

# Hospital admission and surgical approach to ectopic pregnancy in Clinical hospital 'Sveti Duh' from 2015-2020

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**Hospital admission and surgical approach to  
ectopic pregnancy in Clinical hospital 'Sveti Duh'  
from 2015-2020**

**GRADUATE THESIS**



**Zagreb, 2021.**

„This graduate thesis was made at Department of gynaecology and obstetrics, mentored by doc.dr.sc. Ivanka Bekavac Vlatković, and was submitted for evaluation 2021.“.

## LIST OF ABBREVIATIONS

EP – ectopic pregnancy

hCG - human chorionic gonadotropin

IUP – intrauterine pregnancy

IVF – in vitro fertilization

LAP – laparotomy

LPSC - laparoscopy

MTX – methotrexate

TVUS – transvaginal ultrasound

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## SUMMARY

**Introduction:** Ectopic pregnancy is a term for any pregnancy where the implantation occurs outside the uterine cavity. It occurs in approximately 0.6-1.0% of all pregnancies and is most commonly localized within the fallopian tube. Main risk factors associated with ectopic pregnancy are tubal scarring, mainly due to history of infection or surgery, and smoking. Diagnosis relies on the combination of transvaginal ultrasound and measurement of serum  $\beta$ -hCG levels. Ectopic pregnancy may be treated with expectant management, pharmacologic therapy, or surgery. Despite advancements in diagnosis and treatment, hemorrhage due to ectopic pregnancy remains the leading cause of maternal mortality in the first trimester.

**Goal:** The goal of this research paper was to present length of hospital stay and surgical treatment of patients treated for ectopic pregnancy in Clinical hospital 'Sveti duh' 2015 to 2020.

**Method:** Data was collected from the hospital electronic database and books of surgical procedures and then processed in the SPSS (Statistical Package for the Social Sciences) software.

**Results:** Following data collection, 139 patients surgically treated for ectopic pregnancy were included and analyzed in this study. Out of 139 patients surgically treated for ectopic pregnancy, 134 (96,4%) have undergone laparoscopic procedure, while only 5 (3,6%) had open surgery. Salpingectomy was the technique most performed (82,7%), followed by salpingotomy (8,6%). The mean hospitalization time of surgically treated patients was 1,78 days and was dependent on the type of performed procedure.

**Conclusion:** Since the 2015 there has been a decrease in frequency of tubal-sparing surgery as surgical approach for the treatment of ectopic pregnancy. The increase in the frequency of laparoscopic salpingectomy is evident.

**Key words:** ectopic pregnancy, treatment, surgery, hospitalization, salpingectomy

## SAŽETAK

**Uvod:** Ektopična trudnoća je pojam za svaku trudnoću u kojoj se implantacija događa izvan šupljine maternice. Javlja se u otprilike 0,6-1,0% svih trudnoća, a najčešće je lokalizirana unutar jajovoda. Glavni čimbenici rizika povezani s ektopičnom trudnoćom su ožiljci u jajovodu, najčešće zbog prijašnje infekcije ili kirurškog zahvata, te pušenje. Dijagnostička evaluacija pacijentica se oslanja na kombinaciju transvaginalnog ultrazvuka i mjerenja razine  $\beta$ -hCG-a u serumu. Ektopična trudnoća može se liječiti ekspektativnim liječenjem, farmakološkom terapijom ili kirurškim zahvatom. Unatoč napretku u dijagnozi i liječenju, krvarenje zbog ektopične trudnoće ostaje vodeći uzrok smrtnosti majki u prvom tromjesečju.

**Cilj rada:** Cilj ovog istraživačkog rada bio je prikazati duljinu boravka u bolnici i kirurško liječenje pacijentica liječenih zbog ektopične trudnoće u Kliničkoj bolnici 'Sveti duh' 2015. do 2020. godine.

**Metoda:** Podaci su prikupljeni iz bolničke elektroničke baze podataka i knjige kirurških zahvata, a zatim obrađeni u softveru SPSS (Statistical Package for the Social Sciences).

**Rezultati:** Nakon prikupljanja podataka, u ovom je istraživanju analizirano 139 pacijentica kirurški liječenih zbog ektopične trudnoće. Od 139 žena, 134 (96,4%) je imalo laparoskopski zahvat, dok je samo 5 (3,6%) imalo laparotomiju. Salpingektomija je tehnika koja se najčešće izvodila (82,7%), a slijedila ju je salpingotomija (8,6%). Prosječno vrijeme hospitalizacije operativno liječenih pacijentica je bilo 1,78 dana i ovisilo je o odabranom kirurškom pristupu.

**Zaključak:** Od 2015. godine zabilježen je pad učestalosti operacija s namjerom očuvanja oba zdrava jajovoda. Ističe se rastući trend učestalosti laparoskopske salpingektomije.

**Ključne riječi:** ektopična trudnoća, liječenje, operacija, hospitalizacija, salpingektomija



# INTRODUCTION

## DEFINITION

Ectopic pregnancy, also known as eccyesis, is a pregnancy in which the implantation of a fertilized egg occurs at a site other than the uterine endometrium. Most common anatomic site of an ectopic pregnancy (EP) is the fallopian tube (96%), particularly the ampulla, accounting for about 70% (1). The incidence and mortality have varied throughout the years, but hemorrhage caused by EP remains one of the leading causes of pregnancy-related maternal mortality in the first trimester and accounts for approximately 4% of all pregnancy-related deaths in spite of advanced diagnostic methods resulting in earlier detection and therapy (2). Management of ectopic pregnancy relies mainly on pharmacological therapy with methotrexate and surgical treatment, though expectant management can be an option in some cases.

## EPIDEMIOLOGY

### Incidence

The estimated incidence of ectopic pregnancy has fluctuated substantially across time and patient population. Due to several factors, such as outpatient management and increasing number of hospital visits in cases of EP, it is difficult to estimate the incidence. Additionally, when talking about the incidence of EP in the patient population, we express it as a number of ectopic pregnancies per 1000 pregnancies. This denominator proves to be hard to determine with accuracy since many pregnancies face early failures that go unnoticed by the healthcare system, as they do not result in symptomatic presentation and hospitalization.

One of the representative studies, including over 200 United States commercial health plans from 2002 to 2007, reported a rate of 6.4 per 1000 pregnancies, increasing with age (3).

## Mortality

Nowadays, maternal mortality related to ectopic pregnancy has decreased substantially. This can, most likely, be attributed to improved diagnostic methods, leading to earlier diagnosis, and better access to healthcare. A study done in the United States found that EP was responsible for 876 deaths between 1980 and 2007. Between 1980-1984 and 2003-2007, the EP mortality ratio fell by 56.6 percent, from 1.15 to 0.50 deaths per 100,000 live births. During 2003-2007, the EP mortality ratio was 6.8 times higher for African Americans than whites and 3.5 times higher for women over 35 years old than those under 25 years old (2).

## RISK FACTORS

The mechanism(s) that contribute to the risk of extra-uterine implantation are still unknown. The proposed mechanism comprises of factors including anatomic anomalies, i.e. obstruction, abnormalities in tubal motility or ciliary function, abnormal products of conception, and chemotactic factors stimulating tubal implantation. Those factors, which hinder or prevent the passage of an embryo into the uterine cavity, can result in ectopic implantation. Despite the multifactorial etiology, up to 50% of women with an EP have no recognizable risks (4).

Out of all the risk factors determined to cause EP, those with the highest risks include positive history for prior EP and prior tubal surgery, as well as smoking. Other risk factors include age, positive history of spontaneous abortions and history of infertility (5). In vitro fertilization and embryo transfer (IVF-ET) and current IUD use, in addition to the usual risk factors, play an important role in the occurrence of EP (6).

## Previous ectopic pregnancy

Since a previous EP represents the combination of all known and unknown patient risk factors, the risk of a recurrent EP becomes consequently higher.

When compared to other pregnant patients, the probability of repeat EP in patients with a positive history is around three to eight times higher. This risk is linked to both the underlying tubal condition that caused the previous EP and the chosen therapeutic strategy (6,7). For example, the recurrent EP rates after single-dose MTX, salpingectomy, and linear salpingotomy are approximately 8%, 9.8%, and 15.4%, respectively (4).

## Infections

Pelvic infection, especially if recurrent, is a significant cause of tubal pathology and thus results in increased risk of EP. Tubal inflammation is found in up to 90% of EPs, and shows up 6 times more frequently in tubes involving an EP than in normal tubes (4). These infections include chlamydia, gonorrhea, and nonspecific salpingitis. There is evidence linking the rising incidence of EP to an increased incidence of pelvic inflammatory disease (PID), as EP was discovered to be a late sequela of PID (8).

## Infertility and in vitro fertilization (IVF)

Factors contributing to infertility, such as tubal abnormalities, are the probable causes behind the two- to threefold higher incidence of EP in patients with infertility. Even though IVF-ET has been linked to an increased risk of EP in women with a history of infertility, this was only seen in women with tubal infertility and not in women with non-tubal infertility (5,6).

## Contraception

Patients using contraception in the form of an intrauterine device (IUD) or hormones, are at comparatively low risk of conceiving any pregnancy. However, if they do conceive, the chances of extrauterine implantation are higher than in patients not using contraception (4).

## Smoking

Smoking is a dose-dependent risk factor associated with tubal mobility impairment, delayed ovulation and poorer immunity. These effects contribute to a 3.5 higher risk of EP in smokers compared to nonsmokers (4,5).

## ANATOMIC SITES

Fallopian tube is the site of EPs in a vast majority of cases (96%). Bouyer et al. showed that out of 1800 surgically treated cases only 4.5% were extratubal, mainly ovarian (3.2%). The great majority of tubal pregnancies involved the ampullary region (70%), the rest are evenly distributed between the fimbria (11%) and the isthmus (12%). There were no cervical pregnancies observed (1). Other reported sites of extrauterine implantation are the abdomen and the cervix hysterotomy scar. Rarely, intrauterine and ectopic pregnancies may coexist, referred to as a heterotopic pregnancy (4).

## CLINICAL MANIFESTATIONS

EP can be considered in any patient of reproductive age with vaginal bleeding and/or abdominal pain with following characteristics:

- Pregnant patient with unconfirmed IUP
- Pregnant and conceived by IVF

- Unconfirmed pregnancy, especially with amenorrhea of >4 weeks preceding vaginal bleeding
- Rarely, a hemodynamically unstable patient with an unexplained acute abdomen.

First-trimester vaginal bleeding and/or lower abdominal pain are the most common clinical manifestations of EP. In all women presenting to an emergency department with first-trimester bleeding, lower abdominal pain, or a combination of the two, the prevalence of EP ranges between 6% and 16%. Usually, EP clinically manifests six to eight weeks after the last normal menstrual period but can appear later, particularly if the pregnancy is in a location other than the fallopian tube. However, EP can be asymptomatic as well.

At the time of presentation to healthcare, an EP may be intact or ruptured. Rupture should be strongly suspected in a patient with a positive pregnancy test who presents with loss of consciousness and signs of shock, such as pallor, tachycardia and collapse (9-11).

## DIAGNOSIS

EP should be considered in any pregnant patient without evidence of intrauterine pregnancy on transvaginal ultrasound (TVUS) with any of the following:

- Abdominal pain and/or vaginal bleeding, especially in patients presenting with risk factors for EP
- Visualized extraovarian adnexal mass, either complex inhomogeneous or one containing an empty gestational sac, or intraperitoneal bleeding on TVUS
- Abnormally rising serum human chorionic gonadotropin (hCG), typically defined as a <35% over two days but dependent on the initial hCG level

Because the variety of symptoms resembles the numerous abnormalities of early pregnancy, EP is considered the gynecological disease with the most diagnostic errors. Relying solely on clinical features, about half of the women with EP are misdiagnosed at their first presentation (10,11).

## Differential diagnosis

EP is characterized by vaginal bleeding and/or abdominal pain in the presence of a positive pregnancy test.

The differential diagnosis of early-pregnancy bleeding with or without pain also includes implantation bleeding, spontaneous abortion, polyps, subchorionic hematoma and gestational trophoblastic disease (13,14).

## DIAGNOSTIC EVALUATION

Every patient presenting with abnormal uterine bleeding and abdominal pain should be evaluated for EP. Workup should begin with determining that the patient is pregnant, evaluating for hemodynamic instability and determining the site of pregnancy. In some women, in the absence of definite evidence of an EP or IUP on ultrasound, it is impossible to distinguish between the two without performing uterine aspiration, which cannot be done before existence of a viable IUP has been excluded. Such women are diagnosed as having a pregnancy of an unknown location (PUL), of which up to 40% are eventually diagnosed as EPs (11,15).

Currently, a combination of TVUS and measurement of serum  $\beta$ -hCG levels are used to confirm the diagnosis.

### Serum $\beta$ -hCG concentrations

In the diagnosis of ectopic pregnancy, it is extremely important for us to determine the level of  $\beta$ -hCG. Namely, in anembryonic ectopic pregnancy, the level of  $\beta$ -hCG is significantly lower than in normal pregnancy.  $\beta$ -hCG in a normal pregnancy doubles at a constant rate, every 48-72 hours, until it reaches the level of 10,000-20,000 IU/mL (16). However, in a tubal pregnancy with a viable embryo (5-10% cases), serum  $\beta$ -

hCG levels may be normal. Additionally, in an EP serum  $\beta$ -hCG concentration does not follow a normal increasing pattern, but may reach a plateau or a mild decrease.

The  $\beta$ -hCG discriminatory zone is the serum hCG level above which a gestational sac must be visualized in the scenario of a IUP.

- For TVUS, the discriminatory zone is set at 3510 milli-international units/mL. Setting the discriminatory zone at this level makes it easier to diagnose a viable IUP on TVUS, but also increases the risk of a delayed diagnosis of EP, potentially causing complications to arise. In a study of 651 pregnant patients with first trimester bleeding or pain, among viable IUP, 99% of the time a gestational sac was visualized at the discriminatory zone of 3,510 milli-international units/mL (17); IUPs will not be visualized on TVUS 1% of the time at this discriminatory zone.
- For transabdominal ultrasound, the discriminatory zone is set at a higher level of approximately 6500 milli-international units/mL (18).

## Transvaginal ultrasonography

High-definition ultrasonography has allowed for a more accurate diagnosis of both normal and abnormal pregnancies. In healthy IUPs, a TVUS should correctly identify intrauterine gestational sac with almost 100% accuracy at a gestational age of about 5.5 weeks. It is also widely acknowledged that an IUP can only be definitely diagnosed by ultrasound if a yolk sac or embryo is present due to the fact that EP can be accompanied by a 'pseudosac' (11,12). The distinguishing proof of an IUP can rule out EP in majority of cases, except if a heterotopic pregnancy is suspected, where an ectopic pregnancy coincides with an IUP. They are uncommon (1/40 000) and hard to diagnose (19).

If an IUP gestation sac is ruled out, an EP can be diagnosed with evidence of an adnexal mass, often within the fallopian tube.

By itself, TVUS can:

- Diagnose an IUP

Definite evidence includes a gestational sac with an embryo or yolk sac within the uterine cavity. In rare cases, an interstitial pregnancy might be misdiagnosed as an IUP, or a heterotopic pregnancy is misdiagnosed as an IUP only. Ultrasonographic identification of an IUP (gestational sac plus yolk sac or other embryonic products) rules out EP in most cases (12).

- Diagnose an EP

Confirmed diagnosis may be provided by a gestational sac with a yolk sac (with or without an embryo) outside of the uterine cavity (12,20).

Findings that are suggestive of an EP but don't confirm the diagnosis include no intrauterine contents and extraovarian adnexal mass. A complex inhomogenous adnexal mass is the most frequent TVUS finding as it is present in up to 90% of cases (12,21). Suspicion of a ruptured EP might arise in the case of visualized echogenic free fluid, suggestive of blood, surrounding the uterus or in the Pouch of Douglas, although a small amount of fluid in the latter might indicate a transudate, due to an increase in vascular permeability, seen in early pregnancy (11).

### Serum progesterone

Despite being futile in helping discriminate between EP and IUP, levels of serum progesterone may help in distinguishing a viable IUP from nonviable IUP and EP. A study of 177 patients found that as an EP diagnostic marker progesterone demonstrated a sensitivity of 100% at the cutoff of 86.01 nmol/L, whereas for identifying non-viable pregnancies, at the cutoff of 63.2 nmol/L, it demonstrated a sensitivity of 95.40% and a specificity of 90.91% (22).

### Uterine aspiration

If trophoblastic tissue is obtained via uterine curettage, an IUP can be diagnosed with certainty. However, the risk of disrupting a viable pregnancy limits the use of curettage as a diagnostic tool (11). Additionally, the sensitivity of an endometrial suction curette



in identification of chorionic villi from an IUP in the first trimester is about 70%, meaning that the absence of tissue does not definitely diagnose an EP (23).

## Diagnostic laparoscopy

Diagnostic laparoscopy may be required in cases where an EP is suspected but ultrasonography produced no evidence. However, in some cases, small EPs may be missed during the procedure. Seen as the 'gold standard' by many, delayed performing of a diagnostic laparoscopy has even been identified as a factor in fatal cases (11,24).

## TREATMENT

EP can be managed by watchful waiting, medical treatment, or surgery. The most appropriate method depends on the ongoing assessment and on numerous clinical factors, most importantly the patient's clinical picture,  $\beta$ -hCG levels and TVUS findings.

### 1. Expectant management

Since some EPs may resolve spontaneously, through regression or abortion, without harm to the patient, expectant management can be an option for some cases in which there is minimal risk of tubal rupture (11). It is offered as a treatment approach for candidates who have low and declining  $\beta$ -hCG levels without evidence of an extrauterine mass suggestive of an EP on TVUS. Initial levels of  $\beta$ -hCG  $<1000$  IU/L indicate the most useful expectant management (25). Patient on this treatment approach must be carefully monitored for the possibility of tubal rupture, so access to emergency medical services within a reasonable time frame must be secured. Serum  $\beta$ -hCG concentration fall below 15 IU/L is a good indicator of a spontaneous resolution of an unruptured EP (12).

## 2. Medical treatment

Predominant drug is methotrexate (MTX), but other systemic drugs can be used for EP, such as actinomycin D and prostaglandins (9). Pharmacological therapy with MTX is safe and efficient for EP and offers comparable efficacy to surgery, with similar fertility outcomes. MTX acts as a folic acid antagonist targeting rapidly proliferating cells and arresting mitosis. It is suitable for candidates with an unruptured EP and good clinical picture, who are hemodynamically stable and have low volume of free intraabdominal fluid on TVUS, with  $\beta$ -hCG concentration less than 5000IU/L (26).

The most frequent MTX treatment regimen is a single-dose protocol of a deep intramuscular (IM) injection of 50 mg/m<sup>2</sup> of body surface area. Successfulness of therapy is most commonly measured by a decline in  $\beta$ -hCG concentration. EP is likely to resolve 3 to 7 weeks following MTX administration (9). Approximately 14–20% of patients having single-dose treatment will require a repeat dose, indicated if  $\beta$ -hCG concentration declined less than 15% 7 days after therapy (11,27). A meta-analysis of non-randomized research found the success rate of single dose regimen to be only slightly lower than that of multi-dose protocols, 88% and 93% respectively (28).

Multi-dose regimen and direct injection of MTX into the EP are less common methods of medical treatment approach. Direct injection of methotrexate into the ectopic mass, either laparoscopically or with ultrasound guidance, reduces systemic toxicity and sustains a higher therapeutic level. However, there is no significant advantage from this therapeutic approach and in majority of patients it may increase the risk of tubal rupture (11).

Therapy with MTX is contraindicated when there is hemodynamic instability, IUP (including heterotopic pregnancies), clinical picture indicative of impending or ongoing rupture of ectopic mass or in patients with hepatic, renal or hematologic clinically significant abnormalities. Additionally, MTX should be avoided if the patient is hypersensitive to it or breastfeeding.

### 3. Surgical treatment

Indications for surgical therapy are imminent or current rupture, hemodynamic instability, failed pharmacological therapy or contraindications to MTX, as mentioned above. In hemodynamically stable patients, surgery should be considered as an option only if TVUS gave definite proof of a tubal EP or an adnexal mass suggestive of EP; surgery most likely won't lead to a visualization of the mass if TVUS showed none.

The two surgical approaches include laparoscopy and laparotomy, with either conservative (salpingotomy, 'milking' and resection) or radical (salpingectomy) procedures. Laparoscopic salpingectomy is most commonly performed, while organ-saving procedures are associated with higher rates of trophoblast tissue retention (29,30).

#### 3.1. Fimbrial evacuation of tubal pregnancy

Also known as 'milking', extirpation through the fimbrial end is used when the location of the ectopic mass is at the outer portion of the fallopian tube or the fimbrial end. The product is manually 'milked' out of the fimbria, gently pushed until it is fully extruded. Although this technique is 'gentle' and less invasive, it has a greater rate of imperfect removal and hence a higher risk of recurrence and residual trophoblast tissue (9).

Historically, due to its simplicity and less invasive technique it was deemed by many as having the most favorable prognosis for subsequent pregnancies but these claims haven't been confirmed by clinical data (9,31).

#### 3.2. Salpingotomy

A salpingotomy is the surgical evacuation of an EP by dissecting it out of the tube while keeping the Fallopian tube in place to preserve fertility on that side. After the procedure, the main concern is persistent trophoblast so post-operative follow-up includes serial  $\beta$ -hCG measurements to assess the need for systemic MTX treatment in case of

treatment failure (11). The combined results of 2 randomized controlled trials showed that salpingotomy alone was significantly less successful than in combination with a single prophylactic shot methotrexate (2 RCTs, n=163, OR 0.25, 95% CI 0.08-0.76) to prevent trophoblast proliferation (32).

### 3.3. Salpingectomy

Salpingectomy is a radical treatment option including the excision of a segment or all of the fallopian tube. The choice to do partial or complete salpingectomy is influenced by patient's age, condition of the tube, whether they have one or two tubes and their plans for future fertility.

If the ectopic mass is confined to a small part of the midportion segment, either a partial or complete salpingectomy may be done, whilst a large portion involvement or indication for fimbrial removal necessitate total salpingectomy. Total bilateral salpingectomy may be performed electively if the patient requests sterilization or for ovarian cancer risk reduction (33).

### 3.4. Laparotomy versus laparoscopy

The gold standard of surgical methods for extrauterine pregnancies is laparoscopy. Three randomized controlled trials have shown that, as compared to laparotomy, laparoscopic treatment of ectopic pregnancy results in lower costs, shorter hospital stays, less operational time, less blood loss, less analgesic usage, and faster recovery (34-36). Additionally, patients who were randomly allocated to laparoscopy had less adhesions in comparison to those treated with laparotomy, 19% and 64% respectively (37). Thereby, laparotomy is only done in cases when laparoscopy is not possible for either technical, logistic or medical factors (29).

### 3.5. Salpingotomy versus salpingectomy

Tube-sparing salpingotomy is preferred to salpingectomy, as it is less invasive but has comparable rates of future fertility and ectopic pregnancy. However, 8% of patients experience persistent ectopic pregnancy following a salpingotomy (12,38). A randomised controlled trial showed that while salpingotomy bears an increased risk of persistent trophoblast compared to salpingectomy, it does not provide better success rates of future pregnancies by natural conception in women with a healthy contralateral tube (39). Thus, the presumption that women with tubal pregnancy and a healthy contralateral tube might benefit from salpingotomy was rejected, as one healthy tube proved to be enough for equally successful natural conception.

Nowadays, it is a generally accepted notion that the chance of subsequent IUP after salpingotomy is not raised when compared to salpingectomy. Furthermore, conservative surgical procedures expose women to a risk of postoperative tubal haemorrhage, as well as the potential necessity for additional treatment for residual trophoblast. All of this validates current guidelines indicating that laparoscopic salpingectomy is the treatment of choice for EP with contralateral healthy tubes, while in patients with diseased contralateral tubes or history of infertility salpingotomy is the preferable treatment approach (11,29).

## GOAL OF RESEARCH

The goal of this graduate thesis paper is to present length of hospital stay and surgical treatment of patients diagnosed with ectopic pregnancy in Clinical hospital 'Sveti duh' from 2015 to 2020.

## METHOD

This research was a retrospective study done in Clinical hospital 'Sveti duh' at the Department of gynecology and obstetrics. The study included 139 patients who were diagnosed with ectopic pregnancy in the 6-year period from January 1<sup>st</sup> 2015 to December 31<sup>st</sup> 2020.

The data was collected from books of surgical procedures and the hospital electronic database. Data collection and the use of the hospital patient database were permitted by the Ethical committee of the hospital.

Parameters considered included the duration of hospital stay, diagnosis, localization of the ectopic pregnancy, performed procedure and surgical technique of removal. These are presented with descriptive analysis.

Data processing and statistical analysis was done with the help of the IBM SPSS software (Statistical Package for the Social Sciences).

Data are presented in the format of tables and charts.

# RESULTS

In the 6-year period, 139 patients with the diagnosis of ectopic pregnancy were surgically treated in Clinical hospital 'Sveti duh'.

Table 1. Age of patients

N	139
Mean	33,4317
Minimum	16,00
Maximum	43,00

The age of patients ranged from 16 to 43, with the average being 33,43 years.

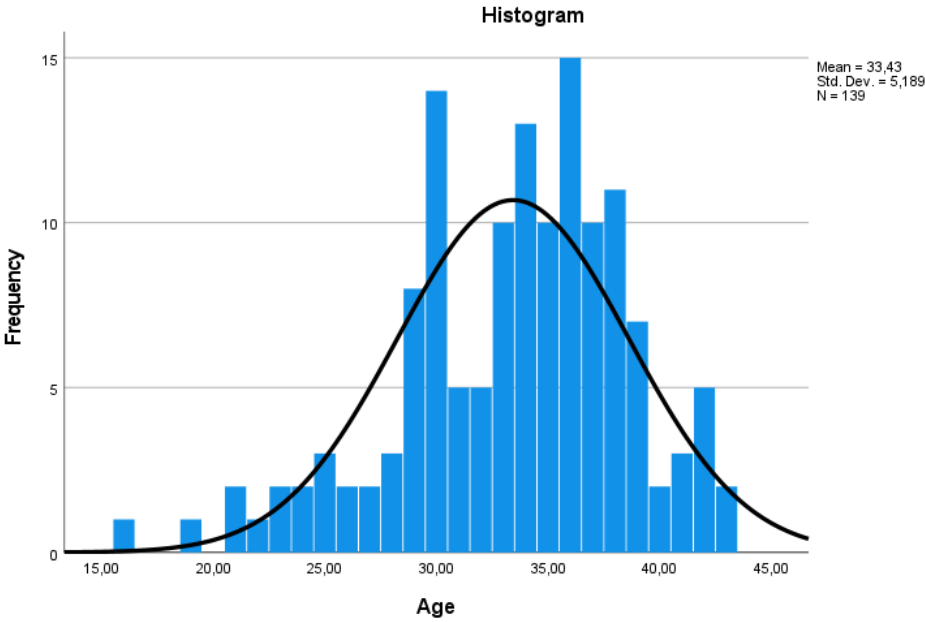


Figure 1. Age distribution of hospitalized patients

Figure 1. Shows the distribution of the frequency of EP with increasing age. Out of 139 patients, the most common age at the time of surgical treatment was 36 years.

Table 2. Length of hospital stay in days

Mean	2,46
Minimum	1
Maximum	7

The average hospital stay was 2,46 days, with the minimum and maximum stay 1 and 7 days, respectively.

Table 3. Localization of ectopic pregnancy

	Frequency	Percent
Tubal EP	135	97,1
Scar pregnancy	1	,7
Cervical EP	1	,7
Interstitial EP	1	,7
Ovarian EP	1	,7
Total	139	100,0

From a total of 139 ectopic pregnancies, as many as 134 (97,1%) were in the fallopian tube. The other, non-tubal, locations (2,9%) included cervical, interstitial, ovarian and cesarean section scar, one of each. Two cases were heterotopic pregnancies with a viable IUP.



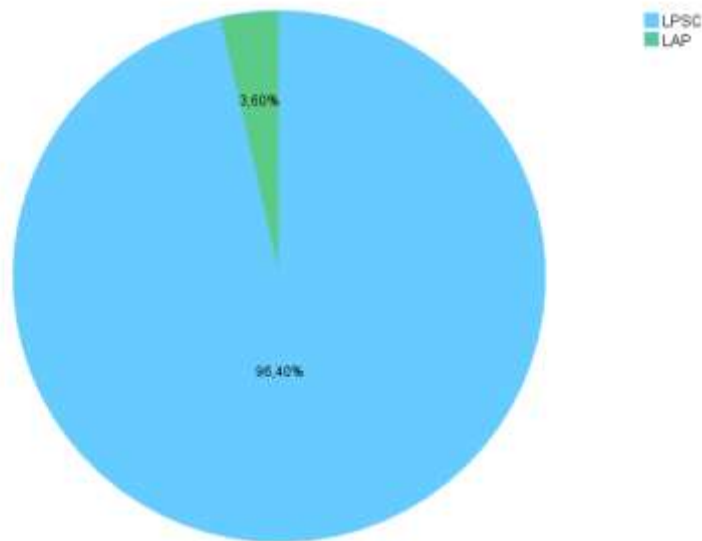


Figure 2. Frequency of laparoscopy versus laparotomy

In Clinical hospital 'Sveti duh', the most common surgical approach to ectopic pregnancy was laparoscopic salpingectomy. Out of 139 operations, only 5 (3.60%) laparotomies were performed. Out of 4 non-tubal pregnancies, 2 were treated by laparotomy.

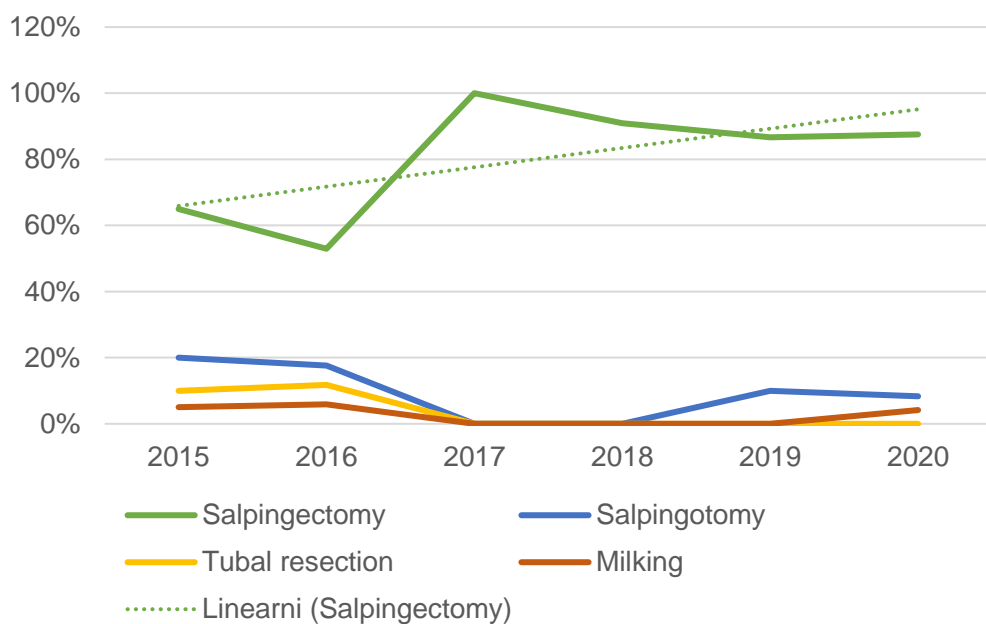


Figure 3. Surgical approach to ectopic pregnancy

Figure 3. illustrates the percentage of surgical approaches performed throughout the 6-year period. The proportion of salpingectomies performed increased steadily, starting at around 65% in 2015 and reaching about 88% by 2020. Out of the tubal-sparing surgical approaches, salpingotomy was most common in 2015 (20%) but by 2020 we have overall decrease in performance rates (8%). On average, 27,8 surgeries were performed annually.

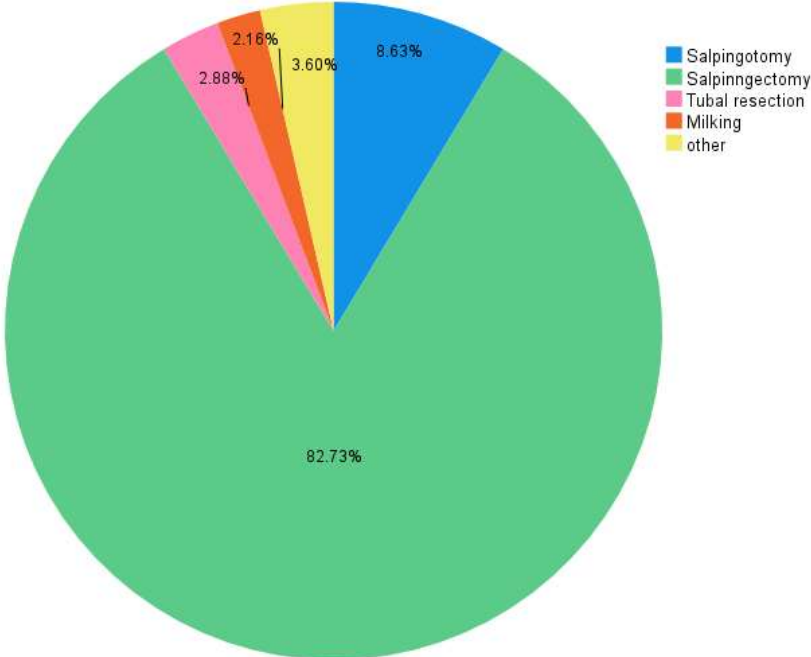


Figure 4. Percentage distribution of surgical approaches

Figure 4. shows the total percentage of surgical approaches performed on all 139 patients included in the survey. From the pie chart it is clear that the majority of patients underwent salpingectomy (82,73%), while the second most common method was salpingotomy (8,63%).

## DISCUSSION

This retrospective study included 139 women hospitalized and treated in the Clinical Hospital "Sveti Duh" for ectopic pregnancy from 2015 to 2020.

According to Bouyer et al. ectopic pregnancy is most commonly localized in the fallopian tubes (95,5%), of which around 75% are in the ampullary region. Extra-tubal pregnancies (4,5%) are rare and include cervical, ovarian, abdominal and scar implantation (1). In Clinical hospital 'Sveti duh', 97,1% of EPs were tubal, while non-tubal locations included cervical, interstitial, ovarian and scar implantation, one (0,7%) of each.

The age of patients ranged from 16 to 43, with the average being 33,43 years.

Our research showed that the average length of hospital stay was 2,46 days, with the minimum and maximum stay 1 and 7 days, respectively.

When taking the type of procedure into consideration, we can see that the duration of hospital stay was around 5 days for the patients who underwent open surgery, compared to 1 or 2 days for the other patients treated via laparoscopic approach. When comparing laparoscopic surgery to laparotomy, multiple studies demonstrated the advantages of laparoscopy, such as lower hospital costs, shorter hospital stay, less blood loss and faster recovery (34-36).

While our findings demonstrate much shorter hospital stay in patients treated via laparoscopy, our study had a small sample size which affects the reliability of the results. Further research should be carried out in Clinical hospital 'Sveti duh' to improve the reliability of these findings with bigger sample sizes.

A study done by Mahboob and Mazhar determined that the average duration of hospital stay for surgically treated patients was 6.5 days. However, in their research operative laparoscopy was not used as primary treatment, laparotomy was the surgical approach of choice (40).

The most prevalent surgical approach to ectopic pregnancy in Clinical Hospital 'Sveti duh' was laparoscopic salpingectomy. Out of 139 surgeries, only 5 (3.60%) were laparotomies. Younger women were more likely to go to laparoscopy which is attributed

to higher expectations of quality of life, including future fertility, body image and self-esteem. Older women were more likely to undergo more radical procedures as

The number of salpingectomies performed increased steadily from roughly 65% in 2015 to around 88% by 2020. Salpingotomy was the most frequent tubal-sparing surgical procedure in 2015 (20%), although overall it has a decreasing trend of frequency, nearing 8% in 2020. This is in line with current research suggesting that salpingotomy does not provide better success rates of future pregnancies by natural conception in women with a healthy contralateral tube, but does increase risk of complications or recurring EP due to persistent trophoblasts (39). Since salpingectomy minimizes these risks and maintains good future fertility, it became the main surgical approach and continues to increase in percentage. On the other hand, salpingotomy was the better option for future fertility in patients with contralateral tubal damage (41). Paull and Robson showed that, in Australia, the proportion of ectopic pregnancies surgically handled via laparotomy has decreased, with a drop from nearly 25% in 2000–01 to 10% in 2013–14. Additionally, it presented a steady drop in the proportion of salpingotomies performed, from roughly 22% in 2000-1 to less than 5% in 2013-14 (41). Comparably, a study from United States presented a decline in proportion of salpingotomies performed, from 13% in 2006 to 6% in 2015 (42).

Overall, with the option of IVF treatment, which does not require functional tubes, salpingotomies and other tubal-sparing procedures became less necessary and allowed for salpingectomies to become prevalent as the concern for fertility and future conception has decreased. A study by Kotlyar et al. demonstrated that patients with EP who underwent salpingectomy and controls who had their tubes left intact and then underwent IVF had comparable rates of implantation, clinical pregnancy, and live birth (43).

## CONCLUSION

Since 2015, there has been a strong trend away from the tubal-sparing surgical approaches for ectopic pregnancy.

The major finding of this research indicates that in Clinical hospital 'Sveti Duh', the most chosen surgical approach for treatment of ectopic pregnancy was salpingectomy (82,73%), with an increasing proportion trend from 2015 to 2020.

Furthermore, laparoscopic approach had been used in the majority of the patients, while laparotomy remains reserved for complicated cases where laparoscopy cannot be performed.

It was shown that the current medical practice for ectopic pregnancy in Clinical hospital 'Sveti duh' is comparable to other countries and follows current international standards. Further research with larger sample size is needed to estimate long-term outcomes of these surgical approaches.

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## REFERENCES

1. Bouyer J, Coste J, Fernandez H, Pouly JL, Job-Spira N. Sites of ectopic pregnancy: a 10 year population-based study of 1800 cases. *Hum Reprod.* 2002;17(12):3224–30.
2. Creanga AA, Shapiro-Mendoza CK, Bish CL, Zane S, Berg CJ, Callaghan WM. Trends in ectopic pregnancy mortality in the United States: 1980-2007: 1980–2007. *Obstet Gynecol.* 2011;117(4):837–43.
3. Hoover KW, Tao G, Kent CK. Trends in the diagnosis and treatment of ectopic pregnancy in the United States. *Obstet Gynecol.* 2010;115(3):495–502.
4. Marion LL, Meeks GR. Ectopic pregnancy: History, incidence, epidemiology, and risk factors. *Clin Obstet Gynecol.* 2012;55(2):376–86.
5. Bouyer J, Coste J, Shojaei T, Pouly J-L, Fernandez H, Gerbaud L, et al. Risk factors for ectopic pregnancy: a comprehensive analysis based on a large case-control, population-based study in France. *Am J Epidemiol.* 2003;157(3):185–94.
6. Li C, Zhao W-H, Zhu Q, Cao S-J, Ping H, Xi X, et al. Risk factors for ectopic pregnancy: a multi-center case-control study. *BMC Pregnancy Childbirth.* 2015;15(1):187.
7. Zhang D, Shi W, Li C, Yuan J-J, Xia W, Xue R-H, et al. Risk factors for recurrent ectopic pregnancy: a case-control study. *BJOG.* 2016;123 Suppl 3:82–9.
8. Kamwendo F, Forslin L, Bodin L, Danielsson D. Epidemiology of ectopic pregnancy during a 28 year period and the role of pelvic inflammatory disease. *Sex Transm Infect.* 2000;76(1):28–32.



9. Alkatout I, Honemeyer U, Strauss A, Tinelli A, Malvasi A, Jonat W, et al. Clinical diagnosis and treatment of ectopic pregnancy. *Obstet Gynecol Surv.* 2013;68(8):571–81.
10. Casanova BC, Sammel MD, Chittams J, Timbers K, Kulp JL, Barnhart KT. Prediction of outcome in women with symptomatic first-trimester pregnancy: focus on intrauterine rather than ectopic gestation. *J Womens Health (Larchmt).* 2009;18(2):195–200.
11. Sivalingam VN, Duncan WC, Kirk E, Shephard LA, Horne AW. Diagnosis and management of ectopic pregnancy. *J Fam Plann Reprod Health Care.* 2011;37(4):231–40.
12. Murray H, Baakdah H, Bardell T, Tulandi T. Diagnosis and treatment of ectopic pregnancy. *CMAJ.* 2005;173(8):905–12.
13. Stanislavsky A. Differential diagnosis for PV bleeding in pregnancy (Internet). *Radiopaedia.org.* (cited 2021 Jun 18). Available from: <https://radiopaedia.org/articles/differential-diagnosis-for-pv-bleeding-in-pregnancy-1?lang=us>
14. Hendriks E, MacNaughton H, MacKenzie MC. First trimester bleeding: Evaluation and management. *Am Fam Physician.* 2019;99(3):166–74.
15. Condous G, Kirk E, Lu C, Van Huffel S, Gevaert O, De Moor B, et al. Diagnostic accuracy of varying discriminatory zones for the prediction of ectopic pregnancy in women with a pregnancy of unknown location: Prediction of ectopic pregnancy. *Ultrasound Obstet Gynecol.* 2005;26(7):770–5.
16. Menon S, Colins J, Barnhart KT. Establishing a human chorionic gonadotropin cutoff to guide methotrexate treatment of ectopic pregnancy: a systematic review. *Fertil Steril.* 2007;87(3):481–4.

17. Connolly A, Ryan DH, Stuebe AM, Wolfe HM. Reevaluation of discriminatory and threshold levels for serum  $\beta$ -hCG in early pregnancy. *Obstet Gynecol.* 2013;121(1):65–70.
18. Kadar N, DeVore G, Romero R. Discriminatory hCG zone: its use in the sonographic evaluation for ectopic pregnancy. *Obstet Gynecol.* 1981;58(2):156–61.
19. Reyftmann L, Dechaud H, Hedon B. Alert for heterotopic pregnancy. *Fertil Steril.* 2007;88(3):759–60; author reply 760.
20. Webster K, Eadon H, Fishburn S, Kumar G, Guideline Committee. Ectopic pregnancy and miscarriage: diagnosis and initial management: summary of updated NICE guidance. *BMJ.* 2019;367:l6283.
21. Dialani V, Levine D. Ectopic pregnancy: a review. *Ultrasound Q.* 2004;20(3):105–17.
22. Feng C, Chen Z-Y, Zhang J, Xu H, Zhang X-M, Huang X-F. Clinical utility of serum reproductive hormones for the early diagnosis of ectopic pregnancy in the first trimester: Reproductive hormones in EP diagnosis. *J Obstet Gynaecol Res.* 2013;39(2):528–35.
23. Hock DL, Amenta PS, Kemmann E. Is the endometrial suction curette useful in the detection of chorionic villi during the first trimester? *Early Pregnancy.* 1997;3(3):225–7.
24. Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, et al. Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. *BJOG.* 2011;118 Suppl 1:1–203.

25. Horne AW, Shaw JLV, Murdoch A, McDonald SE, Williams AR, Jabbour HN, et al. Placental growth factor: a promising diagnostic biomarker for tubal ectopic pregnancy. *J Clin Endocrinol Metab.* 2011;96(1):E104-8.
26. Mukul LV, Teal SB. Current management of ectopic pregnancy. *Obstet Gynecol Clin North Am.* 2007;34(3):403–19, x.
27. Lipscomb GH, Bran D, McCord ML, Portera JC, Ling FW. Analysis of three hundred fifteen ectopic pregnancies treated with single-dose methotrexate. *Am J Obstet Gynecol.* 1998;178(6):1354–8.
28. Barnhart KT, Gosman G, Ashby R, Sammel M. The medical management of ectopic pregnancy: a meta-analysis comparing “single dose” and “multidose” regimens. *Obstet Gynecol.* 2003;101(4):778–84.
29. Taran F-A, Kagan K-O, Hübner M, Hoopmann M, Wallwiener D, Brucker S. The diagnosis and treatment of ectopic pregnancy. *Dtsch Arztebl Int.* 2015;112(41):693–703; quiz 704–5.
30. Farquhar CM. Ectopic pregnancy. *Lancet.* 2005;366(9485):583–91.
31. Sherman D, Langer R, Herman A, Bukovsky I, Caspi E. Reproductive outcome after fimbrial evacuation of tubal pregnancy. *Fertil Steril.* 1987;47(3):420–4.
32. Hajenius PJ, Mol F, Mol BWJ, Bossuyt PMM, Ankum WM, van der Veen F. Interventions for tubal ectopic pregnancy. *Cochrane Database Syst Rev.* 2007;(1):CD000324.
33. Jazayeri A, S Coussons H. Surgical Management of Ectopic Pregnancy (Internet). Medscape. 2021 (cited 2021 Jun 18). Available from: <https://emedicine.medscape.com/article/267384-overview#a3>

34. Lundorff P, Hahlin M, Källfelt B, Thorburn J, Lindblom B. Adhesion formation after laparoscopic surgery in tubal pregnancy: a randomized trial versus laparotomy\*\*Supported by grant 8683 from The Swedish Medical Research Council, Sweden, and by the Göteborg Medical Society, Göteborg, Sweden. *Fertil Steril.* 1991;55(5):911–5.
35. Murphy AA, Nager CW, Wujek JJ, Kettel LM, Torp VA, Chin HG. Operative laparoscopy versus laparotomy for the management of ectopic pregnancy: a prospective trial. *Fertil Steril.* 1992;57(6):1180–5.
36. Vermesh M, Silva PD, Rosen GF, Stein AL, Fossum GT, Sauer MV. Management of unruptured ectopic gestation by linear salpingostomy: a prospective, randomized clinical trial of laparoscopy versus laparotomy. *Obstet Gynecol.* 1989;73(3 Pt 1):400–4.
37. Lundorff P, Thorburn J, Hahlin M, Källfelt B, Lindblom B. Laparoscopic surgery in ectopic pregnancy. A randomized trial versus laparotomy. *Acta Obstet Gynecol Scand.* 1991;70(4–5):343–8.
38. Bangsgaard N, Lund CO, Ottesen B, Nilas L. Improved fertility following conservative surgical treatment of ectopic pregnancy. *BJOG.* 2003;110(8):765–70.
39. Mol F, van Mello NM, Strandell A, Strandell K, Jurkovic D, Ross J, et al. Salpingotomy versus salpingectomy in women with tubal pregnancy (ESEP study): an open-label, multicentre, randomised controlled trial. *Lancet.* 2014;383(9927):1483–9.
40. Mahboob U, Mazhar SB. Management of ectopic pregnancy: a two-year study. *J Ayub Med Coll Abbottabad.* 2006;18(4):34–7.

41. Paull C, Robson SJ. Hospital admission and surgical approach to tubal ectopic pregnancy in Australia 2000 to 2014: A population-based study. *Aust N Z J Obstet Gynaecol.* 2018;58(2):234–8.
42. Hsu JY, Chen L, Gumer AR, Tergas AI, Hou JY, Burke WM, et al. Disparities in the management of ectopic pregnancy. *Am J Obstet Gynecol.* 2017;217(1):49.e1-49.e10.
43. Kotlyar A, Gingold J, Shue S, Falcone T. The effect of salpingectomy on ovarian function. *J Minim Invasive Gynecol.* 2017;24(4):563–78.