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1 **SURGICAL DETERMINANTS OF POST OPERATIVE PAIN IN**
2 **PATIENTS UNDERGOING LAPAROSCOPIC ADNEXECTOMY**

3
4 **Short running title: Post adnexectomy pain.**

5
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9

10 **ABSTRACT**

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

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

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

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

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

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

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38 **INTRODUCTION**

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

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

51 Several authors investigated the benefit of administrating anaesthetics ⁸, others have
52 tried to reduce either port size or per operative intra-abdominal pressure (⁹⁻¹³). All these
53 strategies revolve around the idea, that in order to reduce postoperative pain, surgeons have a
54 role to play and must improve their practices. Strategies to reduce postoperative pain are
55 relevant only if the determinants of postoperative pain are known, and most of them are not, yet
56 ¹⁴.

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

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66 **MATERIAL AND METHODS**

67 **Study design**

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

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

74 The study protocol was approved by the xxxxx.

75

76 **Procedures and surgical outcomes**

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

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

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

100

101 **Outcomes measures**

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

- 104 - Fascia closure (X or U stich)
- 105 - Pneumoperitoneum duration
- 106 - Low Pneumoperitoneum Pressure: $P < 10$ mmHg, (versus $P \geq 10$ mmHg),
- 107 - Medium pneumoperitoneum pressure,
- 108 - Use of 3-mm trocars (versus 5-mm),
- 109 - Intra-operative adhesiolysis (versus not),
- 110 - Bilateral surgery (versus unilateral),
- 111 - Use of Ropivacaine (wound infiltration),
- 112 - Age,
- 113 - Obesity,
- 114 - History of abdominal surgery.

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

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

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

124

125 **Statistical analysis:**

126 Databases were managed using Excel (Microsoft Corporation, Redmond, WA, USA) and
127 statistical analyses were performed using R studio software (1.1.463 version, available online).

128 All potential factors involved in postoperative pain were assessed in univariable analysis. Values
129 of $p < .05$ were considered to denote significant differences.

130 First, we analyzed the main surgical factors associated with no postoperative pain (defined as
131 NRS $<$ 2). Second, we analyzed the main surgical factors associated with intense postoperative
132 pain (defined as NRS \geq 6) requiring opioids.

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149 **RESULTS**

150 **Patient's characteristics**

151 A total of 117 patients who underwent laparoscopy for adnexal surgery were included
152 in this study. Patient characteristics are displayed in Table 1. Median age of the patients was
153 41 years old and the median BMI of 23.85 kg/m².

154
155 **Surgical outcomes**

156 Surgical outcomes are displayed in Table 2. First insufflation was achieved using a "Veress
157 Needle" entry in 40 patients (34.2%) and 77 (66%) had open laparoscopy. Three-millimeters
158 ports were used for 42 patients (36%) and five-mm ports were used for the 75 remaining. Mean
159 (SD, min – max) pneumoperitoneum pressure was of 10.2 mmHg (2.5, 6 –15). Forty-two patients
160 underwent surgery using "low" pneumoperitoneum pressure (P < 10 mmHg), the 75 others had
161 pneumoperitoneum pressure ≥10 mmHg. Median duration of pneumoperitoneum was 01:05
162 (00:26-03:27) hour. An intra-operative adhesiolysis was performed in 41 patients (35%). A fascia
163 closure by an X or U stitch was made in 83 patients (71%). Wound infiltrations with Ropivacaine
164 were performed in 42 patients (36%). None of the patients underwent per or postoperative
165 complication.

166
167 **Immediate postoperative pain parameters**

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

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177 **Univariable analysis**

178 Univariable analysis of the surgical parameters evaluated is presented in Table 4. In
179 patients with low postoperative pain (NRS < or = 2), the only surgical factor significantly
180 associated with postoperative pain is the fascia closure (X or U stich) (OR: 0.2 CI95% [0.0 –
181 0.6], p = .01).

182 In patients with high postoperative pain (defined as NRS ≥ 6), two factors were
183 statistically associated with immediate postoperative pain: fascia closure (X or U stich) (OR: 8.6
184 CI 95% [1.1 – 67.7], p = .04) and duration of pneumoperitoneum longer than 60 minutes (OR:
185 3.3 CI95% [1.1 – 10.0], p = .03).

186 Intraperitoneal pressure had no influence on postoperative pain with no difference in the
187 postoperative NRS (1.9 +/- 2.4 in the low pressure group versus 2.1 +/- 2.2 in the group with
188 pressure > 10 mmHg, p = .57). Similarly, per-operative adhesiolysis and use of Ropivacaine
189 had no statistical influence on postoperative pain (OR: 0.7 CI 95% [0.3 – 1.7], p = .46 in the low
190 pressure group versus OR: 2.7 CI 95% [1.0 – 7.5], p = .06 in the group with pressure > 10
191 mmHg; OR: 1.1 CI 95% [0.5 – 2.6], p = .8 in the low pressure group versus OR: 0.6 CI 95%
192 [0.2 – 1.9], p = .42 in the group with pressure > 10 mmHg). In the same way, the history of
193 surgery had no impact on the amount of postoperative pain in our cohort OR: 1.3 CI 95% [0.6 –
194 2.9], p = .53 in the low pressure group versus OR: 0.5 CI 95% [0.2 – 1.5], p = .22 in the group
195 with pressure > 10 mmHg.

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205 **DISCUSSION**

206 So far, the main determinants of postoperative pain remain unclear. In this work, we
207 focused on collecting extensive data regarding the surgical factors that could be involved in
208 immediate postoperative pain. Fascia closure and duration of pneumoperitoneum longer than
209 60 minutes were the two factors significantly associated with intense postoperative pain.

210 By lack of knowledge regarding the amount of postoperative analgesics needed for each
211 surgery, surgeons are, against their will, actively participating in the opioids epidemic's
212 damages. It has been clearly demonstrated that 3-7% patients undergoing ambulatory surgery
213 develop persistent opioid use³⁻⁶. Bicket et al. in a systematic review that included 6 studies and
214 810 patients, reported that more than two-thirds of patients reported unused prescriptions for
215 opioids after surgery²¹. This is why it is more important than ever to understand surgical factors
216 associated with postoperative pain.

217 Adnexal surgery is usually considered as a short and minor surgery mostly performed
218 ambulatory. Laparoscopy is now considered the approach of choice for adnexal surgery. This is
219 especially true as the large majority of adnexal masses have benign histology (ovarian cancer
220 represents only the 0.4% of all adnexal masses²²). However, in the case of an adnexal mass,
221 the risk of intra-operative rupture increases with the size of the mass; Adnexal mass > 10 cm
222 would thus be associated with a 50% risk of intra-operative spillage, which seems to be linked
223 to the intrinsic limitations of the technique²³. In this setting, the majority of patients will not
224 experience intense postoperative pain. This is in line with data of the literature which considered
225 adnexectomy as minor surgery not at risk of opioid consumption⁶. Another factor that could
226 definitely have an impact on postoperative pain was the history of surgery. Indeed, we could
227 hypothesize that the way a patient respond to pain in the postoperative period could be
228 influenced by his past experience of pain and his personal history. In our cohort, the history of
229 surgery had no impact on the amount of postoperative pain, which is consistent with our finding
230 of the absence of influence of adhesiolysis during surgery. Fascia closure is currently
231 recommended in port > 10 mm since the risk of port site hernia is significant (up to 20% in some

232 series)^{24,25}. While cases of port site hernia have been reported in patients with 5 mm port, their
233 incidence remain rare (less than 1%) and fascia closure in such port is at surgeon's discretion
234 ^{26,27}. The use of Veress needle for first insufflation and development of mini laparoscopy using
235 only < 5 mm ports could reduce the need for fascia closure and thus, postoperative pain. Boza
236 et al.²⁸ have shown in a 110 patients' cohort mini laparoscopic gynecologic surgery using 3-mm
237 trocars resulted in decreased postoperative incisional pain as well as superior cosmetic
238 appearance. In our cohort, the use of 3 mm port was not associated with reduced postoperative
239 pain. One explanation is that adnexectomy is a short surgery and the benefit not large enough
240 to be shown on our cohort. Furthermore, in patients with large adnexal masses, secondary
241 widening of the umbilical fascia to extract the adnexa was required which could have balanced
242 the benefit of performing micro laparoscopy. In our cohort, around half of micro – laparoscopic
243 patients had umbilical fascia stitch impairing the benefit of this surgical approach. Moreover, in
244 our cohort, no patient had direct optical access. This bladeless approach could be interesting to
245 limit postoperative pain and should be studied in further studies. To avoid enlarging the ancillary
246 trocar port, the transvaginal extraction by culdotomy of the surgical specimen could be an option
247 in some patients. It could limit the weakening of the abdominal wall that is associated with
248 increased morbidity.

249 The other parameter that was associated with intense postoperative pain was the
250 duration of pneumoperitoneum. Surgical velocity is achieved by surgical training and reducing
251 the duration of pneumoperitoneum is a goal that should lead to reducing postoperative pain.
252 Besides, it has been reported that the longer the surgery, the higher the risk of postoperative
253 complications²⁹. Pneumoperitoneum, usually with carbon dioxide (CO₂), allows a good
254 visualization of organs. However, the increase of intra-abdominal pressure leads to several
255 metabolic modifications and is free neither of consequences nor risks. Pneumoperitoneum can
256 have several negative impacts such as diaphragmatic elongation (diaphragmatic irritation and
257 diaphragmatic injury) that can result in phrenic neuropraxia, perceived clinically as shoulder
258 pain. In addition, it presents several risks including hypercapnia, subcutaneous emphysema,

Commenté [MOUI]; *Reviewer 2* : Comment 2)

259 gas embolism, pneumothorax, pneumomediastinum, venous thrombosis^{30,31}. While many
260 studies investigated the benefit of lowering abdominal pressure in general surgery especially
261 cholecystectomy, little literature is available for gynecologic surgery^{12,13,32}. Currently available
262 evidence is in favor of a moderate reduction of immediate postoperative pain not significant at
263 24h past surgery³³.

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

Commenté [MOU2]: *Reviewer 2* : Comment 3)

286 laparoscopic surgery performed and further studies should focus on assessing its impact on
287 laparoscopic adnexectomy ³⁵⁻³⁷.

288 **CONCLUSION**

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

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