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Results of a single center experience in 922 procedures

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Emanuele Sturlese*, Onofrio Triolo*, Roberta Grasso*, Antonio Simone Laganà*, Annalisa Retto*, Diego Rossetti**, Salvatore Giovanni Vitale*, Giuseppe Sarpietro***, Rosanna De Dominici*

**Unit of Gynecology and Obstetrics, Department of Human Pathology in Adulthood and Childhood "G. Barresi", University of Messina, Messina, Italy*
***Unit of Gynecology and Obstetrics, Desenzano del Garda Hospital, Section of Gavardo, Gavardo, Brescia, Italy*
****Department of General Surgery and Medical Surgical Specialties, University of Catania, Catania, Italy*

Thromboembolism prophylaxis in laparoscopic surgery for gynecologic benign diseases. Results of a single center experience in 922 procedures

AIM: *The aim of this study is to assess the role of preoperative evaluation risk for venous tromboembolism (VTE) in patients submitted to laparoscopic surgery for gynecologic benign diseases.*
METHODS: *Date from nine hundred twenty-two women affected by adnexal benign diseases treated with laparoscopic procedures were collected and included in this study. VTE risk was assessed by "on line Caprini score calculator". Patients with one or more negative risk factors for Caprini's score underwent to venous thromboembolism prophylaxis (VTP). The remainign of the patients did not recived any VTP. A survey was conducted after three months from the discharge in order to collect the follow up date.*
RESULTS: *In our study 160 patients had a Caprini's score major than 2 and they have been subjected to VTP. A total of 762 patients were considered at low risk for VTE and they did not receive any VTP. In these patients was not registered any event of VTE.*
DISCUSSION: *The results of this study suggest that laparoscopic approach, when carried out in non-oncological patients and without any previous thromboembolic risk factor, is associated with a very low risk of VTE. This study also confirm what was reported by Ageno et al. [6], Nick et al. [7] and ACCP guidelines in 2012 [8] in which routine thromboprophylaxis is recommended for patients with additional risk factors.*
CONCLUSIONS: *Laparoscopic surgery in women for gynecologic benign diseases is associated with a very low risk of thromboembolism and therefore it does not require any mechanical or pharmacological thromboprophylaxis in the absence of risk factors. The systematic evaluation of VTE risk with the help of a standard calculator is highly recommended.*

KEY WORDS: Gynaecology, Laparoscopic surgery, Thromboprophylaxis

Introduction

Thrombosis is defined as the formation or presence of a blood clot within a blood vessel, while embolism is the obstruction or occlusion of a vessel by a transported clot or vegetation, a mass of bacteria, or other material. Venous thromboembolism (VTE), including pulmonary embolism (PE) and deep vein thrombosis (DVT), is the most common preventable cause of hospital-related death. These pathological conditions could be considered a major cause of morbidity and mortality among hospitalized patients submitted to surgery [1]. Pelvic surgical procedures are well-validated to be risk factors for VTE. It has been estimated that death from DVT-associated massive PE amounts as many as 100 new cases-year/100,000 in Italy [2]. DVT typically results

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Correspondence to: Diego Rossetti M.D., Unit of Gynecology and Obstetrics, Desenzano del Garda Hospital, Section of Gavardo, Via A. Gosa 74, 25085 Gavardo, Brescia, Italy. (e-mail: docrossetti@gmail.com)

from one or more of these conditions: venous stasis, blood hypercoagulability (increased clotting), or endovascular damage. They can stem from a wide range of situations. For instance, venous stasis and hypercoagulability may result from immobilization or regional states of low blood flow caused by trauma (especially to the lower legs), burns, shock, obesity, surgery or heart disease, neoplastic diseases and related treatments, previous surgery VTE, advanced age, pregnancy and childbirth, replaced hormone therapy and contraceptive therapy, internal diseases, metabolic diseases, presence of central venous access, use of drugs, congenital and acquired thrombophilic states. The incidence of postoperative venous thrombosis varies depending on a multitude of patient factors, including the type of surgery undertaken. Without prophylaxis, as consequence of general surgery, DVT occurrence can be observed in about 20% of cases, whereas after orthopedic hip surgery DVT can occur in up to 50% of patients[3]. In these conditions, stasis in combination with surgical-related inflammatory status are considered the major contributing factors to DVT. Moreover, the risk of TVP is particulary high in the case of oncological surgery, where release of tumor procoagulants factors, host inflammatory responses and effects of chemotherapeutics drugs represent important contributing factors to trombosis. A summary of the risk factors for DVT is reported in Table I. According to the NICE guidelines, the incidence of DVT ranges from 10% in urological patients to 47% in orthopedic patients [4] . In medical patients, instead, the incidence of thrombosis is around 24%, while in pregnant women and new mothers the incidence is even higher, is estimated to be about three times higher than women in general. Gynecologic-oncology randomized controlled trials reported DVT incidence of 0-14.8 % with prophylaxis and up to 34.6% without prophylaxis [4,5]. Information about the incidence of venous thromboembolism (VTE) following laparoscopic procedures is inadequate and, to our knowledge, there is currently no solid evidence to guide the use of thromboprophylaxis in this setting [6]. Gynecologic laparoscopy is a common technique frequently performed in a low-risk patients. To our knowledge there are few clinical studies specifically designed to assess the incidence of VTE in this scenario. The rates of VTE following laparoscopic procedure appear to be low: a review of 50.427 gynecologic laparoscopies reported symptomatic VTE in only 2 per 10.000 patients [7]. In a multicenter prospective cohort study, 266 consecutive patients undergoing gynecologic laparoscopy in three Italian tertiary care hospitals were evaluated the incidence of clinically relevant venous thromboembolic events. There were neither episodes of CUS (compression ultrasonography) detected DVT or clinically relevant VTE after follow-up. No patient died of fatal pulmonary embolism [6]. Feng at al. reported an incidence of DVT after laparoscopic procedure ranging from 0/3056 patients to 1/100 patients. The reported incidence of pulmonary embolism after laparoscopic procedures ranges from 0/3056 patients to 1/147 [8]. According to literature, gynecological laparoscopic surgery for benign adnexal pathology is frequently associated with a low risk of thromboembolism. There are many validated rating scales for the assessment of VTE risk that are characterized from relevant differences. Kutcher and [9] propose a tool to evaluate risk factors based on numerical score scale; major risk factors are cancer, previous VTE, hypercoagulability with a score of three [7]. ACCP VTE prophylaxis guidelines 2012 suggested the patients to be divided into in three distinct categories: non-surgical patients, not orthopedics surgical patients and orthopedic patients. Compared to the previous ACCP guidelines 2008, the new risk assessment provides a score, according to two different models, the Caprini's model and the Rogers'one, which are world-wide diffused. According to ACCP VTE guidelines, for general and abdominal-pelvic surgery patients at low risk for VTE (Caprini score < 2) [9] we recommend that no specific pharmacologic (Grade 1B) or mechanical (Grade 2C) prophylaxis be used other than

TABLE I - *Risk factors for DVT*

- Surgery Major (longer than 45 minutes)
- Past major surgery (more than 45 minutes) within the last month
- Visible varicose veins
- A history of Inflammatory Bowel Disease (IBD)
- Swollen legs
- Overweight or obese (Body Mass Index of 25 or higher)
- Heart attack within the past month
- Congestive heart failure within the past month
- Serious infection within the past month
- Existing lung disease including emphysema or COPD
- Suffered a stroke within the past month
- Bed rest or restricted mobility during the past month
- Non-removable plaster cast, removable leg brace or mold that has kept you from moving your leg within the last month
- Age
- Current use of birth control or HRT
- Pregnant or had a baby within the last month
- History of unexplained stillborn infant, recurrent spontaneous abortion (more than 3), premature birth with toxemia or growth restricted infant.
- Current or past malignancy, excluding basal cell skin cancer
- Tube in blood vessel or neck or chest that delivers blood or medicine directly to heart within the past month (also called central venous access, PICC line, or port)
- Past personal history or current Deep Vein Thrombosis (DVT) or Pulmonary Embolism (PE)
- Family history of Deep Vein Thrombosis (DVT) or Pulmonary Embolism (PE)
- Personal or family history of positive blood test indicating an increased risk of blood clotting
- Fracture of the hip, pelvis, or leg
- Antithrombin III deficiencyMultiple traumatic injuries (for example multiple broken bones due to a fall or car accident)Spinal cord injury resulting in paralysis
- Spinal cord injury resulting in paralysis

early ambulation. Nowadays laparoscopy is a surgical procedure generally considered safe and effective, widely used in many surgical fields. The potential advantages of this method are represented by the lower impact on healthy tissue, poor postoperative pain, early mobilization and reduction of inpatient surgery, all of which, theoretically, could reduce the risk of postoperative TVE [10]. It has been shown that procedures like adnexa detorsion do not increase the risk of thromboembolism and laparoscopic surgery is minimally invasive with faster recovery times and minimal impact on fertility [17].

Unfortunately, there is no adequate information about the incidence of DVT in patients undergoing laparoscopic surgical procedures. On the one hand, the advantages of laparoscopic surgery, or the least impact on the damaged tissue and the possibility of early mobilization suggest that this procedure might be considered safe in terms of the risk of thromboembolic complications. On the other hand it has seen that laparoscopic surgery induces a state of hypercoagulability similar to that of open traditional surgery due to high levels of circulating coagulation factors such as complex thrombin-antithrombin, prothrombin fragments 1-2 and D-dimer [5,11]. In literature the VTE risk after traditional surgery is well defined, while for laparoscopy a solid scientific evidence is still lacking [12]. A recent study determined a much lower incidence of DVT in patients undergoing laparoscopic surgery for malignancy compared with those undergoing laparotomy [18]. Also in an other study it was indicated low incidence in cancer patients undergoing laparoscopic surgery [19]. The patients with elder age, malignant tumor, cardiovascular comorbidity or large postoperative hemostatics dose should be paid high attention to and the minimally invasive surgery are optimal treatment in preventing DVT [20].

Material and Method

This study was conducted at the Department of Paedriatic, Gynaecological, Microbiological and Biomedical Sciences "G. Barresi" over a period of time ranging from January 2007 to November 2012. The study was approved by the Institutional Review Board and all the patients were thoroughly briefed and provided their written consent to participate which was conducted in accordance with the Declaration of Helsinki. We analyzed 922 consecutive patients, undergoing laparoscopic surgery for adnexal benign disease. Patients with known oncologic diseases, personal history of VTE, pregnant women, anticoagulant therapy or genetic thrombophilia were excluded from the study. The following baseline characteristic were collected: age, body mass index, smoking status, varicose vein, ASA risk class, use of contraceptive therapy, TVP risk preoperative anesthesia, and concomitant treatments. The presence of risk factors for VTE were documented throughout the study period: family history of VTE, recent immobilization (more than 3 days), recent trauma (< 3 months), recent surgery (< 3 months), recent hospital admission for severe medical disorders, use of oral contraceptives or hormone replacement therapy, varicose vein and known thrombophilia. The anesthesiologic risk for VTE was calculated for each patient using the American Society of Anesthesiologists classification of physical status (ASA PS) that is a widely used system for categorizing the preoperative status of patients [21]. In order to assess the adjusted thromboembolic risk in this subset of patients the "Caprini' score" was calculated before surgery (Table I). Patients with a Caprini' score higher than 2 where administered post operatory anticoagulant drugs. The following information on the laparoscopic procedure were also collected: type of procedure (diagnostic laparoscopy, laparoscopy for cystectomy, ovariectomy or salpingectomy), the current procedures (elective or urgency) indication and duration of the procedure, duration of pneumoperitoneum, intraoperative bleeding, duration of general anesthesia, and duration of hospitalization. Operations were performed under general anesthesia, with a Trendelenburg position of 25-30 degrees, arms along the body, legs slightly apart, and a CO_2 flow rate of 6 L/min and intra-abdominal CO_2 pressure of 14 mmHg. The duration of the procedure was 40-45 min. All patients underwent to early ambulation on first postoperative day; the length of postoperative hospital stay was significantly shorter compared to that required for traditional open procedures (1 day). At discharge each patient underwent a thorough clinical check by evaluating the Well's score [13]. Further clinical check was executed after one week from the procedures. Information about the occurrence of symptomatic VTE was collected during a 3 month follow up. Throughout the study period, all patients were instructed to refer to the attending physician in the case of onset of sign or symptoms of VTE. Clinical follow-up by telephone contact was routinely performed at 3 months.

Statistical analysis was performed using SPSS 13 software package (SPSS Inc., Chicago, IL). Continuous data were reported as mean ± standard deviation and percentages for categorical variables. For continuous variables, mean values between the two groups were compared by unpaired Student t test for normally distributed variables and Mann-Whitney U test for skewed variables. The χ^2 test was used to compare categorical variables between groups.

Results

A total of 922 consecutive patients were enrolled in this study. One hundred sixty patients were excluded from the study (17.35 %), 112 of these (70%) because they were pregnant, 10 patients (25.6 %) for previous DVT; 4 patients (2.5%) for cancer; additional 4 patients (2.5%)

TABLE II - *Characteristics of DVT low risk patients.*

Patients Characteristics	Results
Age	36.25+/- 13.74
BMI	24.11 +/- 4.65
Varicose veins	692 no (90.81%) - 70 yes (9.18%)
E/P	695 no (91%) – 67 yes (8.8%)
Smoking	554 no (72,70 %)
	yes (> 10/die) 23 (3.01%)
	yes (<10/die) 185 (24.27%)
ASA risk class	ASA 1. 240 (31.5%)
	ASA 2. 448 (58.79%)
	ASA 3. 72 (9.44)
	ASA 4. 2 (0.26%)

because in therapy with anticoagulant drugs; 4 (2.5%) because affected with known thrombophilia; 16 patients (10%) were excluded because conversion from laparoscopy to open surgery was required during procedure and 10 patients (6.25%) for incomplete data collection.

A total of 762 patients underwent gynecologic laparoscopy surgery for adnexal benign disease.

The main indication for laparoscopic surgery was ovarian follicular cyst in 463 cases (60.8%), endometriosis cyst in 149 cases (19.5%), dermoid tumor in 72 patients (9.45%), ovarian fibroma in 16 patients (2.1%), tubal sterilization in 10 patients (31.1%) and other causes in 52 patients (6.82%). Pre-operatory evaluation with "Caprini's score" was routinely done. On a total of 762 eligible patients the following baseline characteristic were collected: age, BMI, smoking, varicose vein, ASA risk class, use of contraceptive therapy, TVP risk preoperative anesthesia, and concomitant treatments. The basic characteristics of the preoperatory low risk sample analyzed are shown in Table II. The presence of risk factors for VTE were documented throughout the study period: family history of VTE, recent immobilization (more than 3 days), recent trauma (< 3 months), recent surgery (< 3 months), recent hospital admission for severe medical disorders, use of oral contraceptives or hormone replacement therapy, varicose vein and known thrombophilia. In 59 cases (7.74%) patients underwent emergency surgery, while in the remaining 703 cases (92.3%) the procedure was performed electively. The length of the procedure was 42 +/- 17 min, with an average duration of pneumoperitoneum of 32 +/- 17 min. The blood loss during surgery was low in all patients <30 ml. The length of hospital stay was 1.6 +/- 0.3. The anesthesiologic risk for VTE was calculated for each patient using the ASA PS classification: in 314 patients (41.20%) the calculated risk was low, in 448 patients (58.79) was calculated an average risk, while patients for which the calculated risk was high were excluded from the study. Specifically 240 patients (31.5%) are graded as ASA I, 448 patients (58.79%) as ASA II, 72 patients (9.44%) as ASA III and 2 patients (0.26%) as ASA IV. The Caprini' score inferior than 2 allowed us to do not use prophylactic mechanical or medical thromboprophylaxis. No events of venous thromboembolism was observed in our patients after 30 days by the discharge.

Discussion

Laparoscopy has been demonstrated as a valid approach to many gynecologic procedures with better results in terms of minimal perioperative morbidity and shorter hospital stay, with consequent improved quality of life compared to laparotomic approach. The techniques of laparoscopic surgery have found in recent years a widespread application in gynecology, but despite that there are currently no elements demonstrating an increased incidence of VTE in patients treated with this method. There are reasons to assume a possible increased risk of thromboembolism after laparoscopic surgery, since three of the factors of Virchow's triad for venous thrombosis may be present [12]. In fact due to the pneumoperitoneum and prolonged anti-Trendelenburg position can occur an increase in venous stasis in the lower limbs and load he also may occur episodes hypercoagulable and vascular damage. Currently in fact, the latest guidelines of the American College of Chest Physicians [7] recommend routine use of thromboprophylaxis only for patients undergoing gynecological laparoscopic surgery in the presence of additional risk factors. In this study we tried to carefully assess the clinical risk of DVT in patients submitted to gynecological laparoscopic procedures for benign adnexal disease, in order to evaluate the need for a specific thromboprophylaxis in patients undergoing such procedures. The results of this study suggest that laparoscopic approach, when carried out in non-oncological setting and without any previous thromboembolic risk factor, is associated with a very low risk of thromboembolism and therefore it does not require any mechanical or specific pharmacological thromboprophylaxis. The study also demonstrated that early ambulation in these patients, is an effective tool for thromboembolic prophylaxis. Despite the potential risks, literature suggests that this complication is rare, probably due to the lower percentage of damaged tissue, the early mobilization of patients and the short postoperative hospital stay. Moreover our study showed that factors such as the duration of the pneumoperitoneum and the short overall operative time (less than 45 min) do not further increase the risk of occurring DVT [14,15]. In view of some recent evidence, the risk of thrombosis associated with laparoscopic procedures for benign disease is very low. According to Mahdi H et al universal or extended thromboprophylaxis does not appear to be indicated for all patients [25]. The results of our study also confirm what was reported by Ageno et al. [6], i.e. the routine use of

pharmacological thromboprophylaxis in patients undergoing laparoscopic surgery for benign disease is not indicated when an early postoperative mobilization is realized. The results of our study are also in line with the recommendations of the ACCP guidelines in 2008 [7] in which routine thromboprophylaxis is not indicated for patients with a "standard risk" undergoing laparoscopic surgery, and it is recommended for patients with additional risk factors. According to Ramirez et al. there is a paucity of data on the incidence of VTE in patients undergoing minimally invasive surgery, including laparoscopic and robotic surgery. As a result, there are no definitive guidelines referring to prevention of VTEs in patients undergoing minimally invasive surgery [23].
ACCP recommends only early ambulation for patients undergoing laparoscopic surgery, unless they have other risk factors for VTE [26] while ACOG recommends thromboprophylaxis on the basis of patient and procedure risk factors, regardless of whether the procedure is open or performed laparoscopically [27]. ASCO proposes that there are limited data regarding the benefit of thromboprophylaxis in patients undergoing laparoscopic surgery, and consequently propose guidelines stating that patients undergoing laparoscopy lasting longer than 30 minutes should receive pharmacologic thromboprophylaxis with either low-dose unfractionated heparin or low [28-31]. The possibility to assess routinely the risk of VTE with a validated score reduce the post operative adverse events.

Conclusions

In conclusion, this study demonstrated that laparoscopic surgery for benign ovarian or tubal diseases, in preoperatory low grade risk patients (Caprini's score < 2) with the absence of surgical complications and a duration of the procedure less than 45 minutes can be considered as a low thromboembolic risk procedure. In addition, early ambulation alone, in the absence of risk factors, may be considered a valid tool for DVT prophylaxis.

Riassunto

La valutazione del rischio tromboembolico in pazienti che verranno sottoposti a chirurgia addominale rimane un prerequisito fondamentale nell'ottica di ridurre i rischi correlati ad una inadeguata profilassi. Nello specifico, le pazienti sottoposte a chirurgia laparoscopica per patologia annessiale benigna sono spesso considerate a priori a basso rischio tromboembolico. Infatti solitamente ci si trova di fronte a paziente con età inferiore a 40 anni con scarse se non assenti comorbidità e che dovranno subire una procedura rapida e relativamente atraumatica. Non essendoci però forti evidenze scientifiche a riguardo ed essendo comunque presente, seppur basso, un rischio di sviluppare tromboembolia post-operatoria, abbiamo voluto analizzare 922 pazienti operate presso la nostra struttura per patologia annessiale benigna. Di queste 762 sono state considerate a basso rischio per eventi trombo embolici. Tramite l'ausilio dello score di Caprini, abbiamo eseguito una valutazione preoperatoria delle pazienti confermando così il teorico basso rischio tromboembolico. In queste pazienti non è stata eseguita nessuna profilassi (medica o meccanica). È stato poi eseguito un follow up adeguato che ha confermato l'assenza di eventi tromboembolici in queste pazienti. I risultati della nostra esperienza ci consentono di meglio identificare le pazienti a reale basso rischio tromboembolico che dovranno essere operate con tecnica laparoscopica per patologia annessiale benigna.

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