PULMONARY EMBOLISM AFTER GYNECOLOGIC SURGERY-A RETROSPECTIVE STUDY IN CHINA

Hui-Feng Zeng[1], Si-Hua He[2], Yu-Xia Wang[3*]

[1]Department of Reproductive Medicine, The First Affiliated hospital of Jinan University, Guangzhou, Guangdong, China.
[2]Dermatology Hospital of Southern Medical University, Guangzhou, Guangdong, China.
[3]Department of Reproductive Medicine, The First Affiliated hospital of Jinan University, Guangzhou, Guangdong, China.
sunneywang@126.com.

Abstract: To retrospectively analyze the incidence and the characteristics of pulmonary embolism (PE) in patients following gynecologic surgery, and identify the risk factors of PE. A total of 6417 gynecologic surgery cases that were performed from January 2018 to December 2020 at the Department of Gynecology, the First Affiliated Hospital of Jinan University. PE was diagnosed using computed tomographic pulmonary angiography. Clinical data of these patients were analyzed retrospectively. PE was diagnosed in 21 patients (0.33%). The incidence of PE in the malignant tumors was significantly higher than that of benign diseases, which showed a statistically significant difference ($P<0.05$).12 (57.14%) of the 21 PE patients had clinical symptoms or signs, in which 9 (42.86%) cases had respiratory symptoms or signs. 9 (42.86%) patients had no symptoms or signs expect for a SpO_2 level decrease. 12 (57.14%) patients were found to have both PE and deep venous thrombosis (DVT). The interval between the surgeries and the diagnosis of PE was 1-29 days, 10 (47.62%) of the 21 PE patients were diagnosed the day after surgery, and 18 (85.71%) cases were diagnosed within 72 hours after surgery. 17 cases (80.95%) were diagnosed as PE on the day or the next day that symptoms or signs of hypoxia were observed. CTPA was performed in 21 patients, and most emboli mainly located in lobar or segmental arteries. All the 21 patients with PE were classified as no-high-risk PE and no patients died of PE in this study. A substantial number of postoperative PE were lack of typical characteristics. Routine SpO_2 level monitoring can be used for early detection of PE, particularly in asymptomatic patients. Extended prophylaxis, early diagnosis and early treatment should be carried out to cope with high-risk patients especially malignant patients after gynecological surgery.

INTRODUCTION

Venous thromboembolism (VTE) includes deep venous thrombosis (DVT) and pulmonary embolism (PE), among which PE is an important cause of sudden death after surgery (Stein and Matta, 2011). PE is a group of diseases or clinical syndrome which is caused by the sudden blockage of the main pulmonary arteries and their branches by endogenous or exogenous emboli through the circulatory system. In western populations, the annual incidence of PE is 1 per 1000 people, which increase rapidly with age, from 1.4/1000 aged 40-49 to 11.3/1000 aged 80 years or above (Schulman et al., 2009; Bauersachs et al., 2010; Agneli et al., 2013). It is reported that more than 40% of postoperative deaths following gynecological surgery have been attributed to PE (Davis, 2001). In the past, we have always believed that PE is relatively rare in China, compared with the high incidence of PE in western countries. However, in recent years, the incidence of DVT in patients without any preventive measures after gynecological pelvic surgery was 9.6%-15.6%, and the incidence of PE in patients with DVT is as high as 46% in China (Qu et al., 2015; Li and Zhang, 2016). The early symptoms of PE are not obvious and lack of specific clinical manifestations, misdiagnosis and missed diagnosis might appear in clinical work. PE is not uncommon after gynecologic surgery, it should be paid extensive attention by medical institutions and healthcare personnel. To improve diagnosis and treatment of PE, we retrospectively reviewed and analyzed the clinical characteristics and risk factors of 21 patients with PE following gynecological surgery, including a considerable number of asymptomatic cases.

MATERIALS AND METHODS

This retrospective analysis was approved by the hospital ethics committee. A total of 7140 cases who had undergone gynecologic surgery that were retrieved from the hospital medical record system from January 2018 to December 2020 at the Department of Gynecology, the First Affiliated Hospital of Jinan University. The patients who underwent conization, dilatation and curettage, hysteroscopy and laparoscopy were excluded from the 7140 patients, and there were no PE occurred before operation in this population. Ultimately, a total of 6417 cases were incorporated into this report. Acute PE was diagnosed according to clinical manifestations and signs, pulse oxygen saturation (SpO_2), echocardiography, lower extremity doppler ultrasound, arterial blood gas analysis, D-dimer detection and confirmed by computer tomography pulmonary angiography (CTPA) that interpreted by an attending radiologist. The clinical data were retrospectively analyzed, including age, body mass index (BMI), medical history, disease types, clinical characteristics, duration of operation, interval between diagnosis and surgery, interval between the diagnosis and the appearance of symptoms or signs, laboratory and imaging results, treatment and prognosis. Classification of PE severity and the risk of early death were according to 2019 European Society of Cardiology (ESC) guidelines for the diagnosis and management of acute PE (Stavros et al., 2019).

STATISTICAL ANALYSIS

Chi-square test was used to analyze the difference in frequencies between groups. P values < 0.05 were considered to be statistically significant difference. The analyses were performed using the SPSS version 27.0.

RESULTS

Background characteristics of PE following gynecological surgery

Among the 21 patients with PE, the age range 44 to 81 years old, the median age was 56 years old, and 80.9% of them were 50 years old or above. There were 10 cases with body mass index (BMI) greater than 25 kg/m^2 and 2 cases greater than 30 kg/m^2. For the past medical history, 10 patients were complicated with essential hypertension (47.6%), 1 with diabetes, and 1 with anxiety disorder who took anti-anxiety drugs for a long time. None of the patients had a history of VTE. 21 cases with PE were classified as no-high-risk PE.

Incidence of PE after gynecological surgery

The overall incidence of PE following gynecological surgery is 0.33% (21/6417) in our study. Of the 21 PE patients, 13 had benign diseases and 8 had malignant tumors. The incidence of PE in malignant diseases was 2.33% (8/343), and in benign diseases was 0.21% (13/6074). The incidence of PE in the malignant tumors was significantly higher than that of benign diseases, which showed a statistically significant difference ($P < 0.05$). (Table 1)

Relationship between disease types and PE after gynecological surgery

The operative indication in patients with PE included cervical cancer (4/21,19.05%), ovarian cancer (2/21, 9.52%), endometrial cancer (2/21, 9.52%), uterus leiomyoma (4/21, 19.05%), Ovarian benign tumor (4/21, 19.05%), uterine prolapse (3/21, 14.29%), Endometrial polyp (2/21,9.52%). Among malignancies, the incidence of PE in cervical cancer was 2.65% (4/151), in ovarian cancer was 2.74% (2/73) and in endometrial cancer was 1.79% (2/112), no PE was found in other cancers. The incidence of PE in ovarian cancer was higher than those of cervical cancer and endometrial cancer, but there was no significant difference between the three different malignancies respectively ($P > 0.05$) . (Table 1)

Surgical characteristics in PE patients

In our study, the surgical methods of 21 patients with PE following gynecological surgery include 13 cases of laparoscopic surgeries, 6 cases of laparotomy and 2 cases of hysteroscopic surgeries. The incidence of PE in laparoscopic surgeries was 0.43% (13/3000), in laparotomy was 0.65% (6/926) and in hysteroscopic surgeries was 0.10% (2/2064). The incidence of PE in hysteroscopic surgeries was lower than that of laparoscopic surgeries and laparotomy, which showed a statistically significant difference ($P < 0.05$), but there was no significant difference between laparoscopic surgeries and laparotomy ($P > 0.05$) . There were no cases of postoperative PE among the patients underwent vaginal and vulvar surgery. Regarding the surgical position in 21 PE patients, 15 cases (71.43%, 15/21) were lithotomy position and 6 cases (28.57%, 6/21)

were in the supine position. PE occurred among 0.27% (15/5491) of the patients who underwent gynecologic surgery under the lithotomy position, and 0.65% (6/926) of the patients under the supine position. The incidence of PE for lithotomy position was lower than that of supine position, but there was no statistically significant difference (P > 0.05). Lymph node dissection was performed in 7 of the 8 PE patients with malignant tumors. The operation lasted 3 hours or longer in 10 of the 21 PE patients. (Table 1)

Table 1 Univariate analyses of surgical characteristics and disease types

Characteristics	**Total（n=6417）, n**	**With PE (n=21), n (%)**	**Without PE (n=6396), n (%)**	**P value**
Malignant tumor				0.000*
+	343	8(2.33)	335(97.67)	
-	6074	13(0.21)	6061(99.79)	
surgical method				0.026*
Laparoscopic surgery	3000	13(0.43)	2987(99.57)	
hysteroscopic surgery	2064	2(0.10)	2062(99.90)	
laparotomy	926	6(0.65)	920(99.35)	
Other surgical method	427	0(0.00)	427(100.00)	
Surgical position				0.125
lithotomy position	5491	15(0.27)	5476(99.73)	
supine position	926	6(0.65)	920(99.35)	
Malignancies type	**Total (n=343), n**	**With PE (n=8), n%**	**Without PE (n=335), n%**	0.921
Cervical cancer	151	4(2.65)	147(97.35)	
Endometrial cancer	112	2(1.79)	110(98.21)	
Ovarian cancer	73	2(2.74)	71(97.26)	
Other cancer	7	0(0.00)	7(100.00)	

* Significant difference(P < 0.05)

Other surgical method includes vaginal and vulvar surgery

Clinical manifestation of PE patients following gynecological surgery

The interval between the surgeries and the diagnosis of PE was 1-29 days. 10 (47.62%) of the 21 PE patients were diagnosed the day after surgery, and 18 (85.71%) of the 21 PE cases were diagnosed within 72 hours after surgery. The duration between the diagnosis of PE and the appearance of symptoms or signs of hypoxia was 0-2 days. Among the 21 PE patients, 17 cases (80.95%) were diagnosed as PE on the day or the next day that symptoms or signs of hypoxia were observed. The clinical manifestations or signs of PE patients were listed in table 2. 12 (57.14%) of the 21 PE patients had clinical symptoms or signs, in which 9 (42.86%) cases had respiratory symptoms or signs, including dyspnea, cough and chest pain. 8(38.10%) cases had other symptoms or signs, including dizziness, limbs swelling, fatigue, high fever, Perspiration and chill. 9 (42.9%) patients had no symptoms or signs expect for a SpO_2 level decrease to 93% or less after the occurrence of PE. Regarding the physical examination, 5 cases of moist rale, 4 cases of tachypnoea, 2 cases of increased heart rate and 1 case of pleural friction rub were detected by auscultation of the chest. None of the 21 PE patients had the triad of dyspnea, chest pain, hemoptysis simultaneously.

Table 2. Clinical Manifestations and Signs of PE Patients

Symptoms and signs	Cases(n=21)
Asymptomatic PE	9
Symptomatic PE	12*
respiratory symptoms and signs	9*
Dyspnea	9
Cough	2
Chest pain	1
Other symptoms and signs	8*

Dizziness	4
Limbs swelling	3
Fatigue	2
High fever	1
Perspiration and chill	1
physical examination	7*
moist rale	5
tachypnoea	4
increased heart rate	2
pleural friction rub	1

*Some cases have mutiple clinical manifestations or signs

Auxiliary examination of the PE patients after gynecological surgery

Decreased SpO_2 level was found in all 21 PE patients. Arterial blood gas analysis was performed in 9 patients, and 7 cases had hypoxaemia with PaO_2 lower than 80mmHg. D-dimer levels increased 2-40 folds in all 21 PE patients, of which 15 (15/21,71.43%) cases were higher than 2000μg/L. Echocardiography was performed in 15 patients, and the results showed that 12 cases had left ventricular diastolic function dysfunction and 6 cases had pulmonary arterial hypertension. All the 21 PE patients were examined by lower-limb compression venous ultrasonography, and 12 patients were found to have DVT (12/21,57.14%). CTPA was performed in 21 patients, among the 9 asymptomatic cases, 8 cases had emboli located in segmental arteries and 1 case had emboli located in lobar arteries. Among the 12 symptomatic patients, 3 cases had emboli in the pulmonary arteries, 5 cases had emboli in the lobar arteries and 4 cases had emboli in segmental arteries.

Treatment and prognosis of PE patients

There are 16 (16/21,76.19%) patients received subcutaneous low-molecular-weight heparin (LMWH) to prevent VTE before the diagnosis of PE. Once the PE was diagnosed, fundamental treatment such as absolute bed rest, oxygen therapy, respiration, blood oxygen and blood pressure monitoring were performed. Because of respiratory failure, non-invasive ventilator-assisted breathing was used in 1 case. All the 21 PE patients were treated with LMWH 6000 AxaIU every 12 hours. When the condition was stable, warfarin 3mg/day or rivaroxaban 15mg/day was used to continue anticoagulation as the secondary prophylaxis for 3-6 months. For those using warfarin, coagulation function was monitored every 2-3 days to adjust the dosage and international normalized ratio (INR) was controlled at 2-3. During the course of treatment, none of the PE patients experienced major bleeding. After treatment for 2-3 weeks, the conditions of PE patients were improved significantly, and the follow-up CTPA showed that pulmonary artery thrombus disappeared or mainly absorbed. During 3 months follow-up, no patients died of PE in this study.

DISCUSSION

PE is one of the leading causes of morbidity and mortality in hospitalized patients despite a low incidence. In America, 5% to 10% of hospital deaths are due to PE (Park et al., 2009). However, with the improvement of diagnosis and treatment, the fatality rate of hospitalized patients with PE decreased from 12.3% to 8.2% from 1998 to 2005 (Piróg, Jach and Undas, 2016). In the present study, with early diagnosis and effective treatment, no patients died of PE during the follow-up period. Previous studies reported that the incidence of postoperative PE in malignant patients was 2.14%-2.6% (Masao et al., 2010; Clark-Pearson et al., 1990). Martin's study revealed that the incidence of PE was 0.3% of the patients with benign diseases who undergoing gynecological abdominal surgery (Martin et al., 2006). In our study, the overall occurrence of postoperative PE was 0.33% in gynecological procedures, 2.33% and 0.22% in malignant patients and benign patients respectively, which is similar to the results reported in literature. Kodoma's (Junichi et al., 2013) study reported that the incidence of postoperative VTE in patients with ovarian cancer was significantly higher compared with those with other gynecological tumors. Not entirely the same as the data published by Kodama et al. (2013), our study appears to show a higher incidence of PE in women with ovarian cancer compared with those with cervical cancer and endometrial cancer. However, because of limited data for PE with malignant tumors, no statistical differences were found in our study.

It is difficult to predict which individuals are prone to thromboembolic event in clinical practice. Yang et al. (2019) revealed that advanced age, obesity, malignant diseases, laparoscopic surgery, longer operation duration, history of thrombosis may be prone to VTE after gynecologic surgery. There is a well-recognized connection between malignancy and PE. Martino et al. (2006) revealed that malignant patients underwent major abdominal surgery had a 14-fold greater risk of developing a PE compared with patients with benign disease. In our study, the PE incidence in the malignant tumors was significantly higher than that of benign diseases, which was consistent with previous reports (Martin et al., 2006). The high incidence rate of PE in patients with malignant tumors may be due to one or more risk factors such as increasing age, pelvic veins compressed by pelvic tumors, vascular endothelial cell injury during pelvic lymph node dissection, lengthy surgical procedures and chemotherapy (Piróg, Jach and Undas, 2016; Ruidi et al., 2020; Barber and Clarke-Pearson, 2016). What's more, the levels of some potential factors such as platelets, leukocytes, tissue factor-positive microvesicles increased (Yohei and Nigel, 2017), which promoted thrombosis. In our study, the median age of PE patients was 56 years old, and 80.9% of them were 50 years old or above. Among 21 patients with PE, 12 cases had the complications of hypertension or diabetes, which are risk factors for atherosclerosis (Sim, Jeong and Kang, 2010), suggesting these might be risk factors for PE. Okadome et al [9] found that an operation time of three hours or more was identified to be risk factor of PE after gynecologic oncology surgery. The longer operation time, the more bleeding and the more factors that trigger the coagulation system during operative procedure. What's more, the longer the bed rest time, the slower the postoperative recovery, the higher the risk of thrombosis (Ting et al., 2019). In our study, the operation lasted 3 hours or longer in 10 of the 21 PE patients, and Lymph node dissection was performed in 7 of the 8 PE patients with malignant tumors, meaning that longer operation duration may be at higher risk for PE. Obesity is an independent risk factor for VTE, which increasing the risk of VTE by 6.2-fold (Cristina, 2020). There were 10 cases with BMI greater than 25 kg/m^2 in our study, indicating that overweight may be risk factor for PE.

Laparoscopic surgery may be expected to reduce the risk of thrombogenesis due to the less trauma during surgical procedure and earlier mobilization after surgery. However, laparoscopic surgeries also associated with longer operative times and increased intraabdominal pressures that can alter vascular hemodynamics, these eventually lead to venous congestion in the lower extremities (Feng et al., 2001; Alpa et al., 2010). Ageno et al. (2007) found that laparoscopic gynecologic surgery in benign patients is a low-risk procedure for postoperative VTE. In contrast to Ageno's study, Nick et al found that patients undergoing high-complex laparoscopic gynecologic surgery had an increased rate of postoperative VTE (Alpa et al., 2006). Different from the results reported in previous literature, the incidence of PE between laparoscopy and laparotomy was no statistically significant difference in our study, indicating further multicenter randomized clinical trials of larger sample were required to analyze the effects of different surgical methods on PE. However, the incidence of PE in hysteroscopy was lower than that of laparoscopy and laparotomy. The result showed that hysteroscopic procedures may be a-low risk for postoperative PE as which was associated with shorter operative time and less trauma. There is a paucity of data assessing the true incidence of PE in patients undergoing laparoscopic gynecologic surgery. In our study, the incidence of PE in laparoscopic surgery was 0.43%. Because of the lower extremities being elevated in the lithotomy position, the venous return might be easier and the risk for venous thrombosis can be reduce. The incidence of PE among patients underwent gynecologic malignant surgery under the lithotomy position was significantly lower than the supine position (Masao et al., 2010). Similar to the results reported in the literatures, our study found that the incidence of PE for lithotomy position was lower than that of supine position, but there was no statistically significant difference.

The clinical symptoms and signs of PE are lack of specificity, which are similar to the clinical manifestations of respiratory inflammation and angina pectoris. For this reason, a considerable number of patients with PE

are misdiagnosed or unrecognized, and most deaths are discovered on autopsy (Rulido et al., 2006). In our study, the most common clinical manifestation of acute PE was sudden dyspnea. The identification of the symptoms and signs of PE plays an important role in the diagnosis, including careful clinical history and physical examination. Okadome's (Masao et al., 2010) study reported that 35.6% of postoperative PE were asymptomatic and had no signs expect for a low SpO_2 by pulse oximetry monitoring. In our study, 42.9% cases with PE had no symptoms or signs expect for a SpO_2 level decrease after the occurrence of PE. Therefore, routine SpO_2 level and vital signs monitoring is helpful for early detection of postoperative PE. When hypoxemia is detected and the patients were at high risk for thrombosis, PE should be considered and further examination should be performed to confirm the diagnosis. The level of plasma D-dimer is normally less than 500μg/L, and higher level of D-dimer may be associated with the presence of a DVT or PE. In our study, the level of D-dimer in all patients with PE is higher than 500μg/L, and 71.43% cases was higher than 2000μg/L. Crawford et al. (2016) reported that negative D-dimer tests are sensitive in excluding PE and identifying people without PE, but high levels of false-positive test results are also very common. For this reason, a positive D-dimer result requires further imaging tests. Computer tomography pulmonary angiography (CTPA) is considered as the gold standard of imaging modality for diagnosis of acute PE, but probability of PE should be fully evaluated (British Thoracic Society, 2003). All of the 21 patients with PE were diagnosed by CTPA in our study. Emboli mainly located in lobar or segmental arteries in asymptomatic PE cases, however, emboli located in the pulmonary, lobar or segmental arteries in symptomatic ones. Therefore, early identification of PE after surgery may be of clinical significance because most of these emboli are close to the subsegmental arteries.

Elliott et al. (2005) reported that 17% patients were diagnosed with acute PE more than 7 days after symptoms onset, and 5% patients were diagnosed with acute PE more than 25 days after symptoms onset. In contrast, 80.95% of the patients with PE were diagnosed on the day or the next day that symptoms or signs of hypoxia were observed in our study. The longest interval between the discovery of symptoms or signs of hypoxia and the diagnosis of PE was two days. In addition, 85.71% of the patients with PE were diagnosed within 72 hours after surgery, which is consistent to Okadome' s (Masao et al., 2010) report. The longest interval between the operation and the diagnosis of PE was 21 days. This result suggested that the majority of acute PE following gynecologic surgery is considered to occur within three days of surgery and this is the critical period for the prevention of PE. A retrospective cohort study revealed that the incidence of VTE within 30 days of gynecologic malignant surgery decreased from 2.7% to 0.6% when low-molecular-weight heparin (LMWH) was started within 24 hours after surgery and continued for 28 days postoperatively (Schmeler et al., 2013). Therefore, early thromboprophylaxis is very helpful for postoperative patients with high risk factors. In our hospital, LMWH (3000 AxaIU, once a day for a week) was performed 24 hours after surgery for thromboprophylaxia in patients at high risk for PE.

In conclusion, postoperative observation of high-risk patients, especially malignant patients, should be strengthened, and relevant examinations should be carried out as soon as possible once there are suspected clinical manifestations and signs of PE such as dyspnea, chest tightness, chest pain, so as to achieve early detection and early treatment. Still, other than SpO_2 monitoring, few tools are readily available to help identify asymptomatic PE. Routine SpO_2 level monitoring would reduce the diagnostic delay of PE after gynecological surgery, particularly in asymptomatic patients. For those patients with high risk factors such as advanced age, obesity, hypertension, diabetes, long operation duration, thromboprophylaxis is recommended. PE is preventable and treatable, by early prevention, early detection and effective treatment, the incidence and mortality of PE can be reduced.

REFERENCES

Ageno W, Manfredi E, Denatli F, et al. The incidence of venous thromboembolism following gynecologic laparoscopy: a multicenter, prospective cohort study. J Thromb Haemost. 2007, 5(3): 503– 6.

Agneli G, Buller HR, Cohen A, et al. AMPLIFY Investigators. Oral rivaroxaban for the treatment of symptomatic pulmonary embolism. Engl J Med 2013;369: 799-808.

Alpa M Nick, Kathleen M Schmeler, Michael M Frumovitz, et al. Risk of thromboembolic disease in patients undergoing laparoscopic gynecologic surgery. Obstet Gynecol. 2010, 116(4): 956-961.

Alpa M Nick, Kathleen M Schmeler, Michael M Frumovitz, et al. Risk of thromboembolic disease in

patients undergoing laparoscopic gynecologic surgery. Obstet Gynecol. 2010, 116(4): 956-961.
Barber EL, Clarke-Pearson DL. The limited utility of currently available venous thromboembolism risk assessment tools in gynecological oncology patients. Am J Obstet Gynecol. 2016, 215(4): 445.e1-9.
Bauersachs R, Berkowitz SD, Brenner B, et al. EINSTEIN Investigators. Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med 2010; 363: 2499-510.
British Thoracic Society. British Thoracic Society guidelines for the management of suspected acute pulmonary embolism. Thorax. 2003, 58(6): 470-83.
C Gregory Elliott, Samuel Z Goldhaber, Robert L Jensen. Delays in diagnosis of deep vein thrombosis and pulmonary embolism. Chest. 2005, 125(5): 3372-6.
Clark-Pearson DL, Delong E, Synan IS, et al. A controlled trial of two low-dose heparin regimens for the prevention of postoperative deep vein thrombosis. Obstet Gynecol. 1990,75 (4): 684-9.
Cristina Hotoleanu. Association between obesity and venous thromboembolism. Med Pham Rep. 2020, 93(2): 162-168.
Davis JD. Prevention, diagnosis and treatment of venous thromboembolic complication of gynecologic surgery. American Journal of Obstetrics & Gynecology, 2001,184:759-775.
Fay Crawford, Alina Andras, Karen Welch, et al. D-dimer test for excluding the diagnosis of pulmonary embolism. Cochrane Database Syst Rev. 2016(8):CD010864.
Feng L, Song J, Wong F, Xia E. Incidence of deep venous thrombosis after gynaecological laparoscopy. Chin Med J (Engl). 2001, 114(6): 632-5.
Junichi Kodama, Noriko Seki, Chikako Fukushima, et al. Elevated preoperative plasma D-dimer levels and the incidence of venous thromboembolism in Japanese females with gynecological cancer. Oncol Lett. 2013, 5(1): 299-304.
Li Z, Zhang Z. The incidence and risk factors of venous thromboembolism following elective gynecological surgeries without systemic thromboprophylaxis: an observational cohort study in a Chinese tertiary hospital. Clin Exp Obstet Gynecol, 2016, 43(3): 365-369.
Martin A Martino, Elana Borges, Eva Williamson, et al. Pulmonary embolism after major abdominal surgery in gynecological oncology. Obset Gynecol, 2006, 107(3): 666-71.
Masao Okadome, Toshiaki Saito, Daisuke Miyahara, et al. Postoperative pulmonary embolism including asymptomatic cases in gynecologic oncology. Int J Gynecol Cancer. 2010,20 (4): 655-63.
Park B, Messina L, Dargon P, et al. Recent trends in clinical outcomes and resource utilization for pulmonary embolism in the United States: findings from the nationwide inpatient sample. Chest. 2009, 136(4): 983-90.
Piróg MM, Jach R, Undas A. Thromboprophylaxis in women undergoing gynecological surgery or assisted reproductive techniques: new advances and challenges. Ginekol Pol. 2016, 87(11): 773–9.
Qu H, Li Z, Zhai Z, et al. Predicting of venous thromboembolism for patients undergoing gynecological surgery. Medicine (Baltimore), 2015, 94(39): e1653.
Ruidi Yu, Faridah Nansubuga, Jun Yang, et al. Efficiency and safety evaluation of prophylaxes for venous thrombosis after gynecological surgery. Medicine (Baltimore). 2020,99(25): e20928.
Rulido T, Aranda A, Zevallos MA, et al. Pulmonary embolism as a cause of death in patients with heart disease: an autopsy study. Chest. 2006, 129(5):1282-7.
Schmeler KM, Wilson GL, Cain K, et al. Venous thromboembolism (VTE) rates following the implementation of extended duration prophylaxis for patients undergoing surgery for gynecologic malignancies. Gynecol Oncol. 2013,128(2): 204-8.
Schulman S, Kearon C, Kakkar AK, et al. RE-COVER Study Group. Dabigatran versus warfarin in the treatment of acute venous thromboembolism. N Engl J Med, 2009, 361: 2342-52.
Sim DS, Jeong MH, Kang JC. Current management of acute myocardial infarction: experience from the Korea Acute Myocardial Infarction Registry. J Cardiol. 2010, 56(1): 1-7.
Stavros V Konstantinides, Guy Meyer, Cecilia Becattini, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Respir J. 2019, 54(3): 1901647.
Stein PD, Matta F. Epidemiology and incidence: the scope of the problem and risk factors for development of venous thromboembolism. Clin Chest Med. 2011, 27(4): 907-32.
Ting Yang, Sijuan Tian, Yaohui Wang, et al. Evaluation of risk factors for venous thromboembolism in patients who underwent gynecological surgery and validation of a fast-rating assessment table. Med Sci Monit. 2019, 25: 8814-8819.
Ting Yang, Sijuan Tian, Yaohui Wang, et al. Evaluation of risk factors for venous thromboembolism in

patients who underwent gynecological surgery and validation of a fast-rating assessment table. Med Sci Monit. 2019, 25:8814-8819.

Yohei Hisada, Nigel Mackman. Cancer-associated pathways and biomarkers of venous thrombosis. Blood. 2017, 130(13): 1499-1506.