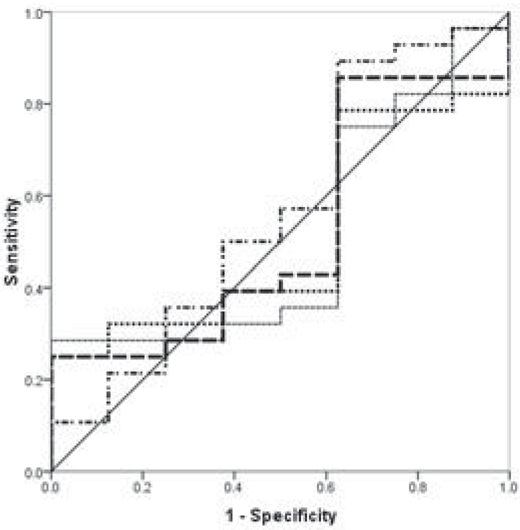

Figure 3. ROC curve of mean time of 4 different swallowing techniques (legend is the same as in Fig. 1)

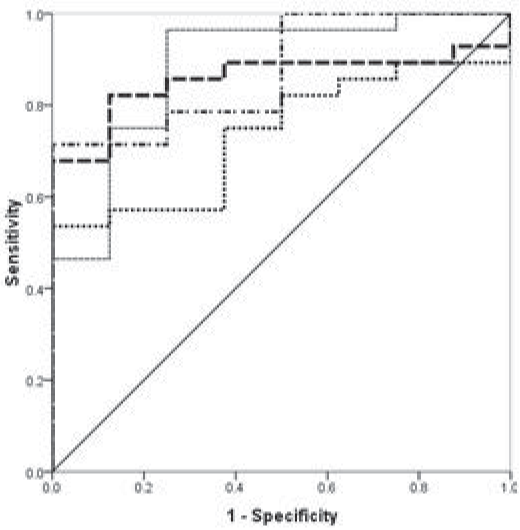

Figure 4. ROC curve of mean transit time of 4 different swallowing techniques (legend is the same as in Fig. 1)

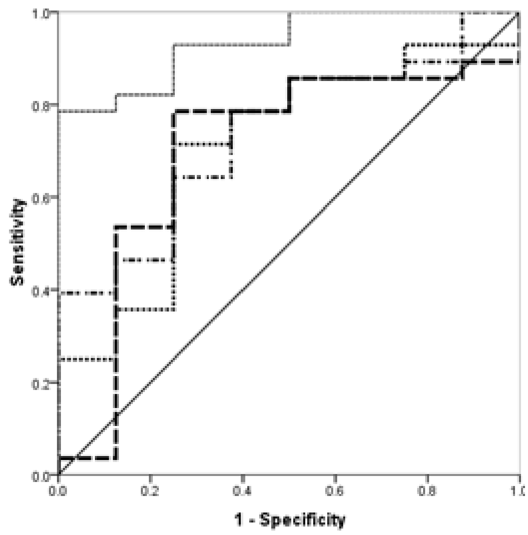

Figure 5. ROC curve of esophageal emptying (Tmax + 10sec) of 4 different swallowing techniques (legend is the same as in Fig. 1)

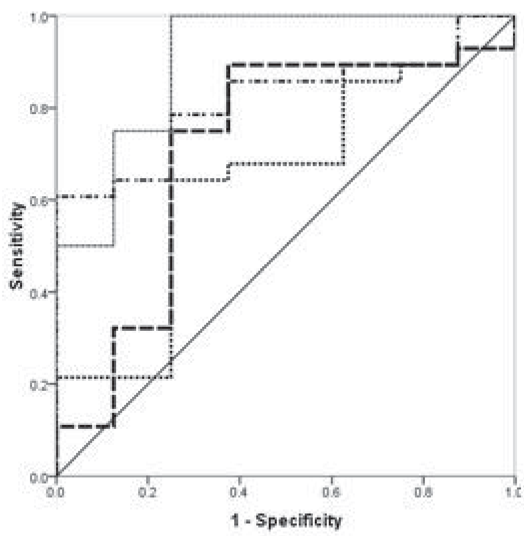

Figure 6. ROC curve of esophageal emptying (12sec) of 4 different swallowing techniques (legend is the same as in Fig. 1)

Table 1. AUC of the 4 ROC curves of the 6 parameters for 4 swallowing techniques.

Parameter	Liquid		Semisolid	
	Single	Multiple	Single	Multiple
Tmax	0.598	0.853	0.730	0.708
Transit time	0.913	0.929	0.719	0.723
Mean time	0.567	0.509	0.522	0.509
Mean transit time	0.875	0.884	0.857	0.737
Emptying (Tmax+10sec)	0.737	0.933	0.701	0.710
Emptying (12sec)	0.817	0.906	0.710	0.638

Single = single swallowing, Multiple = multiple swallowing

The results show that multiple liquid swallows provide best diagnostic result. The areas under the curve (AUC) of multiple liquid swallows were more than 0.85 for almost all parameters, except the mean time. The best diagnostic parameter was “esophageal emptying (Tmax + 10sec)” with AUC of 0.933 followed by “transit time” with AUC of 0.929.

On the contrary, the semisolid swallowing gave varying results, most of which with a marginal difference between the 2 swallowing techniques. “Transit time” and “Esophageal emptying (Tmax+ 10sec)” gave a better AUC for multiple swallowing than single swallowing. But the other 4 parameters gave better AUC for a single swallow than multiple swallows.

Table 2 shows the cutoff values of various parameters for each swallowing technique that provided the best diagnostic sensitivity with specificity equal to or more than 75%. The mean transit time of 8.8 sec. and emptying (12 sec) of 82% for multiple liquid swallowing provided the best sensitivity (96%) of all swallowing techniques. The mean time of any technique gave the worse sensitivity.

Table 2. The cutoff values, sensitivities and specificities of the 6 parameters for 4 swallowing techniques that provided the best diagnostic sensitivity with specificity equal to or more than 75%

Parameter	Liquid						Semisolid					
	Single			Multiple			Single			Multiple		
	cutoff	Sens.	Spec.	cutoff	Sens.	Spec.	cutoff	Sens.	Spec.	cutoff	Sens.	Spec.
Tmax (sec.)	5.13	57	75	3.9	82	88	3.6	82	88	5.7	68	75
Transit time (sec.)	12.1	82	100	17.9	89	88	32.7	71	75	40.0	71	75
Mean time (sec.)	7.2	35	75	10.3	29	75	49.2	25	75	12.0	32	88
Mean transit time (sec.)	7.8	79	75	8.8	96	75	66.1	82	75	22.4	57	88
Emptying (Tmax+10sec) (%)	84.0	64	75	84.0	92	75	62.5	79	75	56.0	71	75
Emptying (12sec) (%)	86.0	78	75	82.0	96	75	50.2	75	75	45.0	64	75

Cutoff = cutoff value, Sens. = sensitivity, Spec. = specificity

Discussion

We used the same swallowing techniques as reported by Tatsch K. *et al*. (4, 7, 15) but instead of creating esophageal condensed image, we simply analyzed the time-activity curve to calculate 6 parameters. The result shows that multiple swallows of liquid bolus give the best sensitivity in detection of esophageal function abnormality. This finding is similar to some other reports.(14-15)

On the other hand, using semisolid bolus, surprisingly we found that single swallowing results in a better diagnostic accuracy. By observation during the study, we found that the consistency of the semisolid bolus changed during the imaging. Water evaporation from the bolus resulted in stickier consistency of the bolus. This was an important factor that could cause variations of the parameters of each swallow with the consequent of decreased diagnostic accuracy. It has been shown in other studies that the swallowing duration increases when the consistency of bolus gets thicker. (17) So if one needs to use semisolid bolus, consistency of the bolus should be strictly controlled.

There were other factors that make semisolid bolus not a good choice for the investigation. Some patients could not swallow the whole bolus at once, this caused the bolus to be spread out and resulted in invalid data analysis. There is a study that shows that the efficiency of semisolid bolus swallowing is low even in non-stroke subjects. (18)

Our results show that mean time and Tmax gave the worse diagnostic accuracy especially in liquid bolus which is difference from the study by Tatsch K, *et al*. (4) This may be because both parameters rely on the starting time of image acquisition as a zero time point. If the start of the acquisition time has not been standardized or corrected before data analysis, it will cause inconsistent results. Other reasons may be explained by the study of Ham HR, *et al* (3) who found that in patients with esophageal functional abnormality, the bolus often separated in two parts with different transit times. The rapid transit part of the bolus is usually larger than that with slower transit. This will result in normal or near normal of the mean time and Tmax parameter. While the starting time point has no influence on the mean transit time because there is no timing factor involved in the calculation of this parameter.

In conclusion, multiple-swallowing technique provides a better sensitivity for detection of esophageal functional abnormality. By using the mean transit time of 8.8 sec or emptying (12sec) of 82% of liquid bolus as a cutoff diagnostic value, it results in the best sensitivity of 96%. It seems that liquid bolus gives a better result than semisolid bolus. However, if the consistency of the semisolid bolus had been well-controlled, it might provide a comparable technique.

Acknowledgements

This research is supported by the Ratchadaphiseksomphot Endowment Fund. The authors would like to thank the staff of the Division of Gastroenterology, Department of Internal Medicine Division of Nuclear Medicine, Department of Radiology, Faculty of Medicine for their good collaboration. The authors, hereby, declare no conflict of interest in conducting this study.

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