Surgical Determinants of Post Operative Pain in Patients Undergoing Laparoscopic Adnexectomy

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SURGICAL DETERMINANTS OF POST OPERATIVE PAIN IN PATIENTS UNDERGOING LAPAROSCOPIC ADNEXECTOMY

Short running title: Post adnexectomy pain.

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ABSTRACT

Objective: The objective of our study was to determine the main surgical factors associated with postoperative pains in patients undergoing adnexectomy.

Material and Methods: Patients that underwent adnexectomy in two French Gynecological centers between July, 2018 to March, 2020 were prospectively included and retrospectively analyzed. The main pre and per operative surgical factors were analyzed to assess their impact on immediate postoperative pain. Analgesic consumption was recorded for each patient and pain was evaluated using the validated numeric rating scale (ranging between 0 – 10).

Results: One hundred and seventeen patients underwent laparoscopic adnexectomy. Eighty-four patients experienced either no or minor postoperative pain (NRS <=2, 84, 72%). Seventeen patients required strong opioids (subcutaneous morphine injection) in the immediate postoperative period.

The only two parameters that had a significant impact on immediate postoperative pain were the realization of a fascia closure and the duration of pneumoperitoneum longer than 60 minutes. Pneumoperitoneum pressure and size of ports were not significantly correlated with postoperative pain.

Conclusion: Fascia closure and increased surgical time were significantly associated with immediate postoperative pain and the need for strong opioids consumption. Surgical training to limit prolonged surgeries should be strongly emphasized to lower postoperative pain and limit opioids consumption.

KEYS WORDS: Adnexal surgery; low pressure laparoscopy; micro-laparoscopy; opioid crisis; postoperative pain.

INTRODUCTION

Between 1990 and 2010, the use of prescription opioids in the USA increased by 10-fold. At the same time, opioids overdoses have tripled and are now the leading cause of preventable death [1,2]. The postoperative period is at high risk for developing opioids addiction as it exposes naïve patients at stress and intense pain requiring powerful and regular analgesics opioids use, with around 3-7% patients developing persistent postoperative opioids consumption [3–6]. Moreover, there is an association between the amount of opioids prescribed postoperatively and the risk of chronic use afterwards [5].

In this context, it is determinant to find strategies to reduce surgical trauma and postoperative pain that could lead to decreasing postoperative opioids consumption. For many years, laparotomy has been the gold standard for performing many surgeries, including gynaecological. The use of laparoscopy has revolutionised the surgical field with its advantages of reduced perioperative morbidity, lower postoperative pain and early recovery [7].

Several authors investigated the benefit of administrating anaesthetics [8], others have tried to reduce either port size or per operative intra-abdominal pressure ([9–13]. All these strategies revolve around the idea, that in order to reduce postoperative pain, surgeons have a role to play and must improve their practices. Strategies to reduce postoperative pain are relevant only if the determinants of postoperative pain are known, and most of them are not, yet [14].

The objective of our study is to determine the main surgical factors associated with postoperative pain in patients undergoing laparoscopic adnexectomy.

MATERIAL AND METHODS

Study design

Patients that underwent adnexectomy in two French Gynecological centers (xxxx and xxxx) between July, 2018 to March, 2020 were prospectively included and retrospectively analyzed.

The inclusion criteria were patients older than 18 years-old with an indication of laparoscopy for adnexal surgery. Patients that required additional procedures during the same operative time and those not eligible for a laparoscopy approach were excluded.

The study protocol was approved by the xxxxx.

Procedures and surgical outcomes

A preoperative prescription of analgesics was usually delivered to the patients that included paracetamol (1 gram), non steroidal anti inflammatory drug (Ketoprofen 100 milligrams) and eventually weak opioids (Tramadol 50 milligrams).

General anesthesia was performed with induction by Propofol as hypnotic, Sufentanil as an analgesic, and Atracurium as a muscle relaxant, followed by intubation, and maintenance with Sevoflurane and Sufentanil. Prevention of vomiting was assured by Dexamethasone 4 milligrams. A tracheal tube was placed routinely by the anesthetist. First insufflation was achieved either using a “Veress Needle” entry or an open laparoscopy, at surgeon discretion. The choice of performing an open laparoscopy was also determined by the nature of the adnexal mass and especially the presence of a solid portion requiring larger port to allow specimen removal from the body. Bladder catheterization was performed for all patients. After the creation of pneumoperitoneum, a 0° laparoscopic camera was inserted through the umbilicus trocar and three working trocars in the lower abdomen, inserted under direct visualization. The size of port was at the surgeon discretion and was based on individual practices, the patient and characteristics of the lesion. Initial pressure was changed into the intraoperative pressure after insertion of all trocars. Insufflation was mediated either by standard insufflator or using Airseal device with a valve-free trocar that provides stable pneumoperitoneum even under constant

suction [15,16]. The patients were placed into the Trendelenburg position to facilitate intraoperative exposure of pelvic organs. Adnexectomy was performed using bipolar and scissors. Extraction of adnexal mass could require the widening of umbilical fascia and/or skin incision. Exsufflation of the intraperitoneal CO2 with Airseal® was automatic; In cases where Airseal was not used, the traps of the trocars were opened to vent the gas. Wound infiltration with Ropivacaine were performed at surgeon discretion.

Outcomes measures

Based on the literature review and the physiological parameters involved in pain, several factors were investigated to search for correlation with postoperative pain:

- Fascia closure (X or U stich)
- Pneumoperitoneum duration
- Low Pneumoperitoneum Pressure: P < 10 mmHg, (versus P ≥10 mmHg),
- Medium pneumoperitoneum pressure,
- Use of 3-mm trocars (versus 5-mm),
- Intra-operative adhesiolysis (versus not),
- Bilateral surgery (versus unilateral),
- Use of Ropivacaïne (wound infiltration),
- Age,
- Obesity,
- History of abdominal surgery.

Postoperative pain was assessed at least every 30 minutes within the following two hours in the PACU by a nurse using the validated numeric rating scale (NRS) ranging from 0 to 10 (where 0 is no pain and 10 the worst imaginable pain) [17–20]

According to the NRS, appropriate analgesics were given: Paracetamol (1 gram) for light pain (NRS < 4), Ibuprofen (200 milligrams) or weak opioids (Tramadol 100 milligrams, Nefopam 20 milligrams) for moderate pain (4 ≤ NRS < 7) and Morphine (titration between 5 and 10 mg of

subcutaneous morphine) for intense pain (NRS ≥ 7). The nurse in the recovery room was completely blinded to the operative technic used and indication for pain relievers was solely based on the NRS.

Statistical analysis:

Databases were managed using Excel (Microsoft Corporation, Redmond, WA, USA) and statistical analyses were performed using R studio software (1.1.463 version, available online). All potential factors involved in postoperative pain were assessed in univariable analysis. Values of $p < .05$ were considered to denote significant differences.

First, we analyzed the main surgical factors associated with no postoperative pain (defined as NRS < 2). Second, we analyzed the main surgical factors associated with intense postoperative pain (defined as NRS ≥ 6) requiring opioids.

RESULTS

Patient's characteristics

A total of 117 patients who underwent laparoscopy for adnexal surgery were included in this study. Patient characteristics are displayed in Table 1. Median age of the patients was 41 years old and the median BMI of 23.85 kg/m2.

Surgical outcomes

Surgical outcomes are displayed in Table 2. First insufflation was achieved using a "Veress Needle" entry in 40 patients (34.2%) and 77 (66%) had open laparoscopy. Three-millimeters ports were used for 42 patients (36%) and five-mm ports were used for the 75 remaining. Mean (SD, min – max) pneumoperitoneum pressure was of 10.2 mmHg (2.5, 6 –15). Forty-two patients underwent surgery using "low" pneumoperitoneum pressure (P < 10 mmHg), the 75 others had pneumoperitoneum pressure ≥10 mmHg. Median duration of pneumoperitoneum was 01:05 (00:26-03:27) hour. An intra-operative adhesiolysis was performed in 41 patients (35%). A fascia closure by an X or U stitch was made in 83 patients (71%). Wound infiltrations with Ropivacaïne were performed in 42 patients (36%). None of the patients underwent per or postoperative complication.

Immediate postoperative pain parameters

Analgesics' consumption and postoperative pain (maximum pain within the following two hours in PACU stay and pain on exiting PACU) are displayed in Table 3. Eighty-four (72%) patients had an immediate low postoperative pain ranging between 0 and 2 on the NRS at most. Eighteen patients (15%) had an immediate high postoperative pain ranging from 6 to 10. Seventy-nine patients (67.5%) used level 1 analgesic such as paracetamol, nefopam or non steroidal anti – inflammatory drugs and seventeen patients (14.5%) used a morphine treatment (subcutaneous morphine injection) in the immediate postoperative period.

Univariable analysis

Univariable analysis of the surgical parameters evaluated is presented in Table 4. In patients with low postoperative pain (NRS < or = 2), the only surgical factor significantly associated with postoperative pain is the fascia closure (X or U stich) (OR: 0.2 CI95% [0.0 – 0.6], p = .01).

In patients with high postoperative pain (defined as NRS ≥ 6), two factors were statistically associated with immediate postoperative pain: fascia closure (X or U stich) (OR: 8.6 CI 95% [1.1 – 67.7], p = .04) and duration of pneumoperitoneum longer than 60 minutes (OR: 3.3 CI95% [1.1 – 10.0], p = .03).

Intraperitoneal pressure had no influence on postoperative pain with no difference in the postoperative NRS (1.9 + /- 2.4 in the low pressure group versus 2.1 +/- 2.2 in the group with pressure > 10 mmHg, p = .57). Similarly, per-operative adhesiolysis and use of Ropivacaïne had no statistical influence on postoperative pain (OR: 0.7 CI 95% [0.3 – 1.7], p = .46 in the low pressure group versus OR: 2.7 CI 95% [1.0 – 7.5], p = .06 in the group with pressure > 10 mmHg; OR: 1.1 CI 95% [0.5 – 2.6], p = .8 in the low pressure group versus OR: 0.6 CI 95% [0.2 – 1.9], p = .42 in the group with pressure > 10 mmHg). In the same way, the history of surgery had no impact on the amount of postoperative pain in our cohort OR: 1.3 CI 95% [0.6 – 2.9], p = .53 in the low pressure group versus OR: 0.5 CI 95% [0.2 – 1.5], p = .22 in the group with pressure > 10 mmHg.

DISCUSSION

So far, the main determinants of postoperative pain remain unclear. In this work, we focused on collecting extensive data regarding the surgical factors that could be involved in immediate postoperative pain. Fascia closure and duration of pneumoperitoneum longer than 60 minutes were the two factors significantly associated with intense postoperative pain.

By lack of knowledge regarding the amount of postoperative analgesics needed for each surgery, surgeons are, against their will, actively participating in the opioids epidemic's damages. It has been clearly demonstrated that 3-7% patients undergoing ambulatory surgery develop persistent opioid use [3–6]. Bicket et al. in a systematic review that included 6 studies and 810 patients, reported that more than two-thirds of patients reported unused prescriptions for opioids after surgery [21]. This is why it is more important than ever to understand surgical factors associated with postoperative pain.

Adnexal surgery is usually considered as a short and minor surgery mostly performed ambulatory. Laparoscopy is now considered the approach of choice for adnexal surgery. This is especially true as the large majority of adnexal masses have benign histology (ovarian cancer represents only the 0.4% of all adnexal masses [22]). However, in the case of an adnexal mass, the risk of intra-operative rupture increases with the size of the mass; Adnexal mass > 10 cm would thus be associated with a 50% risk of intra-operative spillage, which seems to be linked to the intrinsic limitations of the technique [23]. In this setting, the majority of patients will not experience intense postoperative pain. This is in line with data of the literature which considered adnexectomy as minor surgery not at risk of opioid consumption [6]. Another factor that could definitely have an impact on postoperative pain was the history of surgery. Indeed, we could hypothesize that the way a patient respond to pain in the postoperative period could be influenced by his past experience of pain and his personal history. In our cohort, the history of surgery had no impact on the amount of postoperative pain, which is consistent with our finding of the absence of influence of adhesiolysis during surgery. Fascia closure is currently recommended in port > 10 mm since the risk of port site hernia is significant (up to 20% in some

series) [24,25]. While cases of port site hernia have been reported in patients with 5 mm port, their incidence remain rare (less than 1%) and fascia closure in such port is at surgeon's discretion [26,27]. The use of Veress needle for first insufflation and development of mini laparoscopy using only < 5 mm ports could reduce the need for fascia closure and thus, postoperative pain. Boza et al. [28] have shown in a 110 patients' cohort mini laparoscopic gynecologic surgery using 3-mm trocars resulted in decreased postoperative incisional pain as well as superior cosmetic appearance. In our cohort, the use of 3 mm port was not associated with reduced postoperative pain. One explanation is that adnexectomy is a short surgery and the benefit not large enough to be shown on our cohort. Furthermore, in patients with large adnexal masses, secondary widening of the umbilical fascia to extract the adnexa was required which could have balanced the benefit of performing micro laparoscopy. In our cohort, around half of micro – laparoscopic patients had umbilical fascia stitch impairing the benefit of this surgical approach. Moreover, in our cohort, no patient had direct optical access. This bladeless approach could be interesting to limit postoperative pain and should be studied in further studies. To avoid enlarging the ancillary trocar port, the transvaginal extraction by culdotomy of the surgical specimen could be an option in some patients. It could limit the weakening of the abdominal wall that is associated with increased morbidity.

Commenté [MOU1]: *Reviewer 2 : Comment 2)*

The other parameter that was associated with intense postoperative pain was the duration of pneumoperitoneum. Surgical velocity is achieved by surgical training and reducing the duration of pneumoperitoneum is a goal that should lead to reducing postoperative pain. Besides, it has been reported that the longer the surgery, the higher the risk of postoperative complications [29]. Pneumoperitoneum, usually with carbon dioxide (CO2), allows a good visualization of organs. However, the increase of intra-abdominal pressure leads to several metabolic modifications and is free neither of consequences nor risks. Pneumoperitoneum can have several negative impacts such as diaphragmatic elongation (diaphragmatic irritation and diaphragmatic injury) that can result in phrenic neuropraxia, perceived clinically as shoulder pain. In addition, it presents several risks including hypercapnia, subcutaneous emphysema,

gas embolism, pneumothorax, pneumomediastinum, venous thrombosis [30,31]. While many studies investigated the benefit of lowering abdominal pressure in general surgery especially cholecystectomy, little literature is available for gynecologic surgery [12,13,32]. Currently available evidence is in favor of a moderate reduction of immediate postoperative pain not significant at 24h past surgery [33].

Our study suffers from few limitations. First, the relatively small number of patients in our study in relation to the small rate of painful patients requiring morphine injection. This limited number of patients could have influenced our analysis of factors associated with postoperative pain. With only one or two variables associated with postoperative NRS (low or high), a multivariable analysis was not performed, therefore not permitting adjustment on confounding variables. Second, there was only little difference in the pressure used in our cohort. Thus, in our cohort, there was no difference in postoperative pain between the group of patients that had low intraperitoneal pressure and those who had pressure > 10 mmHg. Indeed, the higher pressure used was of 15 mmHg but some surgeons regularly use way higher pressure that could definitely influence pain. While none of our surgeons used pressure higher than 15 mmHg, we could not performed CO2 pressure analysis using narrow measurement ranges. Moreover, most surgeons of our team now use low pressure on a regular basis, thus limiting the probability of demonstrating influence of pressure on postoperative pain. Altogether, our results seem reliable since these patients usually undergo no or little pain following this minor and short surgery, all the more the pressure used is globally low. Eventually, while we focused mainly on surgical factors associated with postoperative pain, anesthesiologic factors such as increased locoregional anesthesia, might play a role in reducing postoperative opioids consumption. In our study, the use of Ropivacaïne had no influence on postoperative pain with no difference in the postoperative NRS. The benefit of the use of Ropivacaïne has been debated, even if its efficacy on postoperative pain following laparoscopic hysterectomy have been demonstrated in prospective randomized trials such as the one of Hortu et al. [34]. Similarly, levobupivacaine injection to trocar sites had different impact on postoperative pain according to the type of

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laparoscopic surgery performed and further studies should focus on assessing its impact on laparoscopic adnexectomy [35–37].

CONCLUSION

In patients undergoing laparoscopic adnexectomy, the two intraoperative parameters associated with immediate postoperative pain are the fascia closure and the duration of pneumoperitoneum. Understanding the factors associated with pain are mandatory in order to improve our pre and per-operative management to reduce analgesics consumption in the immediate postoperative period.

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