Transition zone defect in patients with motor Dysphagia: A Series of Four patients

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ABSTRACT

Introduction: The primary function of the oesophagus is to transfer of liquids and solids to the stomach. There is distinct muscle type as well contraction type above and below transition zone. Defect in coordination and contraction of muscle in this region may leads to abnormal bolus transport resulting in dysphagia. Concurrent high resolution manometry (HRM) and digital fluoroscopy studies showed that defect in transition zone (TZ) was associated with incomplete bolus transport and dysphagia. **Aim:** To evaluate the frequency of transition zone defect responsible for dysphagia in our primary dysphagia patients and also to evaluate response to drugs. **Methods:** From July 2010 to December 2012, we performed the HRM on patients with motor dysphagia who were referred for esophageal function testing. Each patient received 10 liquid swallows. We analyzed the results and the manometric findings. Two of the subjects had additional ambulatory 24-h pH study performed to diagnose gastroesophageal refl ux disease (GERD). **Results:** Among 250 patients, four patients (three male, median age 54 y, range 30-78) had wide transition zone. All four had dysphagia, three predominantly to solid food. Esophago-gastroduodenoscopy was normal in all except one, who had Los Angeles grade A esophagitis. All except one patient with acid reflux had responded poorly to prokinetic therapy. **Conclusion:** Approximately 2% patients with primary motor dysphagia had wide transition zone and they responded poorly to prokinetic therapy.

Keywords: Dysphagia, high resolution pressure topography, Transition zone, Wide transit zone

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INTRODUCTION

Primary function of esophagus is to transport the food bolus from mouth to stomach. Abnormalities in esophageal motility may lead to defect in bolus transport leading to dysphagia. Recent technological advances in esophageal manometry help in better imaging of peristaltic contraction with pressure morphology. Concurrent high resolution manometry and digital fluoroscopy studies [1, 2, 3] showed that defect in transition zone (TZ) was associated with incomplete bolus transport and dysphagia. TZ exist between proximal and distal esophageal contractile segments.

Previous study has shown that break of <2 cm in length in 20 mm Hg isobaric contour or < 3 cm in length in 30 mmHg isobaric contour was associated with complete bolus clearance.[4] Fox M et al[1] reported a case of dysphagia related to wide TZ. They have shown by videofluoroscopy that widened TZ is associated with bolus escape at level of TZ.[1] Combination of both temporal prolongation (>1 sec) and spatial gap (>2 cm in 20 mmHg isobaric contour) was strongly associated with dysphagia.[5] Literature on prevalence of transition zone defect among patients with motor dysphagia and effect of prokinetic therapy on their symptoms are scanty.

AIM & OBJECTIVES: To evaluate the frequency of transition zone defect responsible for dysphagia in our primary dysphagia patients and also to evaluate response to drugs.

MATERIAL AND METHODS:

Study type: Retrospective analysis of symptoms, all manometric data, other investigations as well as response to various drugs.

Study duration: Two and half year period (July 2010 –Dec 2012)

Study subjects: All adult patients with primary motor dysphagia referred to Gastrointestinal Motility unit of Advanced Medical Research Institute (AMRI), Salt Lake, Kolkata were evaluated with high resolution pressure topography (HRPT).

Study process

During two and half years period (July 2010 –Dec 2012), total 250 consecutive patients with primary motor dysphagia referred to Gastrointestinal Motility unit of Advanced Medical Research Institute (AMRI), Salt Lake, Kolkata were evaluated with high resolution pressure topography (HRPT). Among them four patients had wide transition zone.

Past medical record were examined to look for history, previous investigation reports and therapy received by patients. All data were analyzed retrospectively. The study was approved by our institution's Ethics Committee, and all patients provided informed consent.

Esophageal manometry

HRPT was performed water perfused 16 channel catheter which has 8 channels 1 cm apart at the lower end and the remaining 8 channels 3 cm apart (Dent sleeve International Limited, manufactured by Mui scientific, Ontario, Canada). The data were analyzed using Trace 1.2 V software (Geoff Hebbard, Royal Melbourne Hospital, Victoria, Australia). The manometry catheter was introduced into stomach through nasal route. The manometric protocol included a 1 minute period to assess basal sphincter pressure and ten 5 mL water swallows at 30 seconds interval obtained in a supine position. Barium esophagogram, upper gastrointestinal endoscopy finding and other reports were recorded where available.

Length of esophagus (L_E) was obtained from mid upper esophageal sphincter (UES) to mid lower esophageal sphincter (LES) from spatial variation of intra-esophageal pressure during catheter pull through at beginning of manometric study. Center of TZ was defined as location of nadir pressure amplitude (P_{TZ}) in TZ area. Nadir pressure amplitude at center of TZ was obtained with references to intra-thoracic pressure. Upper and lower end of TZ was identified by spatial variation in pressure amplitude along peristaltic contraction. TZ length was obtained from distance between upper and lower end of TZ. Temporal separation was defined as time difference between upper and lower margin of TZ. In our series we considered to have widened TZ if swallow has both temporal prolongation (>1 sec) and spatial elongation (>2 cm in 20 mmHg isobaric contour).[5]

Statistical analysis:

Clinical variables obtained from the medical records were summarized using median and range. Manometric parameters were summarized using mean and standard deviation (SD).

RESULTS:

Of 250 patients with motor dysphagia evaluated by HRPT, 6 patients had widened TZ. Two patients were excluded because two had diffuse weak peristalsis. Patients' characteristics were given in Table 1.

Table. 1 Clinical characteristic of patients

	Age(yr)	Sex	Dysphagia duration (months)	Regurgitation	EGD	CT thorax & neck	24 hr pH study
Case 1	36	M	60	No	Normal	WNL	Percentage of overall time at pH below 4 – 2.1%.
Case 2	47	M	48	No	Normal	--	--
Case 3	39	F	78	No	Normal	WNL	--
Case 4	45	M	30	Yes	LA Gr A esophagitis	--	Percentage of overall time at pH below 4 – 10.2%, Deemester score - 30

EGD, Esophagogastroduodenoscopy; LA Gr A,Los Angeles Grade A; WNL, within normal limit;

All four patients presented with dysphagia (median 54, 30 – 78 months), three had predominant symptoms to solid food and one had symptom to both solid and liquid. Only one patient had history of burning sensation in chest and epigastric region. None had history of nasal regurgitation, bolus obstruction and weight loss. Esophagogastroduodenoscopy was normal in all except Los Angeles grade A esophagitis in one. Barium swallow studies were normal in all patients.

Computed tomography of neck and chest was available in two patients and did not reveal any extramural lesion. The result of previous conventional manometry study was available in two patients and both were normal. HRPT revealed wide transition zone with normal proximal contractile velocity, proximal contractile integrity and distal contractile integrity in all. (Table 2)

Table 2. Manometric parameters (analysis of ten swallow of each patient)

	L_E (cm)	Length of TZ (L_{TZ}) (cm)	Temporal delay (sec)	PCV (cm/sec)	PCI (mmHg cm sec)	DCI (mmHg cm sec)
	Mean ±SD Range	Mean ±SD Range	Mean ±SD Range	Mean ±SD Range	Mean ±SD Range	Mean ± SD Range
Case 1	24±1.8 (24-27)	3.7±0.5 (3-4.4)	3.4±0.6 (2.15-4.13)	3.3±0.7 (1.9-4.1)	581±322 (276-1178)	1633±620 (901-2809)
Case 1 Post treatment P value	--	3.4±0.5 (2.8-4.2) P = 0.1	3.2±0.5 (2.2-3.9) P = 0.46	--	--	--
Case 2	24.9±0.9 (24-26)	3.6±0.42 (2.9-4.1)	3.1±0.6 (2.1-3.9)	3±0.7 (1.8-3.5)	571±270 (310-1078)	1626±582 (890-2768)
Case 3	27±1.1 (26-28)	3.5±0.4 (3-4.1)	3.2±0.5 (2.3-4)	2.9±0.7 (2-4.1)	691±336 (336-1230)	1622±792 (800-3124)
Case 4	21.8±0.8 (21-23)	3.9±0.5 (3.1-4.7)	3.3±0.5 (2.5-3.9)	2.9±0.7 (1.7-3.9)	597±354 (166-1146)	1444±481 (893-2390)

L_E, Length of esophagus; L_{TZ}, Length of transition zone; PCV, Proximal contractile velocity; PCI, Proximal contractile integrity; DCI, Proximal contractile integrity

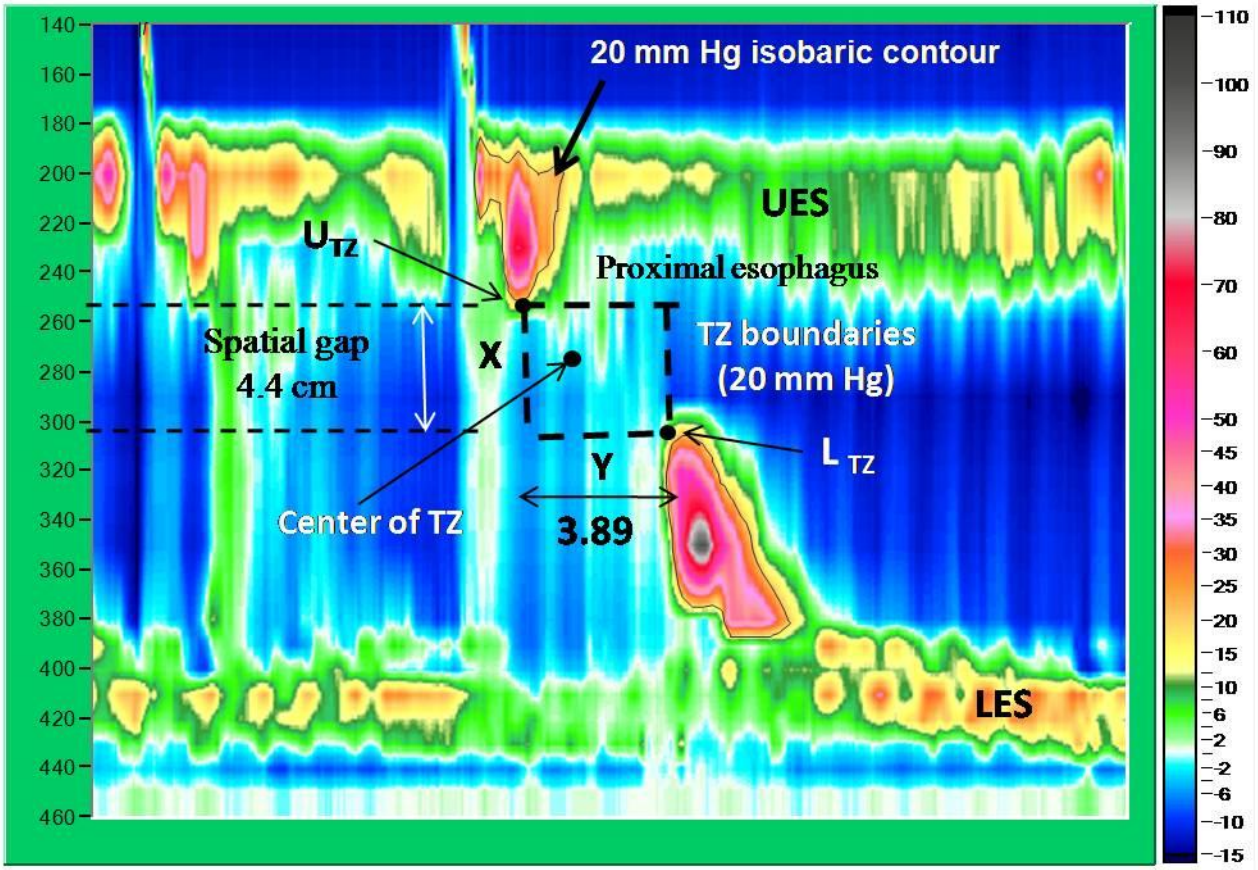

Figure. 1 Pressure topography plot during a peristaltic contraction. Pressure magnitude is encoded in color corresponding to the scale shown at the right side. 20 mmHg isobaric contour was defined. Upper margin of TZ (U_{TZ}) and lower margin of TZ (L_{TZ}) is derived from 20 mm Hg isobaric contour. A TZ boundary (20 mm Hg) is defined. The spatial (*X*) and temporal (*Y*) dimensions of the TZ are shown.

Transition zone length accounts for average 15% (± 2.05, 12.9-17.8) of total esophageal length. Pressure difference among upper and mid esophagus depicted in fig.1 by isobaric pressure zone. There was good relaxation of LES on swallow. Ambulatory 24 hours intra-esophageal pH-metry study was available in one patient before HRPT and report was normal. We did ambulatory 24 hours intra-esophageal pH metry study in a patient with esophagitis and significant acid reflux was observed.

All patients received various prokinetic (DOMPERIDON, ITOPRIDE, LEVOSULPRIDE) during their treatment period. Patients had continued one prokinetic at least for three months before changing onto next one were included in analysis. A patient with significant acid reflux showed improvement with proton pump inhibitor and prokinetic combined therapy. Other three patients showed only

partial improvement in their dysphagia. HRPT was repeated in one patient after one and half year of treatment. There was mild decrease in TZ length after therapy though it was not significant.

DISCUSSION

Since introduction into clinical practice HRPT has been focused mainly into abnormality of distal esophagus and esophago-gastric junction for evaluation of motor dysphagia. While the Chicago classification has extensively characterized contraction abnormality of distal esophagus, but proximal esophageal contraction has not been well described.[6] There are scanty data on abnormality of transition zone in genesis of dysphagia. As per knowledge this first series of transition zone defect in India.

Esophageal peristalsis is neurophysiological process by which bolus transferred to stomach. Neurophysiology and muscle physiology of upper, mid and lower esophagus is complex and different.

Histologically proximal 5% of esophagus is composed of fully striated muscle fiber. Subsequent 35-40% of esophageal length has both striated and smooth muscle.[7] TZ is the area where there is progressive transition from striated muscle to smooth muscle.

Transition in muscle physiology has been associated with reduction in muscle contraction and pressure, shown in conventional manometric study [8] and pressure topographic study.[9, 10]

Bolus transit through TZ depends on smooth coordination between proximal and distal segment of esophagus.

In our series, we found TZ defect was responsible for dysphagia in 1.6% (4/250) of patients. While Ghosh et al found TZ abnormality in <4 % of unexplained dysphagia patients.[5] In our series, three out of six patients had symptoms of gastro-esophageal reflux disease (GERD) as well as had significant reflux in ambulatory 24 hours intra-esophageal pH-metry study. Two had diffuse weak peristaltic contraction and one had widened transit zone (TZ length: 3.9 ± 0.5 cm, Temporal delay: 3.3±0.5 sec, 18% of total esophageal length) with normal PCI and DCI.

Other three patients did not have any symptoms suggestive of reflux. Ambulatory 24 hours intra-esophageal pH-metry study was done in only one patient without symptoms of reflux. We did not perform pH study in others two patients. Patients with diffuse weak peristaltic contraction were excluded from analysis of cause of dysphagia as widened TZ could

be attributed to weak proximal and distal segment contraction.

In our current work, we did not establish direct correlation between TZ defect and impaired bolus transit by concurrent video fluoroscopy. Previous studies already have established this correlation.[1, 2, 3]

Very few studies are available on treatment response in this category of patients. Most of previous studies were case series or done in asymptomatic individual. Tegaserod improves mid esophageal contractility and reduce proximal transition zone resulting in bolus transit.[11]

Cisapride has shown to improve proximal smooth muscle contraction in asymptomatic individuals.[12]

Both these drugs are not available in market now. Other prokinetic was used in all four patients. Only patient with reflux had improvement in dysphagia symptoms. Other three did not have significant improvement of symptoms. We don't know reason for this improvement in reflux patient. As prokinetic drug has good effect on smooth muscle of lower esophagus that reduces reflux episode or improved clearance of acidic fluid. Symptoms improvement might be related to these effects. Other patients did not improve as these prokinetics have little effect on skeletal muscle of upper esophagus. Esophageal dysmotility might be secondary to esophagitis and reflux of acidic fluid. Symptomatic improvement might be attributed to reduction in reflux after prokinetic and proton pump inhibitor therapy.

In our retrospective series, three out of four patients had dysphagia predominantly to solid food. All had intermittent symptoms. Reason for this is still unclear, need more intensive evaluation with concurrent HRPT and video fluoroscopy during solid food swallow. Dysphagia predominantly to solid food might be related to greater dependency of solid food on esophageal peristalsis and smooth coordination in TZ for complete clearance.

CONCLUSION

In conclusion, wide TZ is rare but important cause for unexplained motor dysphagia. During evaluation of unexplained dysphagia, we need to analyze proximal segment separately in addition to distal segment and LES. Patients with wide TZ responded poorly to conventional treatment.

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