

Appendix

Supplementary Tables

Table S1. Case report form.

Date: _____	ID: _____
Case report form	
1. Demographic information	
1.1 Age _____	
1.2 Birthday _____	
1.3 Gender _____ 0. Female 1. Male	
1.4 Height _____ cm	
1.5 Weight _____ Kg	
1.6 Marriage _____ 0. Married 1. Unmarried 2. Divorced 3. Widowed	
1.7 Family Size _____	
1.8 Education Level _____ 0. Primary school or below 1. Middle school or above	
2. Living habits	
2.1 Do you smoke or have you ever smoked? _____ 0. No 1. Yes	
2.2 Do you drink or have you ever drunk? _____ 0. No 1. Yes	
2.3 How fast do you eat? _____ 0. Slow 1. Moderate 2. Fast	
2.4 How about the food temperature? _____ 0. Cold 1. Moderate 2. Hot	
2.5 Do you eat dry or liquid food? _____ 0. Dry 1. Moderate 2. Liquid	
2.6 How often do you eat vegetables? _____ 0. Hardly (less than once per week) 1. Occasionally (one to three times per week) 2. Often (more than four times per week)	
2.7 How often do you eat fruit? _____ 0. Hardly (less than once per week) 1. Occasionally (one to three times per week) 2. Often (more than four times per week)	
2.8 How often do you eat spicy food? _____ 0. Hardly (less than once per week) 1. Occasionally (one to three times per week) 2. Often (more than four times per week)	
2.9 What is your drinking water source? _____ 0. Shallow well or others 1. Deep well water (Closed motorized well greater than 100 meters)	

Table S2. The Adult Functional Gastrointestinal Disease Rome III Diagnostic Questionnaire.

Question	Answer
	0. Never → <i>Skip to question 4</i>
1. In the last 3 months, how often did you have a feeling of a lump, fullness or something stuck in your throat?	1. Less than one day a month 2. One day a month 3. Two to three days a month 4. One day a week 5. More than one day a week 6. Every day
2. Have you had this feeling 6 months or longer?	0. No 1. Yes
3. Does this feeling occur between meals (when you are not eating)?	0. No 1. Yes

- | | | |
|---------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| 4. When you are eating or drinking does it hurt to swallow? | <ul style="list-style-type: none"> 0. Never or rarely 1. Sometimes 2. Often 3. Most of the time 4. Always 0. Never → | <i>Skip to question 8</i> |
| 5. In the last 3 months, how often did you have pain or discomfort in the middle of your chest (not related to heart problems)? | <ul style="list-style-type: none"> 1. Less than one day a month 2. One day a month 3. Two to three days a month 4. One day a week 5. More than one day a week 6. Every day | |
| 6. Have you had this chest pain 6 months or longer? | <ul style="list-style-type: none"> 0. No 1. Yes | |
| 7. When you had your chest pain, how often did it feel like burning? | <ul style="list-style-type: none"> 0. Never or rarely 1. Sometimes 2. Often 3. Most of the time 4. Always 0. Never → | <i>Skip to question 10</i> |
| 8. In the last 3 months, how often did you have heartburn (a burning discomfort or burning pain in your chest)? | <ul style="list-style-type: none"> 1. Less than one day a month 2. One day a month 3. Two to three days a month 4. One day a week 5. More than one day a week 6. Every day | |
| 9. Have you had this heartburn (burning pain or discomfort in the chest) 6 months or longer? | <ul style="list-style-type: none"> 0. No 1. Yes | |
| 10. In the last 3 months, how often did food or drinks get stuck after swallowing or go down slowly through your chest? | <ul style="list-style-type: none"> 0. Never → 1. Less than one day a month 2. One day a month 3. Two to three days a month 4. One day a week 5. More than one day a week 6. Every day | <i>Skip to question 13</i> |
| 11. Was the symptom of food sticking associated with heartburn? | <ul style="list-style-type: none"> 0. Never or rarely 1. Sometimes 2. Often 3. Most of the time 4. Always | |
| 12. Have you had this problem 6 months or longer? | <ul style="list-style-type: none"> 0. No 1. Yes | |
| 13. In the last 3 months, how often | <ul style="list-style-type: none"> 0. Never → | <i>Skip to question 15</i> |

did you feel uncomfortably full after a regular - sized meal?

1. Less than one day a month
2. One day a month
3. Two to three days a month
4. One day a week
5. More than one day a week
6. Every day

14. Have you had this uncomfortable fullness after meals 6 months or longer?

0. No
1. Yes

0. Never →

Skip to question 17

15. In the last 3 months, how often were you unable to finish a regular size meal?

1. Less than one day a month
2. One day a month
3. Two to three days a month
4. One day a week
5. More than one day a week
6. Every day

16. Have you had this inability to finish regular size meals 6 months or longer?

0. No
1. Yes

0. Never →

Skip to question 26

17. In the last 3 months, how often did you have pain or burning in the middle of your abdomen, above your belly button but not in your chest?

1. Less than one day a month
2. One day a month
3. Two to three days a month
4. One day a week
5. More than one day a week
6. Every day

18. Have you had this pain or burning 6 months or longer?

0. No
1. Yes
0. Never or rarely

19. Did this pain or burning occur and then completely disappear during the same day?

1. Sometimes
2. Often
3. Most of the time
4. Always
0. Very mild

20. Usually, how severe was the pain or burning in the middle of your abdomen, above your belly button?

1. Mild
2. Moderate
3. Severe
4. Very severe

21. Was this pain or burning affected by eating?

0. Not affected by eating
1. Worse pain after eating
2. Less pain after eating
0. Never or rarely

22. Was this pain or burning relieved by taking antacids?

1. Sometimes
2. Often

- | | | |
|-------------------------------------------------------------------------------------------------------------------------------|------------------------------|----------------------------|
| | 3. Most of the time | |
| | 4. Always | |
| | 0. Never or rarely | |
| 23. Did this pain or burning usually get better or stop after a bowel movement or passing gas? | 1. Sometimes | |
| | 2. Often | |
| | 3. Most of the time | |
| | 4. Always | |
| | 0. Never or rarely | |
| 24. When this pain or burning started, did you usually have a change in the number of bowel movements (either more or fewer)? | 1. Sometimes | |
| | 2. Often | |
| | 3. Most of the time | |
| | 4. Always | |
| | 0. Never or rarely | |
| 25. When this pain or burning started, did you usually have softer or harder stools? | 1. Sometimes | |
| | 2. Often | |
| | 3. Most of the time | |
| | 4. Always | |
| | 0. Never → | <i>Skip to question 28</i> |
| | 1. Less than one day a month | |
| | 2. One day a month | |
| 26. In the last 3 months, how often did you have bothersome nausea? | 3. Two to three days a month | |
| | 4. One day a week | |
| | 5. More than one day a week | |
| | 6. Every day | |
| 27. Did this nausea start more than 6 months ago? | 0. No | |
| | 1. Yes | |
| | 0. Never → | <i>Skip to question 33</i> |
| | 1. Less than one day a month | |
| | 2. One day a month | |
| 28. In the last 3 months, how often did you vomit? | 3. Two to three days a month | |
| | 4. One day a week | |
| | 5. More than one day a week | |
| | 6. Every day | |
| 29. Have you had this vomiting 6 months or longer? | 0. No | |
| | 1. Yes | |
| | 0. Never or rarely | |
| | 1. Sometimes | |
| 30. Did you make yourself vomit? | 2. Often | |
| | 3. Most of the time | |
| | 4. Always | |
| 31. Did you have vomiting in the last year that occurred in separate episodes of a few days and then stopped? | 0. Never or rarely | <i>Skip to question 33</i> |
| | 1. Sometimes | |
| | 2. Often | |
| | 3. Most of the time | |

	4. Always	
32. Did you have at least three episodes during the past year?	0. No	
	1. Yes	
	0. Never →	<i>Skip to question 39</i>
	1. Less than one day a month	
33. In the last 3 months, how often did food come back up into your mouth?	2. One day a month	
	3. Two to three days a month	
	4. One day a week	
	5. More than one day a week	
	6. Every day	
34. Have you had this problem (food coming back up into your mouth) 6 months or longer?	0. No	
	1. Yes	
35. When food came back up into your mouth, did it usually stay in your mouth for a while before you swallowed it or spit it out?	0. Never or rarely	
	1. Sometimes	
	2. Often	
	3. Most of the time	
	4. Always	
	0. Never or rarely	
36. Did you have retching (heaving) before food came into your mouth?	1. Sometimes	
	2. Often	
	3. Most of the time	
	4. Always	
	0. Never or rarely	
37. When food came into your mouth, how often did you vomit or feel sick to your stomach?	1. Sometimes	
	2. Often	
	3. Most of the time	
	4. Always	
	0. Never or rarely	
38. Did food stop coming back up into your mouth when it turned sour or acidic?	1. Sometimes	
	2. Often	
	3. Most of the time	
	4. Always	
	0. Never →	
	1. Less than one day a month	
39. In the last 3 months, how often did you experience bothersome belching?	2. One day a month	
	3. Two to three days a month	
	4. One day a week	
	5. More than one day a week	
	6. Every day	
40. Did this bothersome belching start more than 6 months ago?	0. No	
	1. Yes	

Table S3. Gastroesophageal Reflux Disease Questionnaire (GerdQ).

Symptoms in previous week Questions	Frequency score for symptom			
	0 day	1 day	2 – 3 days	4 – 7 days
1. How often did you feel burning behind your chest bone (heartburn)?	0	1	2	3
2. How often did you have stomach contents moving upwards to your throat or mouth (regurgitation)?	0	1	2	3
3. How often did you have a pain in the upper stomach region?	3	2	1	0
4. How often did you have nausea symptom?	3	2	1	0
5. How often did you have difficulty getting a good night's sleep because of your heartburn and / or regurgitation?	0	1	2	3
6. How often did you take additional medication for your heartburn and / or regurgitation without your doctor's advice?	0	1	2	3

Table S4. Diagnostic criteria for functional dyspepsia (FD).

Diagnostic criteria for FD
1. The symptoms must include (one or more): a) Bothersome postprandial fullness; b) Early satiation; c) Epigastric pain; d) Epigastric burning; symptoms fulfilled for the last 3 months and onset at least 6 months before diagnosis.
2. Endoscopy indicated the absence of organic diseases including but not limiting to esophagitis, GERD, gastrointestinal ulceration, erosion, malignancies and other organic lesions;
3. Without recent drug – intake history, especially those have gastrointestinal side effects;
4. In the absence of abdominal surgery history;
5. No hypertension, diabetes mellitus, mental disorders, autoimmune diseases or other systematic diseases;
6. Laboratory examinations, abdominal ultrasonography or X – ray examination confirmed no organic abdominal diseases that were related to the liver, gallbladder, pancreas or small intestine.

Table S5. Diagnostic criteria for functional dyspepsia (FD) subtypes.

Diagnostic criteria for FD subtypes
A. Diagnostic criteria for postprandial distress syndrome (PDS)
Must include one or both of the following symptoms a) Bothersome postprandial fullness induced by ordinary meal several times per week; b) Early satiation induced by ordinary meal several times per week. symptoms fulfilled for the last 3 months and onset at least 6 months before diagnosis.
Supportive criteria Upper abdominal bloating or postprandial nausea or excessive belching can be present.
B. Diagnostic criteria for epigastric pain syndrome (EPS)

Must include one or both of the following symptoms

- a) Moderate degree pain or burning centered in the upper abdominal at least once per week;
- b) The pain is intermittent;
- c) Pain or burning are not originated from other abdominal or chest regions;
- d) Defecation or passage of flatus cannot relieve symptoms;
- e) Unsatisfied the criteria for gallbladder and sphincter of Oddi's disorders.

Supportive criteria

- 1. The pain may be of a burning quality but without a substernal component
- 2. The pain is commonly induced or relieved by ingestion of a meal but may occur while fasting

C. Diagnostic criteria for coexistence of EPS and PDS

Subjects fulfilled both PDS and EPS subtype criteria would be taken as overlap of EPS and PDS.

Table S6. Diagnostic criteria for functional esophageal diseases (FED).

Diagnostic criteria for FED
A. Functional heartburn
Must include all of the following:
<ul style="list-style-type: none">a) Burning retrosternal discomfort or pain;b) Absence of evidence that gastroesophageal acid reflux is the cause of the symptom;c) Absence of histopathology – based esophageal motility disorders.
B. Functional chest pain of presumed esophageal origin
Must include all of the following:
<ul style="list-style-type: none">a) Midline chest pain or discomfort that is not of burning quality;b) Absence of evidence that gastroesophageal reflux is the cause of the symptom;c) Absence of histopathology – based esophageal motility disorders.
C. Functional dysphagia
Must include all of the following:
<ul style="list-style-type: none">a) Sense of solid and/or liquid foods sticking, lodging, or passing abnormally through the esophagus;b) Absence of evidence that gastroesophageal reflux is the cause of the symptom;c) Absence of histopathology – based esophageal motility disorders.
D. Globus
Must include all of the following:
<ul style="list-style-type: none">a) Persistent or intermittent, nonpainful sensation of a lump or foreign body in the throat;b) Occurrence of the sensation between meals;c) Absence of dysphagia or odynophagia;d) Absence of evidence that gastroesophageal reflux is the cause of the symptom;e) Absence of histopathology – based esophageal motility disorders.

Table S7. Demographic and clinical characteristics of FD and OD.

	FD (n=149)	OD (n=17)		
		RE (n=13)	ESCC (n=3)	DU (n=1)
Age (years), Mean \pm SD	57.44 \pm 6.71	57.51 \pm 8.79	63.00 \pm 4.00	61.00
Male sex	67 (44.97)	10 (76.92)	2 (66.67)	1 (100.00)
BMI (kg/m ²), Mean \pm SD	24.81 \pm 3.70	27.06 \pm 3.86	24.09 \pm 3.61	21.05
Marriage (Unmarried)	5 (3.36)	0	0	0
Family size, Mean \pm SD	3.56 \pm 1.86	3.23 \pm 1.54	3.33 \pm 2.31	3
Education (Primary school or below)	89 (59.73)	10 (76.9)	3 (100.00)	1 (100.00)
Smoking	40 (26.85)	6 (46.15)	1 (33.33)	1 (100.00)
Alcohol drinking	28 (18.79)	4 (30.70)	1 (33.33)	0
Eating fast	13 (8.72)	2 (15.38)	0	0
Hot food preference	17 (11.41)	2 (15.38)	1 (33.33)	0
Liquid food preference	27 (18.12)	4 (30.70)	1 (33.33)	1 (100.00)
Fresh vegetable preference	143 (95.97)	12 (92.31)	2 (66.67)	1 (100.00)
Fresh fruit preference	66 (44.30)	4 (30.70)	1 (33.33)	1 (100.00)
Spicy food preference	15 (10.07)	1 (7.69)	0	0
Drinking deep well water	87 (58.39)	6 (46.15)	1 (33.33)	1 (100.00)
<i>Helicobacter pylori</i> positive	51 (34.23)	4 (30.70)	0	1 (100.00)

ESCC: Esophageal squamous cell cancer; GC: Gastric cancer; CC: Cardiac cancer; GU: Gastric ulcer; DU: Duodenal ulcer; GERD: Gastroesophageal reflux disease; FD: Functional dyspepsia; PDS: Postprandial distress syndrome; EPS: Epigastric pain syndrome; FED: Functional esophageal diseases; PDS+EPS: Co-occurrence of PDS and EPS; FD+FED: Co-occurrence of FD and FED; SD: Standard deviation; BMI: body mass index.

Table S8. Comparison of symptoms among the control, FD, and OD groups.

Symptoms	Number of participants with symptoms (<i>n</i> , %)					
	Control (<i>n</i> =2099)	FD (<i>n</i> =149)	OD (<i>n</i> =17)	OD/FD	<i>P</i> OD/Control	FD/Control
Nausea	169, 8.05	40, 26.85	4, 23.53	0.997	0.061	<0.001
Vomiting	53, 2.53	15, 10.07	1, 5.88	0.904	0.357	<0.001
Reflux	114, 5.43	19, 12.75	5, 29.41	0.137	0.002	<0.001
Belching	363, 17.29	56, 37.58	7, 41.18	0.772	0.024	<0.001
Globus hystericus	41, 1.95	17, 11.41	1, 5.88	0.777	0.290	<0.001
Chest pain	46, 2.19	24, 16.11	1, 5.88	0.448	0.318	<0.001
Heartburn	428, 20.39	49, 32.89	9, 52.94	0.100	0.003	<0.001
Dysphagia	29, 1.38	15, 10.07	1, 5.88	0.904	0.216	<0.001
Postprandial fullness	372, 17.72	106, 71.14	13, 76.47	0.859	<0.001	<0.001
Early satiation	30, 1.43	18, 12.08	3, 17.65	0.788	0.002	<0.001
Epigastric pain or burning	86, 4.10	85, 57.05	8, 47.06	0.432	<0.001	<0.001

Control: Excludes organic and functional diseases; FD: Functional dyspepsia; OD: Organic dyspepsia.

Table S9. Comparison of symptoms among FD subtypes.

Symptoms	<i>n</i> (%)				<i>P</i> value					
	PDS (<i>n</i> =56)	EPS (<i>n</i> =52)	PDS+EPS (<i>n</i> =9)	FD+FED (<i>n</i> =32)	PDS/ EPS	PDS/ PDS+EPS	EPS/ PDS+EPS	PDS/ FD+FED	EPS/ FD+FED	FD+FED/ PDS+EPS
Nausea	6 (10.71)	13 (25.00)	2 (22.22)	19 (59.38)	0.051	0.668	1.000	<0.001	0.002	0.111
Vomiting	2 (3.57)	7 (13.46)	1 (11.11)	5 (15.63)	0.131	0.365	1.000	0.109	1.000	1.000
Reflux	4 (7.14)	5 (9.62)	0	10 (31.25)	0.908	1.000	1.000	0.003	0.012	0.136
Belching	17 (30.36)	15 (28.85)	5 (55.56)	19 (59.38)	0.864	0.270	0.233	0.008	0.006	1.000
Globus hystericus	3 (5.36)	3 (5.77)	0	11 (34.38)	1.000	1.000	1.000	<0.001	0.001	0.103
Chest pain	6 (10.71)	1 (1.92)	0	17 (53.13)	0.143	0.584	1.000	<0.001	<0.001	0.013
Heartburn	15 (26.79)	11 (21.15)	4 (44.44)	19 (59.38)	0.494	0.493	0.281	0.003	<0.001	0.677
Dysphagia	2 (3.57)	1 (1.92)	0	12 (37.50)	1.000	1.000	1.000	<0.001	<0.001	0.077
Postprandial fullness	50 (89.29)	22 (42.31)	9 (100.00)	25 (78.13)	<0.001	0.584	0.005	0.268	<0.001	0.299
Early satiation	12 (21.43)	0	2 (22.22)	4 (12.50)	<0.001	1.000	0.020	0.296	0.037	0.845
Epigastric pain or burning	2 (3.57)	52 (100.00)	9 (100.00)	22 (68.75)	<0.001	<0.001	–	<0.001	<0.001	0.136

PDS: Postprandial distress syndrome; EPS: Epigastric pain syndrome; PDS+EPS: Co-occurrence of PDS and EPS; FD+FED, Co-occurrence of functional dyspepsia and functional esophageal disorder; – : constant.