Original Article

In-house-Prepared Semisolid Bolus for Esophageal Transit Scintigraphy in Normal Volunteers and its Comparison with Liquid Bolus

Abstract

Background/Aims: Esophageal transit scintigraphy (ETS) is a useful tool for evaluating esophageal motility disorders, although conflicting results are seen due to lack of ideal bolus. Semisolid/solid boluses have shown superiority over liquid boluses, and the present study aims to establish the utility of in-house-prepared bolus in normal volunteers and its comparison with liquid bolus. **Materials and Methods:** Thirty-three healthy volunteers were selected for ETS with in-house-prepared semisolid bolus jelly containing ^{99m}Tc-sulfur colloid. Dynamic studies were acquired in anterior projection with single swallow for both supine and sitting positions. T90% esophageal emptying time (EET) was calculated for whole and three equally divided segments of esophagus and also done with liquid bolus on different day. **Results:** The median value of EET for semisolid bolus for whole esophagus in sitting and supine positions was 11.7 s (interquartile range [IQR]: 8.0–16.7) and 17.7 s (IQR: 12.0–33.0). EET of liquid bolus for whole esophagus in sitting and supine positions was 9.3 s (IQR: 8.0–13.3) and 13.0 s (IQR: 9.7–25.0), respectively. Significantly different EET for whole esophagus and lower one-third esophagus between sitting and supine positions was seen for semisolid (whole esophagus; $P = 0.003$, lower one-third esophagus; $P = 0.025$) and liquid boluses (whole esophagus; $P = 0.032$, lower one-third esophagus; $P = 0.016$). Comparing EET using semisolid and liquid boluses, only lower one-third esophagus in supine position showed significant difference ($P = 0.033$). **Conclusions:** In-house-prepared semisolid radiolabeled jelly is inexpensive, easy to prepare with good radiolabeling. Condensed dynamic images from semisolid bolus were better, sharper, and reproducible in comparison to liquid bolus without fragmentation. This study standardized semisolid bolus and verified its suitability for clinical use.

Keywords: *^{99m}Tc-sulfur colloid, esophageal motor disorders, esophageal transit scintigraphy, liquid bolus, semisolid bolus*

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Introduction

Functional symptoms such as heartburn, epigastric pain, and dysphagia caused by gastrointestinal motility disorders are often ignored despite their common occurrence in the general population. The physicians' awareness for the symptoms related to the underlying gastrointestinal dysmotility affords the successful evaluation and treatment of the patients with possible esophageal motor disorders. Apart from clinical history, a variety of methods are employed to diagnose the esophageal motility disorders (EMDs). However, with the exception of radionuclide scintigraphy, majority of methods are invasive/nonphysiological in nature. Esophageal manometry is considered to be gold standard, which provides indirect assessment of peristalsis, but its major drawback is limited availability, less acceptability to the patients due to invasive nature, and requirement of intubation which itself is an abnormal stimulant in the physiological evaluation of esophageal motility.[1]

Esophageal transit scintigraphy (ETS), since its inception, has seen a number of modifications in the initial scintigraphic procedure in the form of quantitative parameters and functional imaging, or both, for studying the normal esophageal motility and its alteration in EMD.[1,2] The utility of ETS has been extensively reported in different EMDs. Moreover, this technique has shown the possibility to measure the outcome of any therapeutic intervention. It seems to be useful when esophageal manometry is not tolerated or unavailable, or with equivocal or negative manometry

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in high suspicion of the disease. However, despite all the inherent merits of the technique, the exact role of ETS in the evaluation of patients with suspected EMD still remains debatable due to lack of a standardized protocol. Several different ways had been adopted to perform the study in the past such as liquid versus solid versus semisolid bolus, supine versus sitting posture, anterior versus posterior acquisition, swallowing techniques, and quantitative parameters, but many a times lacked reproducibility.[1]

This prospective study was carried out to evaluate the in-house-prepared semisolid bolus in assessing esophageal emptying time (EET) in the ETS in the normal individuals and its comparison with liquid bolus in the same population. The study also aimed to establish the normal quantitative parameters, so the same could be used in patients with variety of EMDs.

Materials and Methods

A total of 33 healthy volunteers (27 men and six women) with the mean age of 30.7 ± 5.2 years (range 21–42) were recruited, under this prospective research project, after written informed consent and the institutional ethical committee clearance. Twenty-seven of 33 volunteers underwent the studies with both liquid and semisolid boluses in sitting as well as in supine positions. For the remaining six volunteers, four underwent semisolid study only, and two volunteers had liquid study only in both sitting and supine positions. Overall, 31 volunteers underwent the studies with semisolid bolus and 29 volunteers underwent studies with liquid bolus in both sitting and supine positions.

The study participants had no complaints or signs of any esophageal disease, had not undergone any gastrointestinal surgery, and were not on any gastrointestinal motility affecting drug for the past 4 weeks. None of the participants suffered from systemic diseases such as diabetes mellitus, systemic lupus erythematosus, and multiple sclerosis. The smokers among the study participants were instructed not to smoke for at least 12 h before the study. Those having recent complaints of vomiting/diarrhea and pregnant/lactating females were excluded from the study. Each participant was asked to fast for a minimum of 6 h before ETS. Every participant was explained about the entire procedure and given the practice of swallowing using plain water before the study.

Preparation of bolus

Each liquid bolus was prepared by adding 7.4 MBq (~200 µCi) of ^{99m}Tc-sulfur colloid in 15 ml of water. The in-house semisolid bolus was prepared using the commercially available edible jelly powder (Weikfield Jelly Crystals) containing sugar (90 g/100 g) and gelling agent with total energy value of 375 kCal/100 g. The jelly powder (~10 g) and around 1.5–2.0 mCi of ^{99m}Tc-sulfur colloid were poured in nearly 20 ml of warm water, stirred well, and allowed to set in the refrigerator for a minimum of 2 h. The semisolid bolus weighing around 2 g of jelly containing approximately 7.4 MBq (~200 µCi) of ^{99m}Tc-sulfur colloid was used for single acquisition. The activity of 7.4 MBq has been previously used regularly in our institute and consistently yielded images of high quality. The stability of radiolabeled semisolid jelly was checked by putting it in the water for approximately 2 h, and it was observed that radiotracer did not leach out from the radiolabeled semisolid jelly. The jelly did not get dispersed also during its transit through esophagus once the study participants were asked to gulp in a single swallow.

Acquisition parameters

Every study participant underwent three consecutive study acquisitions with radiolabeled liquid bolus swallow in sitting and supine positions on a single day, followed by similar three consecutive study acquisitions with radiolabeled semisolid bolus in sitting and supine positions on the different day. The participants were asked to clear the residual esophageal activity between the consecutive acquisitions by drinking the sip of water. Dynamic images with high temporal resolution were acquired after intake of liquid and semisolid boluses in the mouth in anterior projection (240 frames, 0.8 s/frame, 64 × 64 matrix) on SMV Sopha DST XL dual-head variable SPECT gamma camera with low energy all-purpose collimator (GE Healthcare, USA). The patients were instructed to gulp the bolus in single swallow with the start of acquisitions and no further swallow till the completion of each acquisition. The imaging field of view was extended from the pharynx to the stomach both in supine and sitting positions.

Qualitative parameters

Using the available software, the information from all the consecutive frames (n = 240) of the study in each region of interest (ROI) was compressed into a single column, displaying the distribution of the tracer from the pharynx to the cardia of the stomach. The columns thus obtained were arranged serially to generate a space and time matrix where vertical and horizontal dimensions represented the spatial and temporal activity changes, respectively, depicting the dynamics of swallowing in cine mode in the form of condensed dynamic images (CDI). CDI elegantly displayed the dynamic data of swallowing in a single image on y-axis and x-axis.

Quantitative parameters

EET was calculated for all the volunteers after drawing a ROI on the esophagus extending from hypopharynx to gastroesophageal junction for the whole and computer generator segmental esophagus ROIs. Whole EET (T90%) represented the time from maximum activity of the bolus in the proximal esophagus to the clearance of 90% from the entire esophageal ROI. Segmental EETs for upper (U), middle (M), and lower (L) segments (U1/3 T90%, M1/3

T90%, and L1/3 T90%) of esophagus were defined as the time taken for clearance of 90% of the maximal activity in each segment.

Whole and segmental EET were compared for both positions, i.e., supine and sitting and also for both radiolabeled boluses, i.e., liquid and semisolid in the same volunteer. Emptying time for each scintigraphic study was evaluated after three separate swallows. Only the two best out of three studies were selected which were closely related to each other and did not show any fragmentation of bolus or aberrant swallow during the study period. The mean of the two values was taken for the analysis of EET.

Statistics

Data were analyzed using the Statistical Package for the Social Software (SPSS, version 21 Chicago, IL, USA). Normality of quantitative data was analyzed with Shapiro–Wilk test along with visual inspection of histogram, Q-Q plot, and box plot. Because the continuous data were found to have skewed distribution, the quantitative parameters for both types of bolus and positions were calculated as median with interquartile range (25^{th}–75^{th} percentiles). In addition to the quantitative parameters, CDI were also obtained in both types of bolus and position. The time activity curves were generated without background subtraction. Paired *t*-test was applied on each volunteer to calculate the significance of difference between both types of boluses in both the position for whole as well as segmental esophagus. $P < 0.05$ at 95% confidence interval was considered to be statistically significant.

Results

This prospective study comprised of 33 healthy volunteers underwent esophageal transit scintigraphic studies thrice with both semisolid and liquid boluses in sitting and supine positions. The 90% emptying of the semisolid and liquid bolus in sitting and supine positions for the whole and segmental esophagus is mentioned in Tables 1 and 2.

Semisolid bolus

The median values of the 90% emptying of the semisolid bolus for the whole esophagus in the sitting and supine positions were 11.7 s (range: 8.0–16.7) and 17.7 s (range: 12.0–33.0), respectively [Figures 1 and 2]. There was a significant difference in the 90% emptying time of the semisolid bolus between the sitting and supine position for the whole esophagus ($P = 0.003$) and lower third of esophagus ($P = 0.025$), but the difference in 90% emptying time in the upper third ($P = 0.135$) and middle third ($P = 0.132$) of esophagus was nonsignificant [Table 1].

Liquid bolus

The mean values of the 90% emptying of the liquid bolus for the whole esophagus in the sitting and supine positions were 9.3 s (range: 8.0–13.3) and 13.0 s (range: 9.7–25.0), respectively [Figures 3 and 4]. Again, there was a significant difference in the 90% emptying time of the liquid bolus between the sitting and supine position for the whole esophagus ($P = 0.032$) and the lower third esophagus ($P = 0.016$), but no significant difference was seen in the upper third ($P = 0.107$) and middle third ($P = 0.097$) of esophagus as seen with semisolid bolus [Table 2].

Comparison between semisolid and liquid boluses

In supine position, significant difference in 90% emptying time in the lower third of esophagus was observed using semisolid and liquid boluses ($P = 0.033$). However, it was nonsignificant in the upper ($P = 0.134$) and middle third of esophagus ($P = 0.756$) as well as in the whole esophagus ($P = 0.082$).

In the sitting position, we did not find any significant difference in 90% emptying time between semisolid and liquid boluses in the whole ($P = 0.171$) as well as in the segmental esophagus (upper $P = 0.132$, middle $P = 0.201$, and lower $P = 0.101$, respectively).

Table 1: Mean 90% EET for semisolid bolus for segmental and whole esophagus

	Sitting position (seconds)	Supine position (seconds)	Difference of EET between sitting & supine (*P*)
Upper 1/3rd of esophagus	2.5±1.0 (1.3-6.3)	2.9±1.2 (1.3-6.5)	0.135
Middle 1/3rd of esophagus	4.8±2.8 (2.7-13.5)	6.3±4.4 (2.5-23.3)	0.132
Lower 1/3rd of esophagus	12.8±14.0 (3.3-1.0)	24.6±27.7 (6.0-14.0)	0.025
Whole esophagus	18.3±21.0 (5.7-110.0)	36.1±42.4 (8.7-180.0)	0.003

EET: esophageal emptying time

Table 2: Mean 90% EET for liquid bolus for segmental and whole esophagus

	Sitting position (seconds)	Supine position (seconds)	Difference of EET between sitting & supine (*P*)
Upper 1/3rd of esophagus	2.8±1.2 (1.0-6.0)	3.2±1.6 (1.5-7.3)	0.107
Middle 1/3rd of esophagus	5.0±1.9 (1.9-9.3)	6.2±3.3 (2.3-18.3)	0.097
Lower 1/3rd of esophagus	8.0±3.9 (4.0-20.5)	15.5±16.5 (5.0-89.0)	0.016
Whole esophagus	12.1±6.7 (7.0-34.0)	22.5±24.2 (6.0-105.0)	0.032

EET: esophageal emptying time

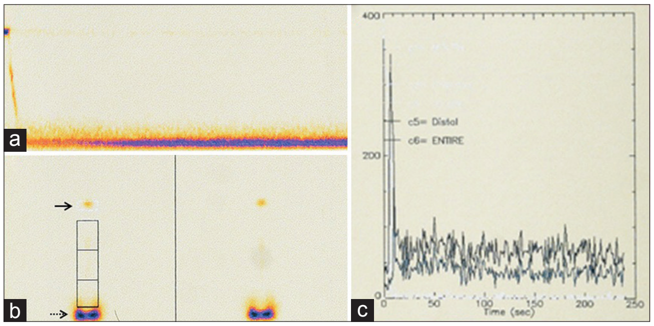

Figure 1: Esophageal transit scintigraphy done with semisolid bolus in sitting position in 25-year-old woman showing condensed dynamic images (a), whole and segmental esophageal region of interest showing transit of semisolid bolus (b) (solid arrow shows tracer activity in the mouth; broken arrow shows tracer activity in the proximal stomach), whole and segmental esophageal time activity curves (c)

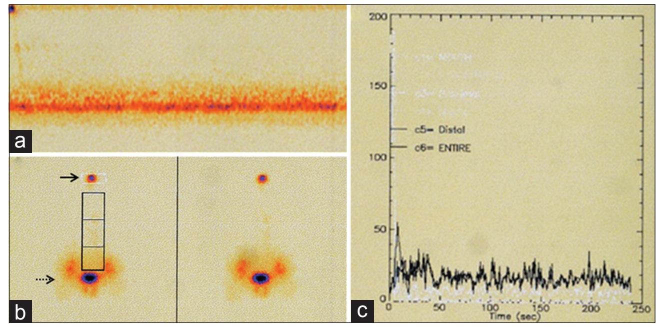

Figure 2: Esophageal transit scintigraphy done with semisolid bolus in supine position in 25-year-old woman showing condensed dynamic images (a), whole and segmental esophageal region of interest showing transit of semisolid bolus (b) (solid arrow shows tracer activity in the mouth; broken arrow shows tracer activity in the proximal stomach), whole and segmental esophageal time activity curves (c)

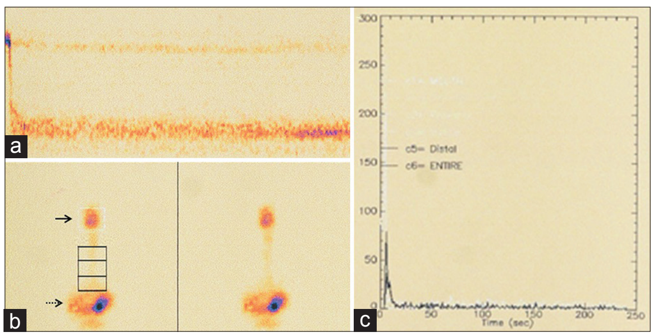

Figure 3: Esophageal transit scintigraphy done with liquid bolus in sitting position in 29-year-old man showing condensed dynamic images (a), whole and segmental esophageal region of interest showing transit of liquid bolus (b) (solid arrow shows tracer activity in the mouth; broken arrow shows tracer activity in the proximal stomach), whole and segmental esophageal time activity curves (c)

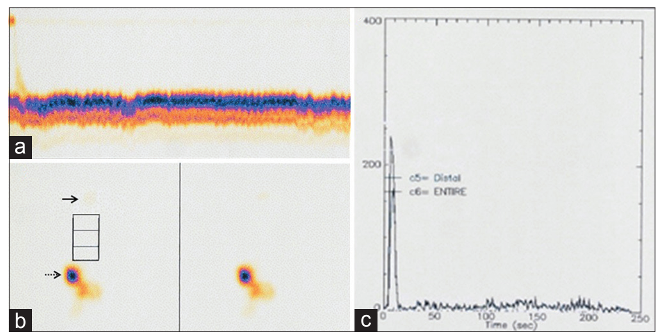

Figure 4: Esophageal transit scintigraphy done with liquid bolus in supine position in 29-year-old man showing condensed dynamic images (a), whole and segmental esophageal region of interest showing transit of liquid bolus (b) (solid arrow shows tracer activity in the mouth; broken arrow shows tracer activity in the proximal stomach), whole and segmental esophageal time activity curves (c)

CDI derived for both liquid and semisolid boluses (in-house-prepared radiolabeled jelly) were normal and showed normal transit pattern without any delay or stasis of activity throughout the esophagus. However, CDI derived from semisolid bolus showed better, sharper, and reproducible images in comparison to the liquid bolus in all the study participants without fragmentation.

Discussion

Kazem in 1972 first described ETS to evaluate the esophageal motility[2] and soon it became a popular option for the evaluation of EMD, being physiological, useful, well-tolerated, performed on outpatient basis, convenient for repeated studies, and noninvasive in nature in comparison to the esophageal manometry. The scintigraphy provides a reproducible quantitative assessment of physiological transit through various segments of the esophagus without any significant whole-body radiation burden.

Esophageal transit is the time required for liquid, solid, or semisolid boluses to transit through esophagus. ETS done with radioactive liquid boluses (water or juices) has shown to be convenient, safe, and reproducible technique, and normal transit time has shown a reference range of 6–15 s.[3-5] Parkman *et al*. in their study of 89 patients of nonobstructive esophageal dysphagia showed that ETS helped in establishing the diagnostic criteria for different esophageal conditions by measuring the esophageal transit time (normal value: <14 s) and retention at 10 min (normal: <18%).[6] However, the liquid bolus itself is not suitable for the assessment of esophageal emptying as its transit is assisted by gravity, although studies acquired in supine position eliminate the assistance of gravity but that is not physiological. The liquid bolus may get fragmented or stuck to esophageal mucosa during its transit, which would provide an erroneous EET. While ETS done with semisolid or solid food is more physiological in nature as they represent a greater challenge to esophageal function and have been shown to be more sensitive for esophageal dysfunction.[1] Semisolid bolus has been used in only few studies because of difference in consensus on the viscosity and nature of semisolid bolus.[7,8] Semisolid boluses are easily swallowed on command and more acceptable then solid boluses to the volunteers undergoing repeat ETS. The solid bolus may get retained in the esophagus for longer time even when other investigations including manometry being normal. The semi- or solid boluses used were baby paste of instant porridge, gelatin capsules of antibiotics, cooked chicken cubes, or eggs.[7-12]

In our study group, normal volunteers were studied with liquid bolus in sitting and supine positions for EET without any significant difference in the upper and middle third of esophagus in EET ($P > 0.05$) between sitting and supine positions. However, a significant difference in the lower one-third and whole esophagus ($P < 0.05$) was observed which had been explained due to pharyngeal pump mechanism in the previous studies.[13-15]

The pharyngeal ejection force propels the leading edge of a liquid bolus to gastro-esophageal junction immediately leaving minimal work to be done by peristalsis. More viscous bolus is propelled over the proximal half of the esophagus, thus requiring more intense peristaltic action to complete transport over the distal half. Thus transit of viscous bolus might reflect peristaltic activity more adequately, particularly in the distal esophagus. Taillefer *et al*.[16] in their study comprising of forty normal volunteers (23 men) showed that EET obtained with liquid bolus in supine position was 1.5 ± 0.5 s, 3.5 ± 1.0 s, and 6.0 ± 2.5 s for upper, middle, and distal esophageal segments, respectively, whereas the emptying time for the entire esophagus in their study was of 9.0 ± 2.5 s with < 10% of residual radioactivity of maximal activity at 2 min in the given ROI, though other investigators showed different values by taking different parameters. Jørgensen *et al*.[4] performed ETS study with liquid in sitting and supine positions and showed significant difference because of the postures with higher values in supine position. Our values for 90% EET for liquid bolus were slightly higher than reported in literature. This was probably due to our technique where we allowed only single swallow to volunteers with each bolus and no more dry swallows were permitted, to avoid aberrant swallow during the acquisition. Klein and Wald[17] in their study of radionuclide ETS in normal controls found that 19% from the control group were abnormal by the criteria of Taillefer *et al*. because of aberrant swallows, and a second swallow was needed to empty the esophagus

In the present study, normal volunteers undergoing EET similarly with semisolid boluses in both sitting and supine positions showed that EET was not significantly different in upper and middle third of the esophagus ($P > 0.05$), but it was significantly different for lower third and whole esophagus ($P < 0.05$). We also compared 90% emptying for semi-solid and liquid boluses in supine position and found significant difference in the lower third esophagus ($p<0.05$) between two different boluses, which might be explained by peristaltic motion of oesophagus, though whole oesophagus, upper and middle third of esophagus did not show statistically significant difference. Even literature has shown that in supine position, solid bolus is more sensitive to detect the subtle changes occurring in EMD from normal volunteers.[18] We did not find statistically significant difference in whole and segmental esophagus using semisolid and liquid boluses in the sitting position. The upright position provides a better physiologic evaluation in relation to normal swallowing and deglutition but gravity augments in propagation of bolus, while in supine position without the help of gravity, it is only esophageal motor activity which propels the bolus forward.[19] It is seen that in supine position, the esophageal transit time is prolonged which can detect the lesion more effectively than sitting position. A study in 28 patients of amyotrophic lateral sclerosis using semisolid and liquid bolus showed that the semisolid bolus produced a higher proportion of pathologic values for the swallowing variables than the liquid bolus.[20] The variation in normal values in semisolid bolus may also be due to difference in ingredients of semisolid prepared differently by different investigators; our values are slightly higher than the values reported in other studies which may be due to difference in the viscosity of the bolus. As the viscosity increases, the esophageal emptying slows down considerably. Esophageal transit of semisolid and solid boluses is significantly slower than that for liquid bolus.[21]

Abnormal swallows had shown fragmentation of bolus in some of the studies. It had been shown that successive swallowing at short intervals interfered with normal contraction pattern, because of interruption of peristaltic wave.[22] Sand *et al*. in their study of 49 healthy volunteers using krypton-81 m liquid bolus showed that only less than half of them had good bolus without fragmentation, whereas the remaining volunteers had residual esophageal activity. They concluded that when test was correctly performed, no esophageal residual activity was observed.[23] Jørgensen *et al*. also found high variation in residual activity in healthy volunteers.[4] In our study, we took the 90% EET as a parameter for esophageal emptying anticipating that complete clearance of radiolabeled tracer would not be achieved during the acquisition period, and nonfragmentation of each bolus during transit was screened before including it for final transit calculation.

The present study was undertaken to evaluate the role of in-house-prepared radiolabeled semisolid jelly in ETS and its comparison with liquid bolus in normal volunteers. Our purpose of using in-house-prepared radiolabeled ^{99m}Tc-sulfur colloid semisolid jelly was to establish its utility as semisolid meal in ETS by looking for its ease of preparation, appropriate binding, inexpensive, and stability during swallowing in the routine practice for ETS. The radiolabeled semisolid bolus was acceptable to volunteers with consecutive multiple swallows in a single session. CDI from in-house-prepared semisolid bolus showed better, sharper, and reproducible images than obtained with liquid in all volunteers without fragmentation. Esophageal scintigraphy and quantitative parameters have been used to assess the treatment response evaluation in patients suffering from malignant or benign conditions.[24-26] A case report distinctly showed the utility of ETS along with

CDI in a symptomatic patient after 3 months of antireflux surgery (Nissen fundoplication), revealing the reflux of semisolid bolus up to mid-esophagus, whereas other investigations (24-h pH monitoring and manometry) were normal.[27] To the best of our knowledge, the semisolid bolus prepared with commercially available edible jelly has never been used before. The exact clinical role of ETS is yet to be defined precisely, but it offers unique characteristics in ETS. Objective quantification of esophageal emptying as a follow-up of either medical or surgical management of esophageal disorders is certainly a valuable technique.

We attempted to standardize a semisolid meal (jelly) for esophageal transit and its suitability for clinical use by establishing the emptying time in normal volunteers. Nonfragmentation and easy swallows of this semisolid meal indicate its acceptability. Opportunity was taken to compare the liquid versus semisolid bolus to evaluate the emptying of the esophagus. CDI generated with the semisolid meal were clearer. This in-house-prepared bolus may discern the transit delay in patients with esophageal motor disorders compared with normal volunteers in the future studies.

Conclusion

This study showed that in-house prepared semi-solid bolus may be standardized with its suitability for clinical use in evaluating the esophageal transit time. The in-house prepared semi-solid radiolabeled jelly was inexpensive, easy to prepare with good radio-labeling. Condensed dynamic images from semi-solid bolus were better, sharper and reproducible in comparison to liquid bolus without any fragmentation during esophageal transit.

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Conflicts of interest

There are no conflicts of interest.

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