Medical diagnose and treatment using high resolution manometry with computer aided system

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ABSTRACT

Nowadays computers analyze medical data almost in every diagnose and treatment steps. We develop new technology which gives us better and more precise diagnose. We chose esophageal high resolution manometry with impedance (HRMI) which has been considered as a „gold standard" test for esophageal motility. HRMI is the next generation of manometry examination which is more sensitive and accurate to EFT. Examination allows physicians to get informations about esophageal peristalsis, amplitude and duration of the esophageal contraction and liquid/viscous bolus transit time from mouth through stomach. In 2008 we examined 80 patients using „old" EFT manometry and 80 patients in 2009 using high resolution manometry (HRMI). Everybody got manometry, endoscopy and X-ray examination. We asked about symptoms which we correlate and connect with data from EFT and HRMI. We tried to find a good algorithm for this purpose in order to do a simple and helpful tool for physician to make right diagnose and treatment decision. Connection between data and symptoms seems to be right and clear, but finding a good algorithm for given data is the main problem.

Keywords: bioimpedance technique, esophageal manometry, high resolution manometry, pH-impedance, esophageal reflux disease, decision tree, support vector machines

1. INTRODUCTION

Esophagus is not only simple tube that transports food from mouth to stomach. It is a straight muscular tube (Fig.1) that is guarded at its two ends by an upper and lower esophageal sphincter [1]. Effective peristalsis is a major determinant of esophageal clearance function. Neuromuscular control mechanisms require fine coordination of the muscles to bring normal functioning of the two sphincters and esophageal peristalsis. Dysfunction may cause the dysphagia, chest pain, vomiting, heartburn.

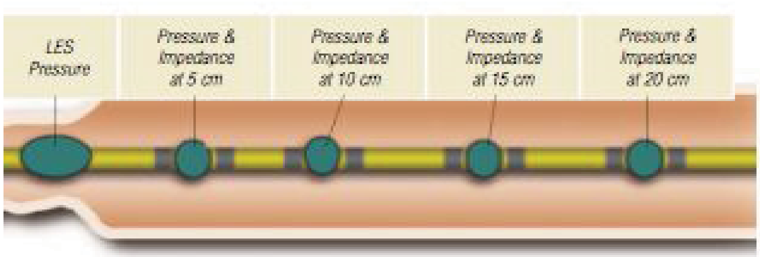

Fig. 1a Manometry probe pressure channels

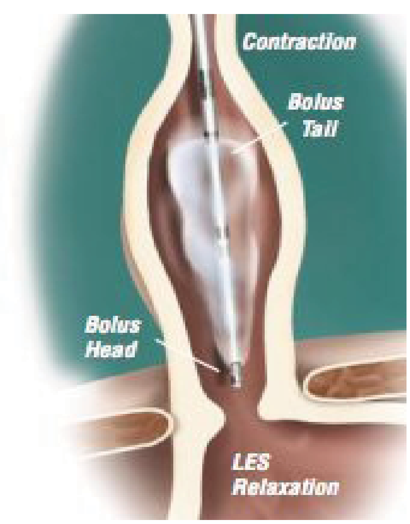

Fig. 1b Manometry probe localizations

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2. REFLUX DISORDERS

Gastroesophageal reflux is the retrograde movement of gastric contents through the lower esophageal sphincter (LES) to the esophagus. The stomach normally secretes acid at a pH 1.5 – 2.0 where in the esophagus is almost neutral (pH 6.0–7.0). Distal esophageal pH will thus decrease dramatically when gastroesophageal reflux occurs. We can divide into two categories depending on whether it is normal physiologic reflux or pathologic reflux which occurs gastroesophageal reflux disease (GERD) [9].

Etiology – pathological reflux of acid gastric contents. There are factors which can contribute to the development of GERD, such as:

1. Incompetent lower esophageal sphincter. Many patients with GERD have a mechanically incompletent LES and if the intraabdominal pressure suddenly rise, reflux of gastric contents will occur. The resistance to reflux provides by the LES depends on several factors: LES pressure, abdominal exposure of the LES, LES length (total). LES pressure is normal pressure in the LES i 10-45 mmHg, and varies with breathing, body position, body movements and the migrating motor complex. Low resting pressure in the LES is common among patients with reflux disease. Hormones and some drugs are also important to LES tone, can decrease LES resting pressure and cause increased reflux. LES length is normal length ≥ 3.0 cm (> 1.5 cm intra-abdominal), its important if some part is located in the intraabdominal region where LES tone is augmented by exposure to intraabdominal pressure. So when the pressure in the abdominal cave increases, the LES is tighten. Hiatal hernias is a function compromised by alternations in the anatomic relationships between the LES and the diaphragmatic crura – contractions of the diaphragmatic crura serve to augment LES tone. In patients with a hiatal hernia the LES is displaced proximally and the diaphragm is distal to the LES. During inspirations there is no increase in LES pressure since the contraction of the diaphragm occurs distal to the LES.
2. Transient lower esophageal sphincter relaxations (TLESR) - is most prevalent mechanism of reflux in GERD patients with normal LES pressure.
3. Delayed esophageal acid clearance – three factors are important: gravity, esophageal motor activity (primary peristalsis – pharyngeal swallow is initiated voluntarily and is the major motor activity, secondary peristalsis – occurs in the absence of a pharyngeal swallow), salivation – natural buffer to acid, it neutralizes an amount of acid that is left after clearance by a peristaltic wave.
4. Gastric abnormalities: outlet obstruction of the stomach – may increase gastric pressure and/or gastric dilatation, vagotomy and diabetic neuropathy – may increase gastric pressure since the normal receptive relaxation of the stomach is interrupted, excessive gastric dilatation – LES sphincter becomes shorter which affects LES competence (aerophagia, overeating, outlet obstruction due to ulcer disease, malignancy), delayed gastric emptying – distended for prolonged periods (can be caused by gastric atony from advanced diabetes, diffuse neuromuscular disorders, vagotomy, pyloric dysfunction and duodenal dysmotility, idiopathic gastric paresis).

Symptoms – wide spectrum of pathological manifestations and may present with a long list of symptoms, such as: heartburn, acid regurgitations, chest pain, dysphasia, chronic cough, hoarseness, laryngitis, asthma.

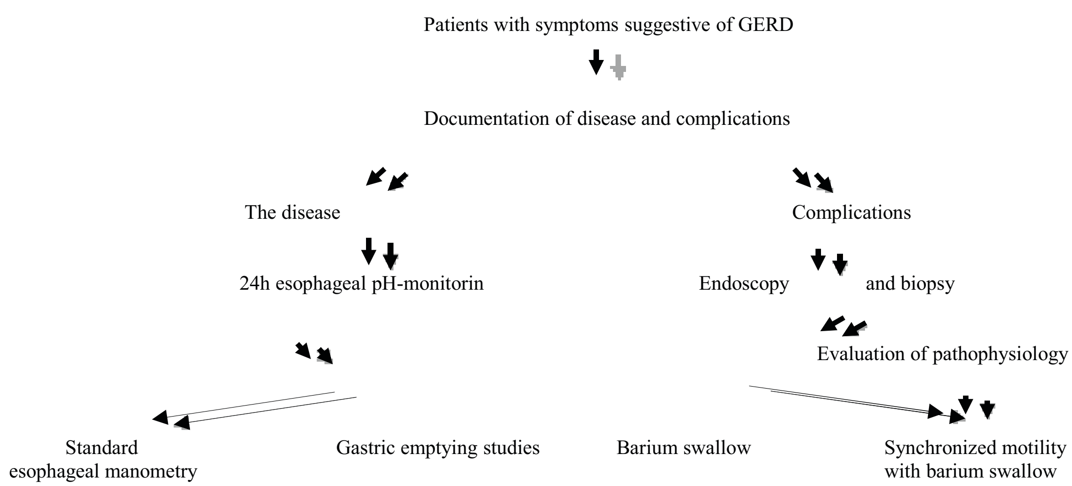

Fig. 2 Differential diagnosis

Diagnostic procedures are the following: endoscopy to asses macroscopic changes in the esophageal mucosa caused by gastroesophageal reflux, also exclude other pathological conditions (cancer) (Fig.3b), radiography with barium swallow provide a detailed assessment of esophageal and gastric anatomy as well as hiatal hernia size (Fig. 3a), esophageal manometry – provides valuable information on pathophysiology, measure LES pressure, position and length, 24h pH recording – it provides parameters: reflux frequency and duration, when reflux occurs, correlations with symptoms and clearance time.

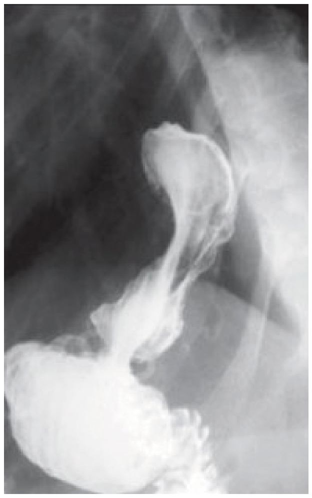

Fig. 3a X-Ray hiatal hernia

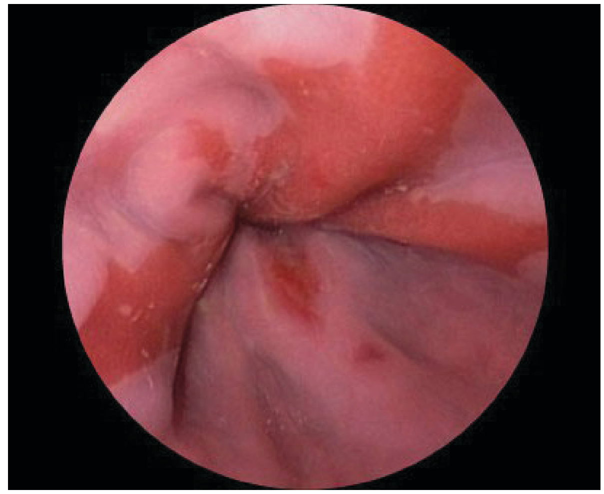

Fig. 3b Esophagitis

Esophageal manometry with impedance (EFT) [6,7] brings us a “gold standard” for motility testing [2,3]. Standard manometry was performed after overnight fast and all known medications which interfere with gastrointestinal secretory or motor function where discontinued for 10 days.

During the examinations EFT catheter was inserted transnasally into the esophagus to a depth of 60 cm (Fig.4). Intragastric position of the catheter is verified by the rise in pressure during deep inspiration. After finding LES (lower esophageal sphincter) - placed in high pressure zone, the catheter was taped to the nose in order to prevent displacement during the study. For the evaluation of the esophageal peristalsis, bolus transport and LES pressure measurement 10 liquid and 10 viscous swallows were given in 20-30s intervals. After that the probe was extubate and the examination finished.

Impedance testing depends upon measurement of changes in resistance (in Ohms) to alternating electrical current when a bolus passes by a pair of metallic rings mounted on a catheter. Impedance is inversely related to the conductivity of the medium surrounding the two electrodes. Liquid containing boluses such as saline with an increased number of ions have a higher conductivity and saliva or air has low conductivity (Fig.5). Thus, by using esophageal impedance monitoring the movements of liquids and gas in the esophagus can be detected. After examination we studied measurements using BioView Sandhill program (Fig. 6).

Table 1. Normal value for Lower Esophageal Sphincter and esophageal motility

LES pressure	10 - 45 mm Hg
LES lenght	≥ 3.0 cm (> 1.5 cm intra-abdominal)
LES relaxation	≤ 12 sec
Motility - contraction	1-6 sec contraction
Motility - velocity	< 8 cm/sec velocity
Motility - effective	Liquid swallows ≥ 80%, TBTT < 12 sec
	Viscous swallows ≥ 70%, TBTT < 13 sec

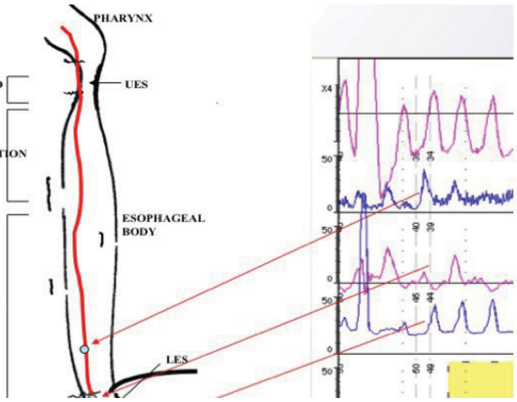

Fig. 4 Pressure readings

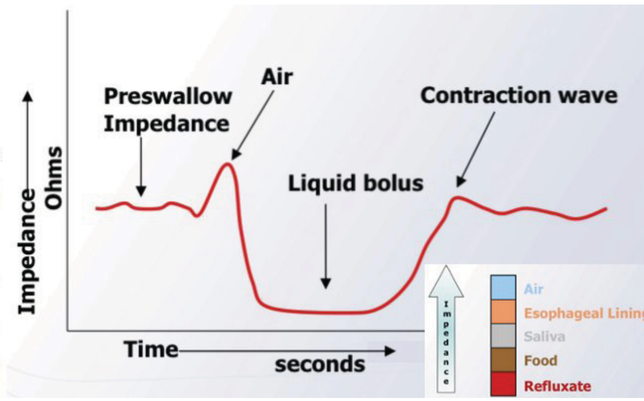

Fig. 5 Bolus transit – impedance

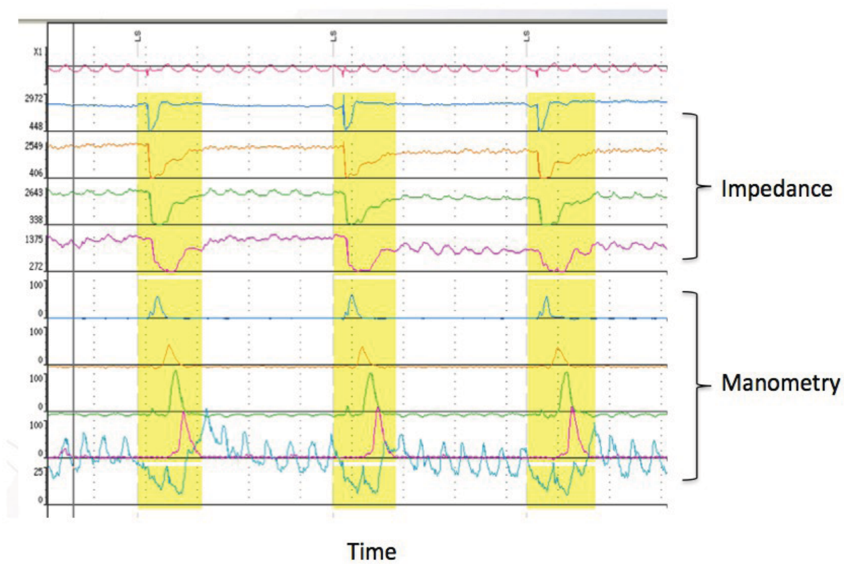

Fig.6 BioView analyze – impedance and manometry

Measurements that we analyze were upper GI endoscopy and X-Ray. We were trying to find esophageal hiatal hernia, chalasia (lower LES pressure) and reflux.

3. MEDICAL MEASUREMENTS

Examinations gave us several parameters that we analyzed (Table 1.). First of all was LES pressure, length and relaxation time that determine how strong barrier between esophagus and stomach is. Its count in mm Hg and normal value is 10 to 45 mm Hg and ≥ 3 cm (>1.5 cm intra-abdominal). LES relaxation could take no longer than 12 sec. Second important informations were motility parameters like: duration of contraction (1-6 sec), velocity (< 8cm/sec) and effective swallows that gave us % of complete liquid and viscous swallows. It was important to ask for symptoms (careful interview), which were most often the following: chest pain, heartburn, chronic cough, pain in the upper abdomen, throat pain. After doing a good interview we can diagnose such diseases like: achalasia, ineffectual lower esophageal sphincter or esophageal hiatal hernia.

4. DATA RETRIEVAL METHODOLOGY

In our investigations linear regression are the most widely used, and extremely powerful statistical techniques modeling the linear relationship between independent variables. Linear regression refers to a model in which the conditional mean of y (a response variable) given the value of X (explanatory variables) is an affine function of X.

Table 2. Parameters of found linear regressions.

Data eft y=a+bx+cz		coeff_estimate	Pr(>|t|)	Mult R^2	Adj R^2	F	p-value
totales ~ intrables	a	0,67093	0,000596	0,7409	0,7377	231,6	2,20E-016
	b	1,03524	2,00E-016				
LESP ~ respres	a	14,5134	9,90E-011	0,09465	0,08348	8,468	0,004664
	b	0,8797	0,00466				
Data hrmi y=a+bx+cz+dv							
totales ~ intrables	a	1,45883	2,00E-016	0,4525	0,4457	66,94	3,29E-012
	b	0,55851	3,29E-012				
LESP ~ respres	a	14,5603	5,48E-008	0,2566	0,2474	27,96	1,03E-006
	b	1,2413	1,03E-006				
totales ~ intrables + TBTVS	a	1,79381	2,00E-016	0,491	0,4783	38,59	1,86E-012
	b	0,52638	2,01E-011				
	c	-0,04703	0,016				
totales ~ intrables + LESP + TBTVS	a	1,602007	9,43E-013	0,5153	0,4969	28	1,95E-012
	b	0,492537	3,12E-010				
	c	0,008905	0,0499				
	d	-0,047008	0,0143				
LESP ~ CBTVS + respres	a	9,38144	0,00277	0,3177	0,3007	18,63	2,28E-007
	b	0,09206	0,00899				
	c	1,28489	2,25E-007				
LESP ~ CBTVS + respres + totales	a	-0,22658	0,95912	0,3834	0,36	16,37	2,29E-008
	b	0,10407	0,00238				
	c	1,15985	1,30E-006				
	d	4,7747	0,00483				
Data eft + hrmi y=a+bx+cz+dv							
totales ~ intrables	a	1,0557	<2e-16	0,7281,	0,7264	439,1	2,20E-016
	b	0,8863	<2e-16				
LESP ~ respres	a	13,7277	2,00E-016	0,242	0,2374	52,35	1,69E-011
	b	1,2199	1,69E-011				
totales ~ intrables + TBTLS + TBTVS	a	1,22406	6,83E-011	0,7422,	0,7375	155,5	2,20E-016
	b	0,86433	2,00E-016				
	c	0,06003	0,02008				
	d	-0,07368	0,00423				
LESP ~ CBTVS + respres	a	9,93572	8,31E-006	0,2669	0,2579	29,67	1,03E-011
	b	0,05665	0,0199				
	c	1,30109	1,56E-012				
LESP ~ CBTVS + percontr + respres	a	13,61093	3,54E-006	0,2841	0,2709	21,43	9,62E-012
	b	0,07765	0,00341				
	c	-0,05804	0,04973				
	d	1,25075	9,49E-012				

Decision tree is a graphic construct showing available choices at each decision node of managing a clinical problem along with probabilities (if known) of possible outcomes for patient's freedom from disability, life expectancy, and mortality. Learning classifiers[8] are divided into unsupervised, which needed sets labeled by physicians to obtain knowledge about patients disease and into supervised classifiers, which under some conditions are able to make classification only with a help of data (from measurements) and distance between examinated patients - points in the multivariable space (PCA). Support vector machines (SVMs) are a set of related supervised learning methods used for classification and regression.

5. DATA RETRIEVAL RESULTS

During measurements we examined two groups of patients: treated after complete examinations (EFT for one group of 83 patients or HRMI for another one also with 83 patients, X-Ray and endoscopy in both sets). Our data variables were the following: totales - Total LES Length (standard > 3cm), intrables - Intra-abdominal LES Length (standard >1.5cm), LESP9 – LES pressure in channel 9 (standard 10-45mmHg), LESP10 - LES pressure in channel 10 (standard 10-45mmHg), LESP - pressure LES (norma 10-45mmHg), CBTLS - Complete Bolus Transit LS (> 80%), TBTLS - Total Bolus Transit Time LS (<12sec), respres - Residual Pressure LES (norma = lub < 8.0mmHg), velocity - Velocity (norma <8cm/sec), percontr - Peristaltic contractions, retcontr - Retrograde contractions, CBTVS - Complete Bolus Transit VS (>70%), TBTVS - Total Bolus Transit Time VS, disease recognised by a physician.

Our research was focused on the mentioned two datasets and the third one emerged from joint two dataset rows (166 rows). In first step we detected linear regressions for continuous variables (totales and LESP were used for response and explanatory variable, and intrables, CBTLS, TBTLS, respres, velocity, percontr, CBTVS, TBTVS only for explanatory variables X) in our three datasets as is seen in Table 2. For each subset of given input variables (for all combinations of them) and every response variable linear regressions were calculated and the one with the lowest p-value and stable coefficient estimates was chosen. Of course, residuals vs fitted and residuals vs leverage plots were quite typical and correct for all chosen regressions, this means with error zero mean and without significant outsiders, but not uniformly sparse (it was caused e.g. by our initial small datasets). Two similar regressions were found in both data files and proved that data was obtained from patients with the same diseases. Additionally, more linear regressions were found in the hrmi dataset and in the third joint one, which points out the hrmi measurement method as a better one. This means more accurate and precise. In the third dataset linear dependencies were almost the same as in the hrmi dataset and even the regressions for all explanatory variable set were found, but its coefficient estimates were not statistically stable. It is assumed that this linearization trend will be stronger and stronger if datasets are larger and measured with greater accuracy and better technically advanced equipment.

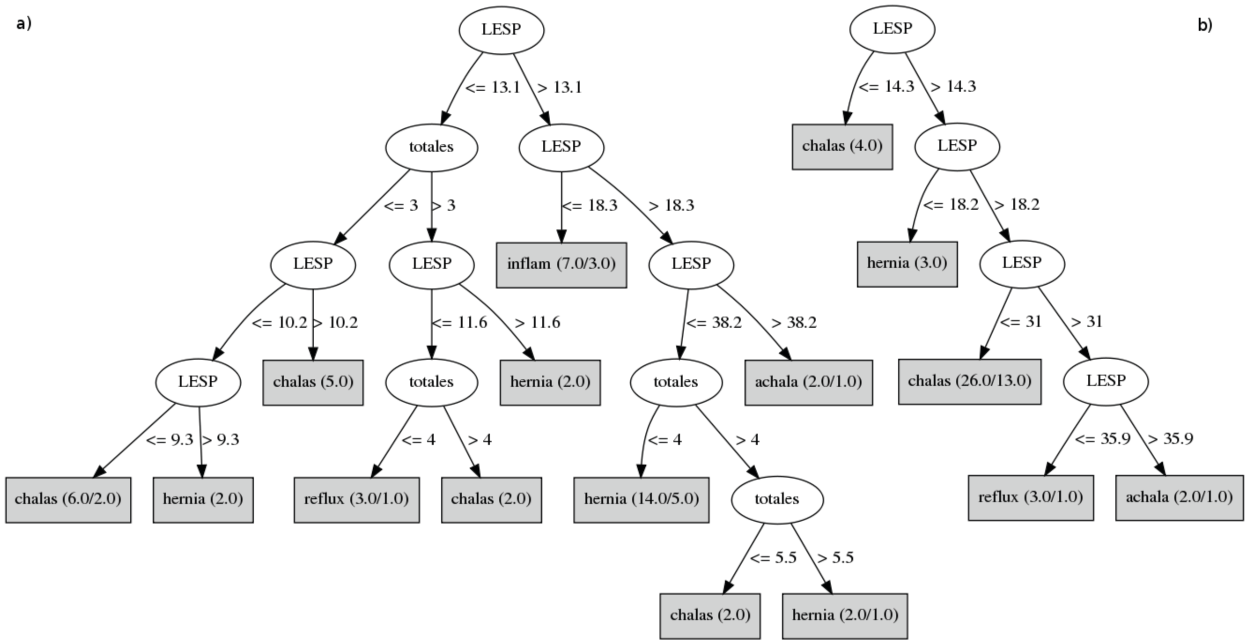

Fig. 7. The decision trees generated a) for eft dataset, b) for hrmi dataset

Second we tried to generate trees for detecting five diseases: achalasia, hiatal hernia, reflux, chalasia, inflammation (only in the eft dataset) which are provided in Fig. 7. First we reduced a number of intermediate node test variables to the ones usually used by medical physicians in order to make similar diagnosis, but in computer. This set contained: totales, intrables, LESP, CBTLS, respres, CBTVS, but we proved that at least in one data set they form linear regressions. Thus, the parameter set was further reduced to only two typical variables: totales and LESP. The found trees should describe diseases as a phisician should do this means for two variables totales and LESP every disease has their ranges and the following symptoms: heartburn, chronic cough, laryngitis, hoarseness, regurgitations, belching for gastroesophageal reflux (LESP <15mmHg, LES lengh <2cm); regurgitations (acid & food), belching, chest pain, heartburn, upper abdominal pain for hiatal hernia (LESP 10–45 mmHg, LES lengh abdominal 0 cm); chest pain, heartburn, vomiting for dysphagia (LESP >30 mmHg, LES lengh 2-3 cm);chest pain, heartburn, vomiting for achalasia (LESP >45 mmHg, LES lengh >2cm); belching, regurgitations, heartburn for chalasia (LESP <10mmHg, LES lengh <2cm).

Trees were generated by procedure J48 from Weka package in R environment from randomly chosen 70% of the given dataset. On the remaining 30% rows of the given dataset trees were tested for disease classification. After such 5 trials a tree with the best classification score was chosen. The whole process was repeated until all diseases were detected by the tree in the entire given dataset. At this initial step trees have still classification errors equal to about 20-40%. In further research we will generate random forests made of such trees, it will improve disease recognition by decreasing classification error. Trees computed on the hrmi dataset were smaller and looked better than trees obtained from the first eft dataset. Thus, the better measurment and more data, the more linear regressions and better compressed classification trees for this kind of medical information. For the third larger dataset subtree prunning was increased by setting smaller confidence threshold for pruning (parameter C set from default value 0.25 to smaller 0.15), but those trees were similar to the trees of eft dataset. Thus, joining two datasets did not stop linearization trend between variables, but worsened clasification tree generation.

Based on raw data we also tried to analyze common symptoms. Trees with these two variables are simple and easy to understand and in differential diagnosis are already known in everyday practice as is depicted in Fig. 8.

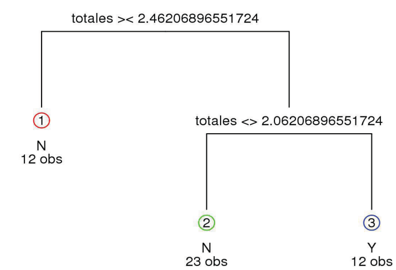

Fig. 8. Tree made for gastroscopy esophagitis, and it fits dysphagia symptoms in everyday practice

6. CONCLUSIONS

Described in this contribution experiment shows possibilities of improving data measurement and in consequence creating better classifiers for detecting patients diseases with a help of data from medical next generation diagnostic equipment. While in differential diagnosis medical physicians usually use only two variables: les length and pressure, we prove that it has basis in linear dependencies between measured variables and it can be used also in data retrieval algorithms. Thus, data retrieval techniques in this case have the same results as expert systems engineering methods. For larger variable sets, by better tuning of algorithm parameters and more precise medical equipment it will be possible to construct computer aided effective diagnosis machines.

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