# Analysis of Risk Factors for Surgical Treatment of Acute Female Pelvic Inflammatory Disease

Ann. Ital. Chir., 2024 95, 4: 724–728 https://doi.org/10.62713/aic.3364

Xu-Wei Chen<sup>1</sup>, Ye-Qin Zhu<sup>1</sup>, Ping Yu<sup>1</sup>, Jun-Qiang Du<sup>1</sup>, Hua-Qing Li<sup>2</sup>

AIM: To investigate the incidence and high-risk factors associated with the surgical treatment of acute female pelvic inflammatory disease (PID).

METHODS: A retrospective analysis was conducted on all inpatients diagnosed with acute female PID, encompassing conditions such as endometritis, salpingitis, tubo-ovarian abscess, ovarian abscess, and pelvic peritonitis, at Dongyang Hospital of Wenzhou Medical University from January 2013 to December 2021. Patients were categorized into two groups: the surgery group (n = 58) and the non-surgery group (n = 399), based on the necessity of surgical intervention (refer to Materials and Methods for surgical indications). Collected data included patient demographics (age, body mass index (BMI)), comorbidities (hypertension, diabetes mellitus), initial laboratory findings upon admission (white blood cell count, absolute neutrophil count, hemoglobin, platelet count, blood urea nitrogen/creatinine, prothrombin time (PT), international normalized ratio (INR), fibrinogen, albumin), surgical records, and postoperative pathology. Univariate and multivariate logistic regression analyses were conducted to ascertain the risk factors associated with the surgical treatment of acute female PID.

RESULTS: Out of 457 hospitalized patients with acute female PID, 58 cases (12.7%) required surgical intervention. Univariate and multivariate logistic regression analyses indicated that advancing age correlated with an increased likelihood of surgical intervention in women with acute PID (odds ratio (OR) = 1.052, 95% Confidence Interval (CI) 1.022–1.082, p = 0.001). Additionally, lower serum albumin levels upon admission were associated with a heightened risk of surgery (OR = 0.913, 95% CI 0.859–0.970, p = 0.003), while elevated fibrinogen levels amplified the risk of surgical intervention in these patients (OR = 1.193, 95% CI 1.008–1.411, p = 0.04). CONCLUSIONS: Elderly women diagnosed with acute PID, especially those presenting with abscess formation, should undergo prompt surgical intervention if they display high-risk factors such as low albumin levels and elevated fibrinogen levels upon admission.

Keywords: acute female pelvic inflammatory disease; surgical treatment; high-risk factors

# Introduction

Acute female pelvic inflammatory disease (PID) denotes a prevalent inflammatory response within the female reproductive tract [1], encompassing conditions like endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis. Predominantly affecting young sexually mature women, its prevalence stands at 1–2% among this demographic [2]. Presently, the primary treatment for acute female PID entails antimicrobial therapy, typically spanning two weeks. Selections commonly include broad-spectrum antimicrobial agents targeting potential pathogens such as Neisseria gonorrhoeae, Chlamydia trachomatis, mycoplasma, anaerobes, and aerobes. When administered appropriately and standardized, antimicrobial agents boast a curative rate of 90% for female PID cases [3].

Correspondence to: Hua-Qing Li, Department of Reproductive Center, Dongyang Hospital of Wenzhou Medical University, 322100 Dongyang, Zhejiang, China (email: 13858964837@163.com). Jun-Qiang Du, Department of Gynecology, Dongyang Hospital of Wenzhou Medical University, 322100 Dongyang, Zhejiang, China (email: dydulv@163.com)

Nevertheless, a significant portion of patients still encounter inadequate response to medical treatment, resulting in prolonged disease duration and heightened risk of complications such as infertility, chronic pelvic pain, and hydrosalpinx, among others, significantly impacting female health [4]. In some instances, patients may develop pelvic abscesses (including pyosalpinx, ovarian abscess, tubo-ovarian abscess, and pelvic abscess stemming from acute peritonitis and acute pelvic connective tissue inflammation [5]), or even experience abscess rupture, necessitating surgical intervention. Particularly concerning pelvic abscesses, the etiology is multifaceted, and clinical presentations are diverse. Delayed surgical intervention may precipitate severe adverse outcomes such as sepsis and multiple organ failure [6]. This retrospective study aims to analyze the high-risk factors associated with surgical treatment of acute female PID, furnishing evidence to guide surgical decision-making in these patients.

<sup>&</sup>lt;sup>1</sup>Department of Gynecology, Dongyang Hospital of Wenzhou Medical University, 322100 Dongyang, Zhejiang, China

<sup>&</sup>lt;sup>2</sup>Department of Reproductive Center, Dongyang Hospital of Wenzhou Medical University, 322100 Dongyang, Zhejiang, China

## **Materials and Methods**

Study Subjects

Data were collected from a cohort of 457 hospitalized patients diagnosed with acute female PID at Dongyang Hospital of Wenzhou Medical University between January 2013 and December 2021.

Inclusion criteria were defined as follows: (1) Diagnosis of acute female PID according to Chinese diagnostic criteria [7]. Patients meeting the minimum diagnostic criteria, which encompass uterine or adnexal tenderness or cervical motion tenderness, were included in the study group. Additional diagnostic criteria included oral temperature >38.3 °C; abnormal vaginal or cervical discharge; presence of a large number of white blood cells revealed in vaginal secretions via wet sheet microscopy with 0.9% sodium chloride solution; elevated erythrocyte sedimentation rate; elevated C-reactive protein; laboratory evidence of cervical infection with Neisseria gonorrhoeae or Chlamydia trachomatis. The most specific diagnostic criteria encompassed histological evidence of endometritis on uterine biopsy; thickening of the fallopian tube wall; tubal fluid accumulation, with or without pelvic fluid accumulation or tubo-ovarian abscess shown on ultrasound or magnetic resonance imaging, indicative of pelvic infection (such as tubal congestion on ultrasound); abnormal findings consistent with PID on laparoscopy. (2) Hospitalization with complete medical records.

Exclusion criteria were: (1) Use of corticosteroids or immunosuppressive agents within three months prior to hospitalization; (2) Presence of liver diseases, malignancies, or other conditions that may affect serum albumin levels; (3) Diagnosis of hematological diseases or use of anticoagulants.

Patients were categorized into surgery and non-surgery groups based on whether surgical treatment was administered. This study received approval from the hospital ethics committee.

#### Data Collection

A retrospective analysis was performed on patient clinical data, encompassing age, body mass index (BMI), presence of hypertension and diabetes complications, as well as initial laboratory test results upon admission (including white blood cell count, absolute neutrophil count, hemoglobin, platelet count, blood urea nitrogen/creatinine, prothrombin time (PT), international normalized ratio, fibrinogen, and albumin levels), surgical records, and postoperative pathology.

#### Treatment Options

All patients underwent cervical microbiological culture following admission. Severity of infection and potential pathogens were assessed based on a comprehensive evaluation of symptoms, physical examination, and auxiliary tests. Mild infection was characterized by patients having a generally good overall condition, body temperature below 38 °C, abdominal pain score of less than 3 (quantified using the Numeric Rating Scale (NRS)), absence of gastrointestinal or bladder irritation symptoms or rebound tenderness, and C-reactive protein (CRP) levels below 50 mg/L.

Moderate infection was indicated by body temperature ranging between 38–39 °C, abdominal pain score between 4–6, absence of gastrointestinal or bladder irritation symptoms, and CRP levels between 50–100 mg/L.

Severe infection manifested as poor general condition, body temperature above 39 °C, abdominal pain score of 7 or higher, acute facial expression, chills, shivering, presence of gastrointestinal or bladder irritation symptoms, abdominal tenderness, rebound tenderness, and CRP levels greater than 100 mg/L.

Taking into account the patient's allergy history, treatment for moderate to severe infections consisted of intravenous ceftriaxone-sulbactam, piperacillin-tazobactam, or imipenem for anti-infection. Patients with mild infections received intravenous cefuroxime, ceftriaxone, or levofloxacin plus metronidazole for anti-infection. Oral doxycycline was administered if pathogen culture indicated positive for Chlamydia or Mycoplasma.

### Surgical Indications

(1) Persistence of fever and worsening symptoms, or enlargement of masses, despite 48 to 72 hours of medical treatment. (2) Resolution of symptoms following antibiotic therapy for tubo-ovarian abscess, but persistent mass observed after 2 weeks of treatment. (3) Rupture of abscess. Surgical intervention involves laparoscopy or open surgery for excision of the affected side's abscess lesion. Intraoperative placement of pelvic drainage tube is carried out, followed by postoperative continuation of antibiotic treatment. Patients were discharged upon achieving cure.

#### Statistical Methods

Statistical analyses of the data were conducted using SPSS 18.0 software (IBM, Chicago, IL, USA). Measurement data were expressed as median (M) and interquartile range (Q25, Q75) if the distribution was non-normal, and the Mann-Whitney U test was utilized. Categorical data were presented as cases (percentage) and analyzed using the  $\chi^2$  test. Significant indicators identified in univariate analysis were incorporated into logistic regression for multivariate analysis, with p < 0.05 considered statistically significant.

## Results

The Incidence of Surgical Treatment in Patients with Acute Female PID

Out of 457 inpatients diagnosed with acute female PID, a total of 58 cases underwent surgical treatment, resulting in a surgical treatment incidence rate of 12.7%. Predominantly, the abscesses were located in the unilateral ovary and fal-

Table 1. Univariate analysis of surgical treatment for acute female PID.

| Classification                               | Conservative treatment group $(n = 399)$ | Surgery group $(n = 58)$ | $\mathrm{U}/\chi^2$ | p       |
|--|--|--------------------------|---------------------|---------|
| BMI  | 22.2 (20.1, 24.6)                        | 22.2 (19.8, 24.8)        | -0.549              | 0.583   |
| Age  | 40 (32, 48)                              | 47 (42, 52)              | -4.337              | < 0.001 |
| Co-existing hypertension                     |  |                          | 5.009               | 0.025   |
| yes  | 15 (3.8)                                 | 6 (10.3)                 |                     |         |
| no   | 384 (96.2)                               | 52 (89.7)                |                     |         |
| Co-existing diabetes                         |  |                          | 6.382               | 0.012   |
| yes  | 13 (3.3)                                 | 6 (10.3)                 |                     |         |
| no   | 386 (96.7)                               | 52 (89.7)                |                     |         |
| Blood urea nitrogen/creatinine               | 0.7 (0.6, 0.9)                           | 0.7 (0.6, 0.9)           | -0.142              | 0.887   |
| White blood cell count (×10 <sup>9</sup> /L) | 10.2 (7.3, 14.2)                         | 11.4 (7.2, 16.0)         | -0.701              | 0.483   |
| Neutrophil count (×10 <sup>9</sup> /L)       | 8.1 (5.1, 11.8)                          | 9.3 (5.5, 13.7)          | -1.071              | 0.284   |
| Hemoglobin (g/L)                             | 123.0 (111.0, 131.0)                     | 120.0 (110.0, 127.5)     | -1.335              | 0.182   |
| Platelet count (×10 <sup>9</sup> /L)         | 251.0 (207.0, 301.0)                     | 272.5 (226.8, 370.3)     | -2.288              | 0.022   |
| Fibrinogen (g/L)                             | 4.5 (3.2, 5.9)                           | 6.0 (4.3, 7.5)           | -4.183              | < 0.001 |
| International normalized ratio               | 1.1 (1.0, 1.2)                           | 1.1 (1.0, 1.2)           | -1.211              | 0.226   |
| PT (S)                                       | 13.8 (13.1, 14.5)                        | 14.1 (13.4, 14.7)        | -1.492              | 0.136   |
| Serum albumin (g/L)                          | 38.9 (35.8, 42.1)                        | 35.2 (31.5, 39.4)        | -4.785              | < 0.001 |

PID, pelvic inflammatory disease; PT, prothrombin time; BMI, body mass index.

Table 2. Multicollinearity assessment of the six indicators.

| Influencing factors      | Tolerance | VIF    |  |
|--------------------------|-----------|--------|--|
| Age                      | 0.949     | 1.053  |  |
| Albumin                  | 0.774     | 1.293  |  |
| Platelet count           | 0.948     | 1.055  |  |
| Fibrinogen               | 0.767     | 1.304  |  |
| Co-existing hypertension | 0.098     | 10.186 |  |
| Co-existing diabetes     | 0.099     | 10.133 |  |

VIF, variance inflation factor.

lopian tube, with 7 cases of bilateral ovary and fallopian tube abscesses (12.1%), 46 cases of unilateral ovary and fallopian tube abscesses (79.3%), 2 cases of unilateral ovary abscesses (3.4%), and 3 cases of unilateral fallopian tube abscesses (5.2%).

#### Univariate Analysis of Surgical Treatment for Acute Female PID

Univariate analysis of surgical treatment for acute female PID revealed that age, initial serum albumin level upon admission, fibrinogen level, platelet count, presence of hypertension, and presence of diabetes mellitus were statistically significant (p < 0.05). Conversely, BMI, initial white blood cell count, absolute neutrophil count, hemoglobin level, blood urea nitrogen/creatinine ratio, prothrombin time, and international normalized ratio showed no statistically significant effect on the need for surgical treatment of acute female PID (p > 0.05) (Table 1).

Multivariate Analysis of Surgical Treatment for Acute Female PID

Prior to conducting the multivariate analysis, a collinearity diagnosis was performed on the six features identified in the preceding step. The results indicated that the variance inflation factors (VIFs) for both Co-existing hypertension and Co-existing diabetes >10 (Table 2). Given the presence of multicollinearity between Co-existing hypertension and Co-existing diabetes, these two variables were excluded from further analysis. Subsequently, a multivariate logistic regression analysis was conducted on the remaining four features. The findings revealed that albumin was a protective factor against surgical treatment for acute female PID (odds ratio (OR) = 0.913, p = 0.003). Conversely, older age (OR = 1.052, p = 0.001) and elevated fibrinogen levels (OR = 1.193, p = 0.04) were identified as risk factors for surgical treatment of acute female PID (Table 3).

# **Discussion**

The principles of antibiotic use and surgical indications in the guidelines for the diagnosis and treatment of PID in women are similar across different countries. This retrospective analysis revealed that the incidence of surgical treatment among inpatients with acute PID was 12.7%, slightly higher than the 10% reported by the Infectious Diseases Collaboration Group of the Chinese Medical Association Obstetrics and Gynecology Branch [3].

In instances of moderate to severe infection, the development of local abscesses is frequently observed. Despite attempts at conservative treatment, abscess formation may persist or worsen. Patients necessitating surgical intervention are typically those presenting with palpable masses in-

Table 3. The multivariate analysis of surgical treatment for acute female PID.

| Influencing factors | В      | S.E   | Wald   | p value | OR    | 95.0% CI      |
|---------------------|--------|-------|--------|---------|-------|---------------|
| Age                 | 0.050  | 0.015 | 11.865 | 0.001   | 1.052 | 1.022-1.082   |
| Albumin             | -0.091 | 0.031 | 8.658  | 0.003   | 0.913 | 0.859 – 0.970 |
| Platelet count      | 0.003  | 0.001 | 3.224  | 0.073   | 1.003 | 1.000-1.005   |
| Fibrinogen          | 0.176  | 0.086 | 4.216  | 0.040   | 1.193 | 1.008-1.411   |

S.E, Std. Error; OR, odds ratio; CI, Confidence Interval.

dicative of such abscesses. The majority of abscesses were found to be located in the unilateral ovary and fallopian tube (79.3%), and all patients who underwent surgical intervention had their lesions excised via laparoscopy or laparotomy. Following surgery, patients experienced improvement and were discharged after receiving continued postoperative antibiotic treatment.

Multivariate analysis revealed associations between age, initial serum albumin levels upon admission, fibrinogen levels, and the necessity for surgical treatment in acute female PID. Notably, the age of patients in the surgery group was significantly higher compared to those in the non-surgery group. Despite the odds ratio (OR) for age being 1.052, it remains meaningful as a reference factor. This observation may be attributed to several factors: firstly, immune function tends to decline in middle-aged and elderly women. Secondly, many patients are in the perimenopausal period, characterized by decreased estrogen levels and weakened reproductive tract barrier function, rendering them more susceptible to microbial invasion and severe infections.

This study observed that the initial serum albumin level upon admission in the surgery group was notably lower than that in the non-surgery group, suggesting that albumin serves as a protective factor for surgical treatment of acute female PID. As widely acknowledged, albumin, primarily synthesized in the liver, plays a crucial role in immune regulation. Patients admitted with low albumin levels often exhibit compromised immune function, rendering them more susceptible to exacerbated infections [8]. The OR value for albumin may not be particularly high, potentially because the measured albumin levels were initial results obtained after admission, while disease progression is a dynamic process. Particularly in cases of uncontrolled inflammation, the body may deplete albumin at a faster rate than anticipated. Therefore, if albumin levels were assessed prior to surgery, the OR value might be higher.

Moreover, this study also identified elevated fibrinogen as a risk factor for surgical treatment of acute female PID. Fibrinogen, a liver-synthesized protein with coagulation functions, holds the highest content among plasma coagulation factors and plays a pivotal role in the clotting process. During an inflammatory response, activation of numerous inflammatory cells leads to an increase in procoagulant substances in the blood and a reduction in anticoagulant substances. This cascade reaction of coagulation significantly

elevates fibrinogen levels [9]. Should inflammation persist and worsen, it can trigger systemic microthrombus formation and compromise microcirculation, ultimately culminating in multi-organ dysfunction or failure. Hence, fibrinogen emerges as a crucial indicator for clinical diagnosis, selection of treatment plans, and assessment of prognosis in inflammatory diseases [10].

The univariate analysis in this study unveiled statistically significant differences in platelet count, co-existing hypertension, and co-existing diabetes regarding the necessity for surgical treatment of acute PID. However, these correlations were not robust in multivariate analysis. Potential explanations for this phenomenon include the following: although platelet levels serve as a crucial indicator of sepsis severity in patients with inflammatory diseases [11] typically decreasing with disease severity—this study did not detect statistically significant differences in platelet counts between the two patient groups. This suggests that patients requiring surgical treatment for acute PID might not have progressed to the stage of severe sepsis. This indirectly implies that elevated fibrinogen levels could potentially serve as an early indicator of the necessity for surgical intervention in acute PID.

Moreover, the relatively limited number of patients with co-existing hypertension and co-existing diabetes, coupled with the multifactorial nature of pelvic inflammation onset and exacerbation, might have influenced the correlation analysis results.

The necessity for surgical treatment in acute female PID arises from the convergence of multiple contributing factors. In managing such patients, it is imperative to conduct a comprehensive assessment that encompasses variables such as age, albumin levels, and fibrinogen levels. This holistic approach enables healthcare providers to effectively evaluate the surgical risk and mitigate the likelihood of disease progression to septic shock.

This study is subject to certain limitations. Being retrospective in nature, it is unavoidably susceptible to selection bias. The efficacy of antibiotic treatment for patients hinges on numerous factors, including pathogen drug resistance, the presence of concurrent infections, and prior treatment received at other healthcare facilities prior to the patient's admission. Additionally, patient preferences regarding the decision to undergo surgery also play a role.

## **Conclusions**

Patients with age-related acute female PID, particularly those with abscess formation, should undergo early surgical intervention if they exhibit risk factors such as low serum albumin levels and elevated fibrinogen.

## Availability of Data and Materials

The data and materials in the current study are available from the corresponding authors on reasonable request.

#### **Author Contributions**

XWC and HQL conceived the study and were in charge of overall direction and planning. XWC and JQD contributed to acquisition of data. YQZ, PY and JQD contributed to analyse the data. XWC and HQL took the lead in writing the manuscript. All authors revised the manuscript critically for important intellectual content. All authors discussed the results and contributed to the final manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

# **Ethics Approval and Consent to Participate**

The experimental protocol was established according to the ethical guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of Dongyang Hospital of Wenzhou Medical University. Application number: SC-2024-110; Approval No.: Dongrenyi 2024-YX-109. Written informed consent was obtained from participants.

## Acknowledgment

Not applicable.

# **Funding**

This research received no external funding.

# **Conflict of Interest**

The authors declare no conflicts of interest.

## References

- [1] Lumbiganon P, Laopaiboon M, Gülmezoglu AM, Souza JP, Taneepanichskul S, Ruyan P, *et al.* Method of delivery and pregnancy outcomes in Asia: the WHO global survey on maternal and perinatal health 2007-08. Lancet (London, England). 2010; 375: 490–499.
- [2] Liu ZH, Liao QP. Strategies for diagnosis and treatment of pelvic inflammatory diseases in China (pp. 10–11). People's Military Medical Press: Beijing, China. 2009. (In Chinese)
- [3] Infectious Diseases Collaboration Group, Gynecology and Obstetrics Branch, Chinese Medical Association. Diagnosis and Treatment of Pelvic Inflammatory Diseases

- (2019 Revision). Chinese Journal of Obstetrics and Gynecology. 2019; 54: 433–437. (In Chinese)
- [4] Haggerty CL, Ness RB. Diagnosis and treatment of pelvic inflammatory disease. Women's Health (London, England). 2008; 4: 383–397.
- [5] Khan ZE, Rizvi JH. Pelvic inflammatory disease and pelvic abscesses. Reviews in Gynaecological & Perinatal Practice. 2006; 6: 185–191.
- [6] Gradison M. Pelvic inflammatory disease. American Family Physician. 2012; 85: 791–796.
- [7] Xie X, Kong BH, Duan T. Obstetrics and Gynaecology. People's Medical Publishing House: Beijing, China. 2018. (In Chinese)
- [8] Zhang Y, Petropoulos S, Liu J, Cheishvili D, Zhou R, Dymov S, *et al.* The signature of liver cancer in immune cells DNA methylation. Clinical Epigenetics. 2018; 10: 8.
- [9] Zhao XC, Zhao GW, Cui YG. Effect of mild hypothermia on coagulation function and inflammation in patients with severe craniocerebral injury. Medical Clinical Research. 2017; 34: 2222–2224. (In Chinese)
- [10] Han ZG, Wang YH, Chen XH, Zhao JH., Application value of fibrinogen, PCT, IFN- $\gamma$  and IL-10 in intracranial infection. Marker Immunoassay and Clinic. 2017; 24: 1163–1166. (In Chinese)
- [11] Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, *et al.* Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Intensive Care Medicine. 2013; 39: 165–228.

**Publisher's Note**: Annali Italiani di Chirurgia stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.