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Prognosis Predictors of Pelvic Inflammatory Disease among the Hospitalized Patients

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Abstract

Introduction: Serious reproductive health consequences linked to pelvic inflammatory disease (PID) include infertility and ectopic pregnancy. Thus, it is important to identify patients likely to have a poor prognosis in choosing the best initial treatment. The aim of our study was to identify the valuable prognosis predictors of PID among the hospitalized patients and determined cut off values of quantitative independent prognosis predictors.

Material and methods: Hospital records for women hospitalized with PID were retrospectively examined. The PID patients were divided into two sub-groups according to their clinical outcome. Prognostic factors were evaluated by T-test, χ2-test, and logistic regression analysis. The cut-off values of age, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and ESR combined with CRP were calculated by receiver-operator curve analysis.

Results: Independent prognosis predictors of PID were advanced age (OR=1.031, 95% CI=1.002-1.062; P=0.036), elevated ESR (OR=1.029, 95% CI=1.013-1.046; P<0.001), increased CRP (OR=1.096, 95% CI=1.027-1.169; P=0.006), and presence of endometriosis (OR=5.700, 95% CI=1.123-28.943; P=0.025). The cut-off values of age, ESR, CRP, and ESR combined with CRP were 35 years, 30.5 mm/hr, 7.0 mg/dL, and 25 mm/hr and 6.5 mg/dL respectively.

Conclusions: The initial treatment of patients who are elderly, and/or who have endometriosis, elevated ESR, or increased CRP should be carefully decided. Evaluation of ESR together with CRP is recommended to gain a more accurate prediction of disease outcome.

Keywords: Pelvic inflammatory disease; C-reactive protein; Erythrocyte sedimentation rate; Risk factors; Sexually transmitted disease

Abbreviations: PID: Pelvic Inflammatory Disease; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; IUD: Intrauterine Device; MPV: Mean Platelet Volume; TOA: Tubo-Ovarian Abscess; ROC: Receiver-Operator Curve; AUC: Area Under The Curve

Introduction

The known risk factors of pelvic inflammatory disease (PID) include age<25 years, age at first sexual intercourse <15 years, lower socioeconomic status, being single, adverse pregnancy outcome, self-reported history of a sexually transmitted disease, and exposure to Chlamydia trachomatis [1-3]. Although risk factors of PID are almost fully understood, there are still several important unanswered questions about PID, particularly the question of which patients are likely to have a poor clinical course. Serious reproductive health consequences linked to PID include infertility and ectopic pregnancy. Thus, it is important to identify patients likely to have a poor prognosis in choosing the best initial treatment.

In previous studies, prognosis predictors including epidemiological factors, clinical signs, ultrasonography findings, and laboratory data obtained on admission were evaluated to examine their association with a clinical course of PID. Age, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), previous intrauterine surgery, presence of endometriosis, and intrauterine device (IUD) use have been implicated as relevant prognostic factors in some studies but sometimes controversial results have been reported [4-14]. Furthermore, in recent studies, mean platelet volume (MPV) in patients with PID were lower than those in the control group and platelet indices were noted to be factors related to some inflammatory diseases [15-19] Among the factors mentioned above, elevated ESR and CRP values have been reported to be main prognosis predictors of PID but the cut-off values for these reads have not been accurately determined.

Our study is a comprehensive report of previous studies mentioned above and the aim was to identify the valuable prognosis predictors of PID among the hospitalized patients and determined cut off values of quantitative independent prognosis predictors.

Methods

This retrospective study enrolled women with PID treated at the Department of Obstetrics and Gynecology, CHA University Gumi Hospital, Gumi, Republic of Korea, between January 2008 and December 2012. Centres for Disease Control and Prevention (CDC) criteria were used for PID diagnosis. The decision of whether hospitalization was necessary was based on the judgment of the provider and also whether the patient met any of the following suggested criteria: (i) surgical emergency cannot be excluded, (ii) no response to oral antimicrobial therapy, (iii) inability to follow or tolerate outpatient therapy, or (iv) severe illness with nausea, vomiting, or high fever [20]. Exclusion criteria included age<18 years or >70 years, presence of chronic disease,

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pregnancy, and admission diagnosis of tubo-ovarian abscess (TOA) on admission. Following exclusions, 279 women were studied. When conducted, combination therapy comprised triple antibiotic therapy with metronidazole, aminoglycoside, and cephalosporin. Patients received these antibiotics until clinical symptoms and signs improved.

The PID patients were divided into two sub-groups according to their clinical outcome. The median duration of hospitalization for all cases was 7 days. One group comprised 117 patients discharged within 7 days and only given a conservative treatment (favorable clinical course group). The other group comprised 162 patients who needed hospitalization for more than 7 days and/or diagnosed with pyosalpinx or TOA after being hospitalized on day 2 (poor clinical course group). There were 267 cases of uncomplicated PID and 12 cases of complicated PID suspected as pyosalpinx or TOA after the second day of hospitalization. The patients with complicated PID were included in the poor clinical course group.

Factors used for prediction of prognosis were obtained on admission. Patients diagnosed before admission or upon entry with endometriosis were included. Intrauterine operations included embryo transfer (ET), intrauterine insemination (IUI), dilatation and curettage (D&C), and hysteroscopy (HSC). These were categorized into one group because all involved insertion of instruments into the uterine cavity through the cervix. The subdivisions for intrauterine operation (favorable/poor clinical course) were ET (0/0), IUI (0/0), D and C (28/56), and HSC (19/21).

The results obtained were statistically analyzed with the Statistical Package for Social Sciences software program (SPSS, Chicago IL, USA). T-and χ2-tests were used for data analysis as appropriate. Binary logistic regression analysis was performed to reveal the independent prognosis predictors of PID. A P-value<0.05 was considered statistically significant. The cut-off values for age, ESR, CRP, and ESR combined with CRP were calculated by the receiver-operator curve (ROC) analysis.

Results

Among the 279 females diagnosed with PID, 117 (41.9%) were in the favorable clinical course group and 162 (58.1%) were in the poor clinical course group. Using T-test and χ2-test, mean age, platelet count, ESR, CRP, presence of endometriosis, and rate of IUD use were higher in the poor clinical course group than in the favorable clinical course group. There were no significant differences between the groups in terms of MPV level and rate of previous intrauterine surgery (Table 1).

Independent prognosis predictors of PID were advanced age (OR=1.031, 95% CI=1.002-1.062; P=0.036), elevated ESR (OR=1.029, 95% CI=1.013-1.046; P<0.001), increased CRP (OR=1.096, 95% CI=1.027-1.169; P=0.006), and presence of endometriosis (OR=5.700, 95% CI=1.123-28.943; P=0.025). Platelet count and IUD use were not independent prognosis predictors (Table 2).

A ROC curve was constructed and used to select cut-off values for the occurrence of poor prognosis. The area under the curve (AUC) for age was 0.63 and the cut-off value was 35 years of age, yielding a sensitivity of 51.9% and specificity of 66.7% (Figure 1A). For ESR, the AUC was 0.78 and the cut-off value was 30.5 mm/hr, yielding a sensitivity of 75.2% and specificity of 72.2% (Figure 1B). For CRP, AUC was 0.77 and the cut-off value was 7.0 mg/dL, yielding a sensitivity of 79.5% and specificity of 46.9% (Figure 1C). For ESR combined with CRP, AUC was 0.79 and the cut-off value was 25 mm/hr and 6.5 mg/dL, respectively, yielding a sensitivity of 81.5% and specificity of 73.5% (Figure 1D).

Discussion

The present study was a comprehensive analysis of the effect of multiple variables on the poor prognosis of PID. Advanced age, elevated ESR, increased CRP, and presence of endometriosis were independent prognosis predictors of PID.

Patient age was previously implicated as a potential prognosis predictor of PID [4]. Age was also reported as an independent factor predictive of TOA in acute PID, with an age exceeding 35 years old a benchmark that strongly correlated with an increase in the risk for PID surgery as a result of failed conservative treatment [6,7]. The present

Factors	Favorable clinical course group (n=117)	Poor clinical course group (n=162)	95% CI	*P*-value
Age	30.47 ± 9.07	35.42 ± 11.01	2.578-7.322	<0.001
MPV	7.52 ± 0.88	7.60 ± 0.78	-0.392	NS
Platelet count	300910 ± 90470	334320 ± 123238	6.967-59.846	0.01
ESR	23.03 ± 21.65	47.20 ± 27.26	18.400-29.944	<0.001
CRP	3.37 ± 4.91	8.50 ± 6.74	3.755-6.501	<0.001
Intrauterine surgery	47(40.2%)	77(47.5%)	-1.933	NS
Endometriosis	2(1.7%)	13(8.0%)	0.040-0.216	0.029
IUD use	10(8.5%)	31(19.1%)	0.044-0.251	0.016

Values are given as a mean standard deviation or number (percentage). CI: Confidence Interval; MPV: Mean Platelet Volume; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; IUD: Intrauterine Device; NS: Non-Significant; PID: Pelvic Inflammatory Disease

Table 1: T-test and χ2-test of factors related to the clinical course of PID.

Factors	Odds ratio	95% CI	*P*-value
Age	1.031	1.002-1.062	0.036
Platelet count	-	0.998-1.004	NS
ESR	1.029	1.013-1.046	<0.001
CRP	1.096	1.027-1.169	0.006
Endometriosis	5.700	1.123-28.943	0.025
IUD use	-	0.788-4.469	NS

CI: Confidence Interval; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; IUD: Intrauterine Device; NS: Non-Significant; PID: Pelvic Inflammatory Disease

Table 2: Multivariate analysis of factors related to the clinical course of PID.

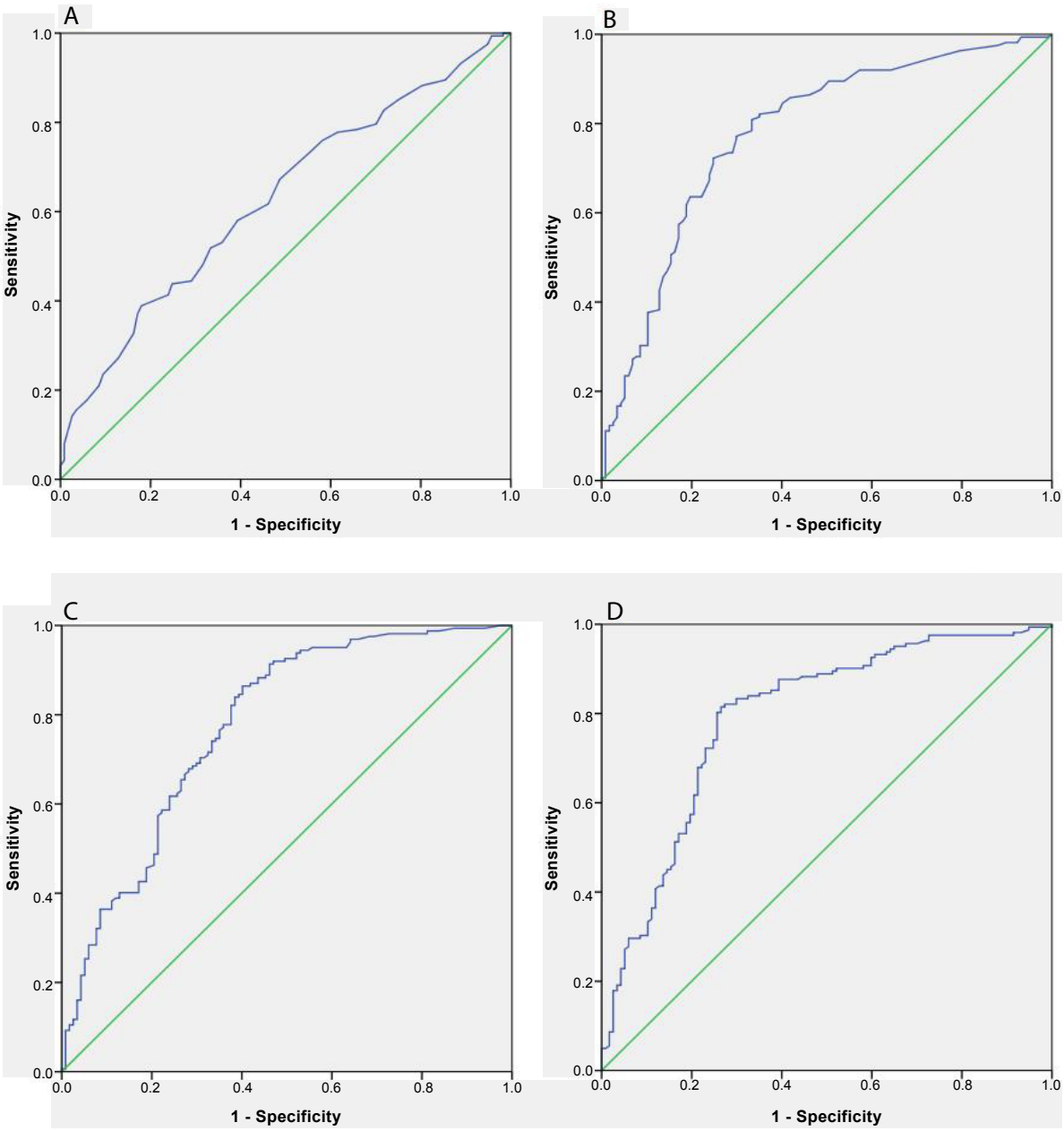

Figure 1: The cut-off value for age (A), erythrocyte sedimentation rate (ESR; B), Creactive protein (CRP; C) and ESR combined with CRP (D) calculated by receiver operator curve analysis.
(A) The area under the curve (AUC) was 0.63 and the cut-off value was 35 years, yielding a sensitivity of 51.9% and specificity of 66.7%.
(B) The AUC was 0.77 and the cut-off value was 30.5 mm/hr, yielding a sensitivity of 75.2% and specificity of 72.2%.
(C) The AUC was 0.77 and the cut-off value was 7.0 mg/dL, yielding a sensitivity of 79.5% and specificity of 46.9%.
(D) The AUC was 0.79 and the cut-off value was 25 mm/hr and 6.5 mg/dL, yielding a sensitivity of 81.5% and specificity of 73.5%.

data corroborate advanced age as an independent prognosis predictor of PID, with a cut-off value of 35 years. Possible explanations for age as an influence in a poor clinical outcome in women with PID are inherent weakness or vulnerability of the subjects, a tendency not to seek medical help at an advanced age, and delayed diagnosis due to a reduced suspicion of PID among gynaecologists [4]. PID patients over 35 years of age require careful initial management.

The consensus is that ESR and CRP are related with poor prognosis in PID and that these factors reflect PID severity. In a previous study, ESR with CRP levels were useful for assessing the severity of acute PID [8]. Another study concluded that ESR>50 mm/h was the best predictor of TOA and prolonged hospital stay in PID patients [5]. Our study findings echo these observations and add to the weight of evidence of an association between ESR and CRP and poor clinical course. ROC analysis indicated an ESR and CRP cut-off value of 30.5 mm/hr and 7.0 mg/dL, respectively (ESR: sensitivity of 75.2% and specificity of 72.2%, CRP: sensitivity of 79.5% and specificity of 46.9%). Furthermore, the cut-off value of ESR combined with CRP was >25 mm/hr and >6.5 mg/dL, a sensitivity of 81.5% and specificity of 73.5%. The cut-off value of ESR combined with CRP was more predictive than the separate cut-off

values. Thus evaluation of ESR together with CRP is recommended to provide a more accurate prediction of the disease prognosis. There is a possible explanation as to why elevated ESR and CRP are important prognosis predictors of PID. Elevations in ESR and CRP are manifest as histologically evident tissue injury and inflammation. It is more likely that the ESR and CRP values reflect the severity of the clinical findings for PID. Assuming the capacity of recovery at baseline is similar, higher ESR and CRP values for PID patients reflect longer hospitalization periods.

In women hospitalized with PID, the reported 14% prevalence of endometriosis was higher than the reported 6-10% prevalence of endometriosis [10,12]. Besides, our study revealed that endometriosis was related to a poor prognosis of PID and patients with endometriosis had 5.7-fold higher probability of having a poor prognosis. A possible link between endometriosis and poor prognosis of PID is the role of endometriosis in the pelvic cavity. Endometriosis is an immunologically aberrant disease that makes the pelvic cavity vulnerable to infection as the bloody, exposed nature of endometriosis can serve as an incubator for bacteria, facilitating the spread of infection. Therefore, patients who have endometriosis with PID-related symptoms may be in need of careful evaluation and intensive management when they require hospitalization.

The transcervical intrauterine route is commonly used in operative gynecological procedures in women. The vagina is an area of the body that is abundant with normal bacterial flora. Thus surgery through the vagina has the potential for post-procedure infection [21]. A history of intrauterine surgery history has been reported as being independently related with the clinical course of PID [4]. However, the clinical course of PID was not presently associated with previous intrauterine surgery. The different results may be due to the proportion of ET patients. In the study of Friedler et al., severe PID was considered a potential complication of ET and the percentage of their patients with ET linked with severity of PID was 30% [22]. With our patients the percentage was 0%. Therefore, prospective studies that include subdivisions of previous intrauterine surgery may be required to confirm whether certain/all types of intrauterine surgery are associated with the poor prognosis of PID.

Low MPV level might correlate with the poor prognosis of PID, because MPV level was significantly decreased in patients with PID in a recent study [15]. However, in the present study neither MPV nor platelet count was independently associated with PID prognosis. Despite this, the present data do indicate the value of platelet indices. Platelet indices warrant further study as prognostic predictors of PID, given their importance in the diagnosis and prognosis of inflammatory diseases [16,18,23].

IUD use has been associated with poor prognosis and is a predictive factor of TOA in acute PID in one study, while other recent studies found no correlation [4,6,7]. We can suggest several reasons for the discrepancy between studies. IUDs were developed to minimize inflammation in the uterine endometrium; a consequence may be infections in the upper genital tract [24-26]. The type of IUD and the duration of use might also have a bearing on its infection risk. For example, the PID rates are lower among women who had an IUD inserted more recently [27]. In our study, most of the IUD users received the first or last IUD insertion in the prior 5 years and IUDs were removed on the admission day. Consequently, the contribution of IUD use to PID might be lower in our cases.

Even though this study was retrospective, it might have a high predictive value due to the large number of subjects. In addition, it included various inflammatory markers and clinical findings of PID that were successful in obtaining significant cut-off values for independent prognosis predictors. Advanced patient age, elevated ESR, increased CRP, and presence of endometriosis were independent prognostic predictors of PID and the cut-off value of age was 35 years and that of ESR combined with CRP was 25 mm/hr with 6.5 mg/dL. The cut-off value of ESR combined with CRP was more predictive than the separate cut-off values. Consequently, the initial treatment of patients who are elderly, and/or who have endometriosis, elevated ESR, or increased CRP should be carefully decided and evaluation of ESR together with CRP is recommended to gain a more accurate prediction of disease outcome.

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