ORIGINAL ARTICLE

Association between 24-hour combined multichannel intraluminal impedance-pH monitoring and symptoms or quality of life in patients with laryngopharyngeal reflux

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Objective: To evaluate the association between the parameters of 24-hour multichannel intraluminal impedance (MII)-pH monitoring and the symptoms or quality of life (QoL) in laryngopharyngeal reflux (LPR) patients.
Design: Prospective cohort study without controls.
Setting: University teaching hospital.
Methods: Forty-five LPR patients were selected from subjects who underwent 24-hour MII-pH monitoring and were diagnosed with LPR from September 2014 to May 2015. Reflux Symptom Index (RSI), Health-related Quality of Life (HRQoL), Short Form 12 (SF-12) Survey questionnaires were surveyed. Spearman's correlation was used to analyse the association between the symptoms or QoL and 24-hour MII-pH monitoring.
Results: Most parameters in 24-hour MII-pH monitoring showed weak or no correlation with RSI, HRQoL and SF-12. Only number of non-acid reflux events that reached the larynx and pharynx (LPR-non-acid) and number of total reflux events that reached the larynx and pharynx (LPR-total) parameters showed strong correlation with heartburn in RSI ($R = 0.520$, $P < 0.001$, $R = 0.478$, $P = 0.001$, respectively). Multiple regression analysis showed that there was only one significant regression coefficient between LPR-non-acid and voice/hoarseness portion of HRQoL ($b = 1.719$, $P = 0.022$).
Conclusion: Most parameters of 24-hour MII-pH monitoring did not reflect subjective symptoms or QoL in patients with LPR.

Laryngopharyngeal reflux (LPR) is the most widely investigated extra-oesophageal syndrome, and it is defined that the gastric contents reflux into larynx and pharynx. LPR-related symptoms include sore throat, cough, hoarseness, globus.[1]

LPR frequently results in a negative effect on patients, especially on social functioning.[2] Reflux Symptom Index (RSI), Health-related Quality of Life (HRQoL), and Short Form 12 Survey (SF-12) were used to measure patients' quality of life and subjective symptoms. PPI treatment showed an improvement on the symptoms and quality of life (QoL) with LPR when RSI, HRQoL and SF-12 are used to measure patients' symptoms.[3]

Currently, ambulatory 24-hour double-probe pH monitoring test, which was developed and used for diagnosing gastro-oesophageal reflux disease, is regarded as gold standard for the diagnosis of LPR. However, it is often difficult for some patients to tolerate the pH monitoring test. Furthermore, the test has sensitivity from 50% to 80% for detecting LPR.[4,5] In a review of latest studies, it has been found that only 54% of patients with laryngoscopic findings of LPR have abnormal oesophageal acid exposure of pH probe.[6]

Consequently, other diagnostic tools such as multichannel intraluminal impedance (MII), pharyngeal pH monitoring and hypopharyngeal MII were developed more recently. Impedance monitoring detects both acid and non-acid reflux in gaseous and liquid forms by measuring electrical resistance between different points of the oesophagus. Concurrent impedance and pH recordings could detect significantly more events qualifying as reflux in the pharynx than pH recordings alone. A substantial majority of these events were gaseous refluxes both with and without minor pH drops.[7] With pH monitoring, impedance could offer improved detection of reflux events of LPR.[6] However, there are few studies about 24-hour MII-pH monitoring for diagnosing LPR and the parameters of 24-hour MII-pH monitoring test have not been clearly determined.

The aim of this study was to evaluate the association between the parameters of 24-hour MII-pH monitoring and the symptoms or quality of life in patients with LPR.

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Subjects and methods

Subjects and study design

Fifty-two patients who underwent 24-hour MII-pH monitoring were selected prospectively from outpatients who visited our hospital with a chief complaint of LPR symptoms such as globus sensation, hoarseness and chronic cough from September 2014 to May 2015. The patients with number of total reflux events that reached the larynx and pharynx (LPR-total) parameter ≥ 1 on 24-hour MII-pH monitoring test were selected. Patients with a history of any oesophageal or gastric surgery and use of proton pump inhibitor were excluded.

All included patients completed the RSI, HRQoL, SF-12 questionnaires. Age, gender, past medical history such as hypertension and diabetes mellitus, and social history such as smoking, alcohol and coffee were determined from their medical history. The investigators had obtained the institutional review board approval before the start of the study.

24-hour MII-pH monitoring[8]

The dual-channel MII-pH catheter models (ZAI-BL-54, 55, 56, ComforTEC Z/PH single use probe with 2.3 mm diameter, Sandhill Scientificd, Inc. WI, USA) were used based on the patient's oesophageal length and the correct model was selected. The configuration of this catheter allowed recording the changes in intraluminal impedance at 5, 7, 12, 14, 25 and 27 cm above the LES. In addition, pH was monitored at 6 cm above the LES (distal, pH 8) and 25 cm above the LES (proximal, pH 1). Distal pH sensor was positioned at relative to the LES (25 cm, 22 cm, 19 cm from proximal pH sensor at ZAI-BL-54, 55, 56, respectively). After inserting the fiberoptic scope into the nasal cavity to place the probe using direct visualisation, dual-channel MII-pH catheter was inserted transnasally to the opposite side and the blue visualisation band 1 cm below the proximal pH sensor at the proximal edge of the UES was placed.

DeMeester score was calculated at proximal pH and distal pH areas using the following six parameters: (i) total percentage time of pH <4.0, (ii) percentage time of pH <4.0 in the upright position, (iii) percentage time of pH <4.0 in the recumbent position, (iv) total number of acid reflux events, (v) total number of acid reflux events longer than 5 min and (vi) duration of the longest acid reflux event.

Then, acid exposure time and reflux episode at pH 1 and pH 8 were checked. We defined acid reflux episodes as a drop in pH to less than 4 for at least 5 s. Total acid exposure time was measured as the total time of acid reflux episodes divided by the monitoring time.[6]

We also calculated the symptom-associated probability (SAP), symptom sensitivity index (SSI), symptom index (SI) from 24-hour MII-pH monitoring, but SAP and SI were used in this study because some papers found that SI and SAP are useful quantitative measures of the association between reflux episode and symptoms. The symptom index was calculated as the number of symptoms associated with LPR divided by the total number of symptoms. When the patient recorded different types of symptoms, indices were determined for separate symptom. Three different indices: (i) SI-cough (%), (ii) SI-globus (%) and (iii) SI-heartburn (%) were used in this study.[9] SAP was defined as the probability that the patients' symptoms were related to reflux based on a statistical analysis of a contingency table consisting of four possible combinations of symptoms and reflux. We calculate the SAP as $(1 - P) \times 100\%$.[10]

Among many parameters of 24-hour MII-pH monitoring, we used the following eight parameters: (i) number of non-acid reflux episodes that reached the larynx and pharynx (LPR-non-acid), (ii) number of acid reflux episodes that reached the larynx and pharynx (LPR-acid), (iii) number of total reflux episodes that reached the larynx and pharynx (LPR-total), (iv) total acid time (%), (v) all reflux time (%), (vi) longest bolus exposure time (=longest time), (vii) distal reflux episode and (viii) proximal reflux episode.

Each MII tracing was manually analysed. A liquid reflux episode defined by impedance was defined as a retrograde drop in impedance by more than 50% of baseline in the distal two channels. A gas reflux episode was detected as an increase in impedance of 50% or greater in two consecutive channels with ohms of >8000. Total reflux time (%) was defined as the sum of bolus clearance time of all individual reflux episodes divided by the monitoring time. Total acid time (%) was calculated as the total time of acid reflux episodes divided by the time of monitoring. A distal reflux episode was defined as a reflux that reaches the two impedance sensors closest to the lower oesophageal sphincter. A proximal reflux episode was defined as a reflux that reaches the two impedance sensors closest to the oropharynx.[8,11]

The questionnaires

We evaluated the QoL and subjective symptoms reported by patients using three surveys: RSI, LPR-HRQoL and SF-12 version 2.0.

The RSI, which is a highly validated survey, includes nine questions that assess the response to treatment and evaluates the severity of LPR symptoms. The survey estimates the grade of symptoms and its severity through a six-point Likert scale, which ranges from 0 to 5. A high score shows that patients have more severe symptoms, where 0 means no symptom.[12]

LPR-HRQoL is known to be a reliable and valid QoL rating scale described by Carrau *et al.*[13] This method can be used to assess the QoL of LPR patients through a simple survey comprising 43 questions across five different categories including cough, hoarseness, throat clearing, swallow and overall impact of acid reflux. The questionnaire uses a seven-point Likert scale question in four categories and a 10-point Likert scale question in one category of the overall impact of acid reflux. A score of 0 indicates no symptoms, and high score indicates more severe symptoms.

The SF-12 version 2.0 contains 12 questions and is designed and validated to evaluate the quality of life in large population studies; it consists of eight items measuring physical and mental health outcomes. These items include physical functioning, social functioning, role-physical, bodily pain, general health, vitality, role-emotional and mental health. Data from these items are used to construct the physical and mental component summary measures (PCS and MCS).[14]

Statistical analysis

All statistical analyses were performed using SPSS, NY, USA 18.0 software. Spearman's correlation was used to analyse the association between each patient's symptom or QoL and 24-hour MII-pH monitoring. The parameters of 24-hour MII-pH monitoring related to the symptoms and QoL were evaluated by multiple logistic regression. The difference was considered to be statistically significant when the *P* value was less than 0.05.

Ethical considerations

This reliability study has been approved by the local ethics committee.

Results

A total of 45 patients were included in this study, and all patients had undergone 24-hour MII-pH monitoring, and parameters of 24 hour MII-pH monitoring were summarised in Table 1. Clinical characteristics of patients are summarised in Table 2. Nineteen males and 26 females were included, and the mean age was 57.8 ± 14.7 years.

Table 3 shows the correlation coefficients between RSI and the parameters of 24-hour MII-pH monitoring. Similarly, Table 4 shows the correlations between HRQoL and 24-hour MII-pH monitoring, and Table 5 shows the association between SF-12 and 24-hour MII-pH monitoring.

There were no significant correlations between DeMeester score or acid exposure time at pH1 and many parameters of RSI, HRQoL and SF-12. Also, reflux episode at pH1 showed no significant correlations with RSI, HRQoL and SF-12 except for throat clearing in RSI ($R = 0.300$, $P = 0.045$). Also, DeMeester score, acid exposure time and reflux episode

Table 1. Summary of 24 hour MII-pH monitoring

Parameters		Mean ± SD	
pH1	DeMeester score	0.84 ± 0.14	
	Acid exposure time (%)	0.02 ± 0.06	
	Reflux episode	0.43 ± 1.29	
pH8	DeMeester score	1.03 ± 0.70	
	Acid exposure time (%)	0.06 ± 0.20	
	Reflux episode	0.56 ± 1.20	
MII	LPR-non-acid	4.46 ± 3.30	
	LPR-acid	0.91 ± 2.35	
	LPR-total	5.37 ± 4.38	
	Total acid time (%)	0.04 ± 1.14	
	All reflux time (%)	0.43 ± 0.87	
	Longest time (min)	2.19 ± 3.52	
	Distal reflux episode	9.17 ± 6.72	
	Proximal reflux episode	7.00 ± 5.51	
Reflux symptom index (SI)	Cough (%)	6.46 ± 11.46	1/45 (2.22%)†
	Globus (%)	5.11 ± 9.51	0/45 (0.00%)†
	Heartburn (%)	3.11 ± 15.30	1/45 (2.22%)†
Reflux symptom-associated probability (SAP)	Cough (%)	18.42 ± 36.14	4/45 (8.88%)‡
	Globus (%)	16.20 ± 35.71	3/45 (6.66%)‡
	Heartburn (%)	0.00 ± 0.00	0/45 (0.00%)‡

MII, multichannel intraluminal impedance; SD, standard deviation.
†SI>50%.
‡SAP>95%.

Table 2. Subjects characteristics

Characteristics	No. (%)
Sex (Male : Female)	19 : 26 (42.2% : 57.8%)
Hypertension	15 (33.3%)
Diabetes mellitus	3 (6.7%)
Cigarette smoking	7 (15.6%)
Alcohol	12 (26.7%)
Coffee	14 (31.1%)

Table 3. Correlations between RSI and 24-hour MII-pH monitoring

		pH1			pH8			MII		
		DeMeester score	Acid exposure time (%)	Reflux episode	DeMeester score	Acid exposure time (%)	Reflux episode	LPR-non-acid	LPR-acid	LPR-total
Hoarseness	*R*	−0.038	−0.026	−0.088	−0.192	−0.094	−0.208	0.200	−0.059	0.214
	P	0.805	0.865	0.567	0.206	0.539	0.171	0.187	0.698	0.157
Throat clearing	*R*	0.268	0.261	0.300*	0.217	0.186	0.163	0.001	0.105	0.044
	P	0.076	0.083	0.045	0.152	0.220	0.285	0.994	0.492	0.773
PND	*R*	0.090	0.087	0.194	0.177	0.218	0.194	0.026	−0.033	0.008
	P	0.556	0.570	0.202	0.246	0.150	0.202	0.864	0.827	0.958
Swallowing difficulty	*R*	−0.140	−0.135	−0.046	−0.077	−0.012	0.040	0.067	0.130	0.066
	P	0.358	0.376	0.764	0.616	0.939	0.792	0.663	0.394	0.668
Cough (supine, post-meal)	*R*	−0.021	−0.035	−0.077	−0.108	−0.037	−0.066	0.119	−0.058	0.053
	P	0.891	0.818	0.615	0.481	0.810	0.666	0.436	0.706	0.729
Dyspnoea, Aspiration	*R*	−0.092	−0.086	−0.101	0.031	0.080	0.106	0.109	0.009	0.054
	P	0.546	0.572	0.509	0.840	0.603	0.488	0.477	0.952	0.725
Cough	*R*	−0.075	−0.088	−0.041	−0.105	−0.088	−0.165	−0.030	−0.198	−0.059
	P	0.626	0.567	0.787	0.493	0.565	0.279	0.847	0.191	0.700
Globus	*R*	0.236	0.232	0.267	0.181	0.149	0.130	−0.180	0.217	−0.089
	P	0.119	0.125	0.076	0.235	0.330	0.395	0.236	0.152	0.561
Heartburn	*R*	−0.042	−0.033	0.058	0.130	0.095	0.166	0.520*	0.027	0.478*
	P	0.786	0.831	0.704	0.396	0.534	0.275	<0.001	0.858	0.001
Total	*R*	0.022	0.022	0.084	−0.006	0.066	0.040	0.288	0.020	0.279
	P	0.887	0.887	0.585	0.968	0.664	0.793	0.055	0.895	0.063

		MII					Reflux symptom index (SI)			
		Total acid time (%)	All reflux time (%)	Longest time (min)	Distal reflux episode	Proximal reflux episode	Cough (%)	Globus (%)	Heartburn (%)	SAP Cough (%)
Hoarseness	*R*	−0.214	0.152	0.067	0.316*	0.228	0.045	0.090	0.051	0.065
	P	0.163	0.320	0.662	0.035	0.131	0.771	0.558	0.741	0.671
Throat clearing	*R*	0.139	0.026	0.116	0.062	−0.022	0.292	0.309*	0.107	0.166
	P	0.367	0.863	0.448	0.685	0.884	0.052	0.039	0.485	0.276
PND	*R*	0.277	−0.044	−0.024	0.046	0.013	0.033	−0.094	0.246	−0.017
	P	0.069	0.775	0.875	0.762	0.934	0.828	0.537	0.103	0.913
Swallowing difficulty	*R*	0.060	0.019	−0.121	0.103	0.016	0.153	0.114	0.261	0.153
	P	0.698	0.903	0.428	0.500	0.917	0.317	0.454	0.083	0.314
Cough (supine, post-meal)	*R*	−0.057	−0.067	−0.107	0.152	0.080	−0.009	0.108	0.370*	−0.014
	P	0.711	0.662	0.484	0.318	0.603	0.954	0.480	0.012	0.927
Dyspnoea, Aspiration	*R*	0.228	0.149	0.065	0.182	0.162	0.152	0.296*	0.046	−0.047
	P	0.136	0.328	0.672	0.231	0.287	0.318	0.048	0.766	0.757
Cough	*R*	−0.064	0.077	0.040	−0.019	0.028	0.164	−0.117	0.107	0.360
	P	0.679	0.616	0.792	0.901	0.857	0.281	0.446	0.483	0.015*
Globus	*R*	−0.035	−0.211	−0.123	−0.215	−0.256	0.395*	0.170	0.353*	0.295
	P	0.822	0.163	0.419	0.155	0.089	0.007	0.264	0.017	0.049*
Heartburn	*R*	0.281	0.287	0.266	0.357*	0.388*	−0.063	0.064	−0.159	0.292
	P	0.065	0.056	0.077	0.016	0.009	0.682	0.676	0.297	0.051
Total	*R*	0.123	0.150	0.087	0.308*	0.222	0.260	0.263	0.249	0.415
	P	0.425	0.326	0.571	0.040	0.143	0.085	0.081	0.100	0.005*

RSI, Reflux Symptom Index; MII, multichannel intraluminal impedance; LPR, laryngopharyngeal reflux; SAP, symptom-associated probability.
*$P < 0.05$.

Table 4. Correlations between HRQoL and 24-hour MII-pH monitoring

		pH1			pH8			MII		
		DeMeester score	Acid exposure time (%)	Reflux episode	DeMeester score	Acid exposure time (%)	Reflux episode	LPR-non-acid	LPR-acid	LPR-total
Hoarseness	*R*	−0.205	−0.196	−0.258	−0.179	−0.155	−0.141	0.147	0.007	0.168
	P	0.177	0.197	0.086	0.239	0.310	0.355	0.337	0.963	0.271
Throat clearing	*R*	−0.050	−0.055	−0.094	0.083	−0.002	0.006	0.063	−0.115	0.047
	P	0.745	0.719	0.541	0.586	0.987	0.969	0.679	0.452	0.757
PND	*R*	0.105	0.098	0.052	0.219	0.137	0.184	0.100	0.023	0.126
	P	0.493	0.523	0.735	0.148	0.370	0.227	0.513	0.880	0.408
Swallowing difficulty	*R*	−0.142	−0.138	−0.154	0.044	−0.008	0.123	−0.005	0.269	0.086
	P	0.353	0.366	0.312	0.774	0.961	0.419	0.975	0.074	0.574
Cough (supine, post-meal)	*R*	0.041	0.046	−0.027	0.232	0.122	0.215	0.149	0.112	0.176
	P	0.791	0.763	0.859	0.124	0.425	0.156	0.329	0.465	0.249
Total	*R*	−0.105	−0.105	−0.178	0.071	0.012	0.073	0.157	−0.024	0.152
	P	0.492	0.493	0.242	0.642	0.939	0.632	0.304	0.874	0.320

		MII					Reflux symptom index (SI)			
		Total acid time (%)	All reflux time (%)	Longest time (min)	Distal reflux episode	Proximal reflux episode	Cough (%)	Globus (%)	Heartburn (%)	SAP Cough (%)
Hoarseness	*R*	−0.100	0.154	0.078	0.262	0.226	0.202	0.192	0.016	0.252
	P	0.519	0.312	0.609	0.082	0.136	0.184	0.207	0.919	0.095
Throat clearing	*R*	−0.021	0.156	0.212	0.179	0.167	0.154	0.078	−0.086	0.306
	P	0.890	0.306	0.161	0.240	0.273	0.311	0.611	0.575	0.041*
PND	*R*	0.111	0.025	0.107	0.171	0.148	0.228	0.279	−0.302*	0.145
	P	0.474	0.868	0.486	0.260	0.332	0.131	0.064	0.043	0.342
Swallowing difficulty	*R*	0.158	−0.021	−0.038	0.152	0.081	0.157	0.103	0.081	0.297
	P	0.307	0.891	0.804	0.319	0.598	0.304	0.501	0.596	0.048*
Cough (supine, post-meal)	*R*	0.222	0.062	0.085	0.288	0.258	0.035	0.028	−0.153	0.010
	P	0.148	0.686	0.580	0.055	0.087	0.818	0.856	0.315	0.950
Total	*R*	0.093	0.073	0.077	0.277	0.266	0.207	0.178	−0.109	0.202
	P	0.547	0.634	0.617	0.065	0.077	0.172	0.242	0.476	0.183

HRQoL, Health-related Quality of Life; MII, multichannel intraluminal impedance; LPR, laryngopharyngeal reflux; SAP, symptom-associated probability.
*$P < 0.05$.

at pH8 showed no correlations with any parameters of RSI, HRQoL and SF-12.

LPR-non-acid and LPR-total were correlated with heartburn in RSI, and LPR-acid was correlated with PCS in SF-12 ($R = 0.520$, $P < 0.001$, $R = 0.478$, $P = 0.001$, $R = -0.350$, $P = 0.018$, respectively). Any other parameters of RSI, HRQoL and SF-12 showed no correlation with LPR-non-acid, LPR-acid and LPR-total.

Total acid time (%), all reflux time (%) and longest time (min) parameters of 24-hour MII-pH monitoring showed no correlations with RSI, HRQoL and SF-12. Distal reflux episode showed significant correlations with four parameters of the symptoms or quality of life; hoarseness, heartburn, total score in RSI and MCS in SF-12 ($R = 0.316$, $P = 0.035$, $R = 0.357$, $P = 0.016$, $R = 0.308$, $P = 0.040$, $R = -0.373$, $P = 0.012$, respectively). Proximal reflux episode showed no significant correlations with symptoms or quality of life except for heartburn in RSI ($R = 0.388$, $P = 0.009$).

Six significant correlations were found between the reflux symptom index and symptoms or quality of life; cough (%) and globus in RSI, globus (%) and throat clearing in RSI,

Table 5. Correlations between SF-12 and 24-hour MII-pH monitoring

		pH1			pH8			MII		
		DeMeester score	Acid exposure time (%)	Reflux episode	DeMeester score	Acid exposure time (%)	Reflux episode	LPR-non-acid	LPR-acid	LPR-total
PCS	*R*	−0.247	−0.258	−0.157	−0.262	−0.274	−0.195	−0.080	−0.350*	−0.172
	P	0.102	0.087	0.304	0.083	0.069	0.200	0.601	0.018	0.257
MCS	*R*	−0.057	−0.078	0.005	−0.005	−0.090	0.040	−0.277	−0.071	−0.279
	P	0.708	0.613	0.976	0.975	0.558	0.792	0.065	0.643	0.063

		MII					Reflux symptom index (SI)			
		Total acid time (%)	All reflux time (%)	Longest time (min)	Distal reflux episode	Proximal reflux episode	Cough (%)	Globus (%)	Heartburn (%)	SAP Cough (%)
PCS	*R*	−0.075	−0.139	−0.235	−0.154	−0.146	−0.052	−0.070	0.084	−0.098
	P	0.628	0.364	0.120	−0.311	0.339	0.736	0.648	0.563	0.520
MCS	*R*	0.023	−0.184	−0.161	−0.373*	−0.292	0.182	−0.030	0.073	0.222
	P	0.883	0.225	0.292	0.012	0.051	0.232	0.846	0.632	0.143

SF-12, Short Form 12 Survey; MII, multichannel intraluminal impedance; PCS, Physical Component Score; MCS, Mental Component Score; LPR, laryngopharyngeal reflux; SAP, symptom-associated probability.
*$P < 0.05$.

globus (%) and dyspnoea or aspiration in RSI, heartburn (%) and cough (supine or post-meal) in RSI, heartburn (%) and globus in RSI, and heartburn (%) and PND in HRQoL ($R = 0.395$, $P = 0.007$, $R = 0.309$, $P = 0.039$, $R = 0.296$, $P = 0.048$, $R = 0.370$, $P = 0.012$, $R = 0.353$, $P = 0.017$, $R = -0.302$, $P = 0.043$, respectively). There were no other correlations between the reflux symptom index and RSI, HRQoL and SF-12.

Also five significant correlations were found between the reflux symptom-associated probability and symptoms or quality of life. SAP-globus (%) and SAP-heartburn (%) showed no correlations with symptoms. SAP-cough (%) showed significant correlations with cough, globus, total score in RSI, throat clearing and swallowing difficulty in HRQoL ($R = 0.360$, $P = 0.015$, $R = 0.295$, $P = 0.049$, $R = 0.415$, $P = 0.005$, $R = 0.306$, $P = 0.041$, $R = 0.297$, $P = 0.048$, respectively).

Multiple regression analysis showed that there was only one significant regression coefficient between LPR-non-acid and voice/hoarseness portion of HRQoL ($b = 1.719$, $P = 0.022$).

Discussion

We evaluated the association between the parameters of 24-hour MII-pH monitoring and the symptoms or quality of life in patients with LPR. We found that a few parameters had weak or moderate correlation with RSI, HRQoL and SF-12. However, no parameters of 24-hour MII-pH monitoring had a strong correlation with symptoms or quality of life.

There is a no specific test for diagnosing LPR. Laryngoscopy and 24-hour pH monitoring have not established as reliable tools for the diagnosis of this disease.[15] Ambulatory 24-hour pH monitoring was considered by many experts as the gold standard for diagnosing LPR. In spite of the wide acceptance of 24-hour pH monitoring as the gold standard for diagnosing LPR, it is not widely used by otolaryngologists as a diagnostic tool. The reasons for this contain poor compliance, high cost, difficulty in quantifying intermittent events and its unavailability.[16]

With the use of 24-hour pH monitoring, pharyngeal reflux episodes below pH 4.0 are considered diagnostic for LPR. For interpretation of the distal oesophageal probe data, abnormal studies are defined as the percentage of time the pH is lower than 4.0: either 8.1% of the time in the upright position, 2.9% of the time in the supine position or 5.5% of the total time are considered abnormal results.[12]

While 24-hour pH monitoring remains the gold standard for confirming the diagnosis of gastro-oesophageal reflux, the addition of multichannel intraluminal impedance technology improves diagnostic accuracy for detecting LPR events. Ambulatory multichannel intraluminal impedance evaluation allows for identification of gaseous as well as liquid refluxate and detection of non-acid reflux events that tend to be significant in confirming LPR.[17]

Strength of the study

The 24-hour MII-pH monitoring has more complex parameters than conventional 24-hour pH monitoring;[18] 24-hour MII-pH monitoring reliability has not previously been rigorously investigated, so in this study it was compared with another widely available diagnostic tool – endoscopy and ambulatory 24-hour pH monitoring. For example, PPI-refractory, endoscopy-negative patients are the optimal candidates for this test. The sensitivity of pH-only monitoring in these patients with endoscopy-negative reflux symptoms is <71%.[19] According to a consensus study by Sifrim *et al.*, when impedance testing is added to pH monitoring, the sensitivity of reflux monitoring approaches 90%.[20] In fact, using only acid pH monitoring lacks the capability of accurately diagnosing LPR. Furthermore, we employed computerised autoscan and manually detection analysis to measure reflux episodes of proximally directed decreases in impedance for more accurate diagnosis.

Synopsis of key findings

At first, we calculated correlation coefficients between RSI, HRQoL and SF-12 and 55 parameters of 24-hour MII-pH monitoring such as number of acid or non-acid or total reflux events, acid or non-acid refluxate (min), total % time reflux. But, no correlation was found in most parameters of 24-hour MII-pH monitoring; therefore, we included 17 parameters in the results.

Comparison with other studies

In a previous study, 24-hour pH monitoring could not show the severity of patient's reflux laryngitis symptoms or signs. Only the heartburn symptom is associated with laryngopharyngeal and oesophageal reflux.[21] Similar results were observed in many studies using 24-hour MII-pH monitoring. In a previous study, symptom index (SI), symptom sensitivity index (SSI) and symptom-associated probability (SAP) showed discrepancy with 24-hour MII-pH monitoring.[10] Also, the reflux finding score (RFS) showed no significant association with 24-hour MII-pH monitoring.[6] However, Loots *et al.* found that 24-hour MII-pH monitoring increases the probability of demonstrating a positive gastro-oesophageal reflux symptom correlation compared with conventional 24-hour pH monitoring.[22]

But, there were no researches about correlation between 24-hour MII-pH monitoring and RSI, HRQoL and SF-12 reflecting QoL and subjective symptoms of patients. In this study, we evaluated not only SI, SSI and SAP but also subjective symptoms and QoL using RSI, HRQoL and SF-12 in LPR patients, and most of the Pearson correlation results showed that there were meaningless coefficients or low coefficients in a statistically meaningful correlation.

Clinical applicability of the study

We showed 24-hour MII-pH monitoring has weak correlations with symptoms and QoL of LPR patients. However, given its portability, applicability to home or clinic, this monitoring test has greater utility and therefore may be preferred for diagnosing LPR and both acid and non-acid reflux outcome data collection.

Conclusion

Most parameters of 24-hour MII-pH monitoring did not reflect subjective symptoms or QoL in patients with LPR. For the future, study with larger number and control is needed.

Keypoints

- Most parameters in 24-hour MII-pH monitoring showed weak or no correlation with subjective symptoms or QoL in patients with LPR.
- Only number of non-acid reflux events that reached the larynx and pharynx had a significant correlation with voice/hoarseness of HRQoL.

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The authors have no financial relationships or conflicts of interest to disclose.

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