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A Model for Prediction of Pelvic Inflammatory Disease and Acute Appendicitis in Childbearing-aged Women who Visit the Emergency Department with Abdominal Pain

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Purpose: We evaluated important factors for pelvic inflammatory disease (PID) and acute appendicitis, respectively, and we developed scoring systems for use in screening for PID or acute appendicitis in childbearing-aged women who visit the emergency department (ED) with abdominal pain.

Methods: By performance of multivariable logistic regression analysis, we found statistically significant factors for PID and acute appendicitis in prospectively collected registries, and we developed scoring systems for screening of each disease. The performances of these scoring systems were compared using the area under the receiver operating characteristics (ROC) curve.

Results: A total of 1048 patients were registered. Among them, 279 patients diagnosed as PID (155 patients) or acute appendicitis (124 patients) were finally analyzed in this study. The significant factors that favored PID were a length of pain onset more than two days, a history of coitus within four weeks, fever, a history of abortion, vaginal secretions, taking a painkiller for dysmenorrhea, diffuse low abdominal tenderness, no migration of pain, absence of gastrointestinal symptoms, and no leukocytosis. The significant factors that favored acute appendicitis were directly contrary to the significant factors for PID. Each of these variables was assigned a score of 1 or 2. The ROC areas of PID and acute appendicitis were 0.896 and 0.910, respectively.

Conclusion: In order to screen for PID and acute appendicitis, among other diseases, using eleven important factors, we developed scoring systems for childbearing-aged women who present with abdominal pain. Conduct of further prospective study that will utilize these scoring systems is needed.

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접수일: 2012년 8월 6일, 1차 교정일: 2012년 8월 20일
게재승인일: 2012년 10월 27일

Key Words: Pelvic inflammatory disease, Appendicitis, Abdominal pain

Introduction

Making the diagnosis of childbearing-aged women who are admitted to the emergency department (ED) with abdominal pain is more complicated than that of male patients. Furthermore, patients who have infectious diseases at the upper gynecological organs or more progressive gynecological infection at the intra-abdominal organs with a resolved infection at the low gynecological organs could be misdiagnosed as various diseases that have similar symptoms[1-4]. These kinds of misdiagnosis might lead inappropriate treatment for patients in the ED. Especially, a patient who has pelvic inflammatory disease (PID) or PID-related diseases might be discharged from the ED after only symptomatic treatment for abdominal pain without a confirmed diagnosis, antibiotic treatment and follow-up. To avoid situations like this, more sophisticated and unpleasant gynecological examinations for differentiating between different gynecological diseases, in conjunction with consulting a surgeon for making the differentiation of surgical abdominal diseases, are required. This complex process may prolong the stay of patients in the ED and result in overcrowding in the ED, and some patients have expressed dissatisfaction with this process. However, emergency physicians may not always make the accurate diagnosis of PID or acute appendicitis by using only the physical examination and routine ED laboratory results. Finally, patients may need expensive studies such as ultrasonography, abdominal-pelvis computed tomography (CT) and magnetic resonance imaging (MRI) for a precise diagnosis, and CT is hazard to childbearing-aged women due to the radiation exposure[5-7]. Therefore, we

evaluated the clinical predictive factors that are easy to ask and examine when screening for PID and acute appendicitis in childbearing-aged women who present with abdominal pain, and then we developed a scoring system that is feasible to use in the ED.

Material and Methods

1. Design, registry and predictor variables

This study is a prospective cross-sectional analysis. We have collected the registries of childbearing-aged women who presented with abdominal pain at urban EDs from April 2008 to October 2010. This study was approved by the institution review board (IRB number 20100203/6-2010-77/92) at our hospital, which is metropolitan academic teaching hospital with 40,000 annual ED visitors. The enrolled subjects were childbearing-aged women who presented to the ED with abdominal pain. But the patients who were pregnancy, those who had abdominal pain and presented with known diseases and those who were before the age of menarche or after menopause were excluded from our study. Patients were also excluded if they had undergone prior abdominal surgery such as appendectomy. The registries of the childbearing-aged women included information about age, the onset of pain, the marriage status, the obstetric history, a history of gynecologic infection (PID), a history of abortion, a history of other gynecologic diseases, the last menstrual period, the presence of vaginal secretions and dysmenorrhea, taking a painkiller for dysmenorrhea, a history of sexual contact, the use of an intrauterine device, fever (body temperature >37.8 degree centigrade), the location of pain, migration of pain, the location of abdominal tenderness, the presence of rebound tenderness, the gastrointestinal (GI) symptoms (nausea, vomiting, diarrhea and postprandial pain), the urinary symptoms (dysuria, hematuria and frequency) and costovetebral angle tenderness (CVAT). This registry was recorded by emergency physicians at the first medical examination. The laboratory data, included the total leukocyte count, the C-reactive protein (CRP) level and the urinary sediment for pyuria, was examined by quantitative analyses. The final diagnosis was identified by performing chart review. PID was confirmed by gynecologist's examination according to the 2006 CDC guideline for PID and PID-related diseases. Tubo-ovarian abscess (TOA) and Fits-Hugh-Curtis syndrome (FHCS) were included in the PID-related diseases, which were diagnosed by using trans-vaginal sonography or CT. Acute appendicitis was diagnosed by abdominal ultrasonography or CT and this was followed by a surgeon performing appendectomy and it was finally confirmed by pathological examination.

2. Statistical analysis

Statistical analysis was performed using SPSS version 12.0 (SPSS Inc., Chicago, IL). Univariate analyses involved identified Two-independent samples test for the nominal variables and Student t test for the continuous variables. We identified the significant predictive variables for PID and acute appendicitis, respectively, by the use of multivariable logistic regression analyses, along with the 95% confidence interval (CI). All the items that were included in our registry and the laboratory findings were for assessing the predictive variables within the statistical analysis. Variables were removed from the predictor variables based on the chi-square p-value in the multivariable logistic regression model, beginning with the variables with the highest *p*-values. After multivariable logistic regression analysis, the adjusted prevalence odds ratios (ORs) and the associated 95% CIs of the statistically significant predictive variables that affect the diagnosis of PID and acute appendicitis, respectively, were obtained. We created applicable weighted clinical risk scores for PID and acute appendicitis, respectively, by using the β-coefficients corresponding to each predictor in the final analyses. Each distribution of β-coefficients between the maximum and minimum values was divided into 2 intervals, and we assigned a proper score to each of the predictive variables with a range of scores of 1 or 2. We then made the PID score and acute appendicitis score for the screening models, respectively. The performances of both scores were evaluated by using the receiver operating characteristics (ROC) areas. Two cutoff points for each of the ROC areas were selected by using the points according to the sensitivity or specificity over 95%, and the likelihood ratios were obtained for each of the cutoff points of the PID score and the acute appendicitis score, respectively. Finally the proportions

of the probability of PID and acute appendicitis were calculated and divided into the low, intermediate and high risk groups, respectively.

Results

1. Study population and characteristics

A total of 1048 eligible childbearing women patients were registered in our study. The registries of 14 patients did not have complete data for some variables and analyses were excluded from the statistical analysis. Table 1 shows the disease categories of the enrolled patients. There were 155(14.8%) patients who had PID and PID-related diseases and 124(11.8%) patients who had acute appendicitis. Finally 279 patients were analyzed in this study. The range of age was between 13 and 51, and the mean age of the enrolled patients was 28.9±8.0 years old.

2. Multivariable logistic regression analyses

The clinical characteristics of the study population with PID and acute appendicitis are shown in Table 2. After the multivariable logistic regression analysis, the number of statistically significant predictive variables for PID and acute appendicitis was ten for each. The statistically significant predictive variables that favored PID were a length of pain onset more than 2 days, a coitus history within 4 weeks, fever, a history of abortion, vaginal secretions, taking a painkiller for dysmenorrhea, diffuse low abdominal tenderness, no migration of pain, the absence of GI symptoms and no leukocytosis (white blood cell count ≥10,000/μL). The significant predictive variables that favored acute appendicitis were a length of pain onset less than 2 days, no fever, no history of abortion, the absence of a coitus history within 4 weeks, no vaginal secretions, not taking painkiller for dysmenorrhea, localized right low quadrant tenderness, the presence of GI symptoms, migration of pain, and leukocytosis (Table 3).

Table 1. The diseases categories of the registered patients

Diseases categories	N (%)*
PID† &PID†-related diseases (PID†, TOA†, FHCS§)	155 (14.8)
Other gynecologic diseases	150 (14.3)
Gastrointestinal diseases	344 (32.8)
Acute appendicitis	124 (11.8)
Urologic diseases	103 (9.8)
Unconfirmed diseases	306 (29.2)
Total	1064

* N: number
† PID: pelvic inflammatory disease
‡ TOA: tubo-ovarian abscess
§ FHCS: fitz-hugh-curtis syndrome.

3. Clinical risk score for PID and acute appendicitis

Each of these significant predictive variables was assigned a range of scores of 1 or 2. These weights were determined using the distribution of the β-coefficients from the multivariable logistic regression analyses. The β-coefficients for the PID model ranged from 0.909 to 2.255, with 1.632 being the midpoint, and the β-coefficients for the acute appendicitis model ranged from 0.799 to 2.117, with 1.498 being the midpoint. We assigned a weight of 1 to the predictors with a β<1.632 and a weight of 2 to the predictors with a $\beta \geq 1.632$ for the PID score. We also assigned a weight of 1 to predictors with a β<1.498 and a weight of 2 to predictors with a $\beta \geq 1.498$ for the acute appendicitis score. The total scores of PID and acute appendicitis were 12 points and 14 points, respectively. The ROC areas for the each scores were 0.896(95% CI: 0.859-0.933) for PID and 0.910(95% CI: 0.875-0.944) for acute appendicitis.

4. Validity and performance of the PID and acute appendicitis risk scores

Among the PID and acute appendicitis scored, lower and higher risk score cutoff points were assigned by using the sensitivity and specificity that were over 95%, respectively. The lower and higher cutoff points were 3 and 8 for PID, and 6 and 10 for acute appendicitis. We obtained sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio for the PID and acute appendicitis according to each cutoff point, respectively (Table 4). Finally, the proportions of the probability of PID and acute appendicitis were divided by into the low, intermediate and high risk groups by using these cutoff points, respectively. The proportions of risk for PID and acute appendicitis were 3.2% and 1.7% for the low risk

Table 2. The clinical characteristics of PID and acute appendicitis

Clinical characteristics Overall	PID* 155 (100)	Acute appendicitis 124 (100)	*p*-value
Age (years)			
Mean±SD†	28.9±7.7	28.9±8.5	0.997
Marital status			
Married	57 (36.8)	50 (46.7)	0.545
Pain onset (days)			
Mean±SD†	4.1±4.5	1.4±1.8	<0.0001
≥2	105 (67.7)	35 (28.2)	<0.001
PID* history			
Yes	43 (27.7)	15 (12.1)	0.001
Abortion			
Yes	72 (46.5)	28 (22.6)	<0.0001
Artificial abortion			
Yes	50 (32.3)	21 (16.9)	0.004
Other noninfectious gynecologic diseases			
Yes	16 (10.3)	8 (6.5)	0.253
Menstruation			
Last period (days ago)			
Irregular	57 (36.8)	58 (46.8)	0.092
Metrorrhagia			
Yes	55 (35.5)	47 (37.9)	0.667
Menorrhagia			
Yes	52 (33.5)	45 (36.3)	0.633
Vaginal secretions			
Yes	119 (76.8)	69 (55.6)	<0.0001
Dysmenorrhea (≥one times/years)			
Yes	111 (72.1)	81 (65.3)	0.227
Taking a painkiller for dysmenorrhea			
Yes	72 (46.8)	44 (35.5)	0.059
Sexual contact			
Yes within one month	121 (78.1)	52 (41.9)	<0.0001
Intrauterine device			
Yes	12 (7.7)	5 (4.0)	0.199
Fever (≥37.8 degree centigrade)			
Yes	37 (23.9)	15 (12.1)	0.012
Migration of pain			
Yes	57 (36.8)	80 (64.5)	<0.0001
Location of tenderness			
Diffuse upper	69 (44.5)	15 (12.1)	<0.0001
Localized right upper quadrant	57 (36.8)	4 (3.2)	<0.0001
Diffuse lower	67 (69.1)	30 (23.2)	0.001
Localized right lower quadrant	69 (44.5)	105 (84.7)	<0.0001
Rebound tenderness			
Yes	63 (40.6)	70 (56.5)	0.009
GI† symptoms (nausea/vomiting/diarrhea/postprandial pain)			
No	89 (57.4)	45 (36.3)	0.001
Urologic symptoms (dysuria/hematuria/frequency/residual urine/cloudy)			
No	129 (83.2)	114 (91.9)	0.031
CVAT§			
Yes	42 (27.1)	14 (11.3)	0.001
Elevation of the WBC‖ count (>10,000/μL)			
Mean±SD†	10597±4011	13364±4729	0.011
Yes	72 (46.5)	91 (73.4)	<0.0001
Elevation of the CRP¶ level (>0.5 mg/dL)			
Mean±SD†	6.52±7.42	4.33±6.80	<0.0001
Yes	110 (71.0)	71 (57.3)	0.017
Pyuria (white blood cell count ≥5/HPF**)			
Yes			
No	99 (65.1)	97 (78.9)	0.013

* PID: pelvic inflammatory disease, † SD: standard deviation, † GI: gastrointestinal, § CVAT: costovertebral angle tenderness, ‖ WBC: white blood cell, ¶ CRP: c-reactive protein, ** HPF: high power field.

group, 49.5% and 32.3% for the intermediate risk group and 96.9% and 93% for the high risk group, respectively (Table 5).

Discussion

PID is a clinical syndrome that has been defined by the Centers for Disease Control and Prevention (CDC) as a spectrum of upper genital tract infections that includes any combination of endometritis, salpingitis, pyosalpinx, TOA and pelvic peritonitis. In the 2006 center for disease control (CDC) guideline, there were minimum criteria and additional supportive criteria for making the diagnosis of PID[8]. The minimum criteria included cervical motion tenderness (CMT), uterine tenderness and adnexal tenderness. The supportive criteria included an increase of the body temperature (BT), leukorrhea, vaginal secretions, an elevated erythrocyte sedimentation rate or CRP level, and cervical infection with Neisseria gon-

Table 3. The statistically significant predictive variables of PID and acute appendicitis by multivariable logistic regression analysis

Predictor variables	PID* ROC† 0.896				Acute appendicitis ROC† 0.910			
	B†	OR§	95% CI‖	*p*-value	B†	OR§	95% CI‖	*p*-value
Pain onset								
<2 dyas								
≥2 days	2.255	9.538	4.417-20.596	<0.001	2.117	8.303	3.734-18.461	<0.001
Fever (>37.8˚C)								
Yes	1.442	4.228		0.005				
No					1.499	4.476	1.610-12.441	0.004
Abortion								
Yes	1.142	3.132	1.440-6.816	0.004				
No					1.244	3.468	1.582-7.601	0.002
Vaginal secretions								
Yes	1.087	2.965	1.424-6.173	0.004				
No					1.098	2.997	1.402-6.407	0.005
Taking a painkiller for dysmenorrhea								
Yes	0.933	2.542	1.219-5.300	0.013				
No					0.962	2.616	1.238-5.526	0.012
Sexual contact								
Yes within one month	1.546	4.693	2.257-9.757	<0.001				
No within one month					1.816	6.144	2.812-13.426	<0.001
Location of tenderness								
Diffuse lower or bilateral	0.909	2.482	1.186-5.195	0.016				
Localized right lower quadrant					1.743	5.713	2.566-12.721	<0.001
Migration of pain								
Yes					1.050	2.858	1.357-6.019	0.006
No	1.342	3.827	1.878-7.798	<0.001				
Gastro-intestinal symptoms								
Yes					0.779	2.178	1.054-4.503	0.036
No	0.909	2.481	1.230-5.001	0.011				
Elevation of the WBC count (>10,000/μL)								
Yes					0.854	2.348	1.086-5.077	0.03
No	1.010	2.745	1.299-5.799	0.008				

* PID: pelvic inflammatory disease
† ROC: receiver operating characteristics
† B: beta-coefficient
§ OR: odds ratio
‖ CI: confidence interval.

orrhea or Chlamydia trachomatis. Acute PID infections are associated not only with psychological, economic and public health burdens, but also with long-term sequelae, including infertility, ectopic pregnancy, recurrent PID, chronic pelvic pain and cancer[9-13]. Making the differential diagnosis between PID and acute appendicitis using only a physical examination and laboratory findings has been of the oldest unsolved problems in EDs. There have been many attempt to screen for gynecological infection, such as sexually transmitted diseases and PID, and to create a feasible technique for rapidly detecting the chlamydial and gonococcal infections in EDs[14-20]. There have been some studies about the under-recognition, misdiagnosis and under-treatment of chlamydial and gonococcal infection in EDs[1,2,4]. The clinical diagnosis of PID is imprecise and difficult because of the wide variations of signs and symptoms; many women with PID exhibit subtle, vague or mild symptoms[21-23]. PID might progress to peritonitis in the pelvic cavity or the intra-abdominal space due to ascending infection, which is mainly Chlamydia trachomatis and some other organisms. FHCS is complication of uncured PID and it might develop by ascending infection of the causative organisms from the pelvic cavity to the capsule of the liver[24,25]. Therefore, FHCS should be treated with the same regimen as that of PID. We also considered that FHCS was a PID-related disease and it was counted in the criteria of PID. The characteristics of FHCS patient are pleuritic RUQ pain, migration of pain from the low abdomen to the upper abdomen and sometimes to the right CVAT[24].

The length of stay in the ED may be increased by conducting further studies and examination for making the differential diagnosis. We might overcome this weak point for childbearing women with abdominal pain by conducting screening programs or creating a scoring system. We developed some different scoring systems for predicting PID and acute appendicitis in childbearing women with abdominal pain from previous studies[17]. We assigned a range of scores of 1 or 2 points to each of the significant predictive variables by using the distribution of the β-coefficients from the multivariable logistic regression analyses. We categorized the risk groups of the PID and acute appendicitis scores into the low, inter-

Table 4. Validity of prediction method for the PID and acute appendicitis according to each scores

Diagnosis	Cutoff point	Sensitivity	Specificity	PPV*	NPV†	PLR‡	NLR§
PID‖	≥3	99.4 (95.9-100)	24.2 (17.2-32.9)	61.9 (55.5-68.0)	96.8 (81.5-99.8)	1.31 (1.19-1.45)	0.03 (0.00-0.20)
	≥8	40.9 (33.2-49.1)	98.4 (93.7-99.7)	96.9 (88.4-99.5)	57.3 (50.3-64.0)	25.40 (6.33-101.60)	0.60 (0.53-0.69)
Acute appendicitis	≥6	99.2 (94.9-100)	37.7 (30.1-45.9)	56.2 (49.3-62.8)	98.3 (89.7-99.9)	1.59 (1.41-1.80)	0.02 (0.00-0.15)
	≥10	64.5 (55.4-72.8)	96.1 (91.3-98.4)	93.0 (84.9-97.1)	77.1 (70.4-82.7)	16.56 (7.48-36.68)	0.37 (0.29-0.47)

95% Confidence interval in parentheses.
* PPV: positive predictive value
† NPV: negative predictive value
‡ PLR: positive likelihood ratio
§ NLR: negative likelihood ratio
‖ PID: pelvic inflammatory disease.

Table 5. Risk status and proportions according to the risk score for PID and acute appendicitis

	PID*		Acute appendicitis	
Risk Status	Interval of the score	Proportion (%)	Interval of the score	Proportion (%)
Low	0~2	1/31 (3.2)	0~5	1/59 (1.7)
Intermediate	3~7	90/182 (49.5)	6~9	43/133 (32.3)
High	≥8	63/65 (96.9)	≥10	80/86 (93.0)

* PID: pelvic inflammatory disease.

mediate and high risk groups. So for the high PID risk patient, the emergency physician should first call a gynecologist to conduct a gynecologic examination with trans-vaginal ultrasonography. In contrast, for the acute appendicitis risk patients, the emergency physician should first confirm acute appendicitis by using abdominal ultrasonography or CT and then a surgeon should be consulted according to the results of these studies.

Further study will be needed for prospectively validating our scoring system in our hospital and other hospital.

Our study had the following limitations. First, our study was a single-center study. Second, some other predictor variables such as the socioeconomic status, a medication history of oral contraceptives, condom use, smoking and the number of sexual partners were not counted in our study.

Conclusion

We developed scoring systems for childbearing-aged women who present with abdominal pain to screen for PID and acute appendicitis, among other diseases, by using eleven important factors. Further prospective study that will use these scoring systems is needed.

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