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Laparoscopic nerve lysis for deep endometriosis improves quality of life and chronic pain levels: a pilot study.

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Laparoscopic nerve lysis for deep endometriosis improves quality of life and	1
chronic pain levels: a pilot study.	2

	Abstract	3
<u>Objectives:</u>	To assess the benefit of surgical management of patients with	4
	endometriosis infiltrating pelvic nerves in terms of pain, analgesic consumption, and	5
	quality of life (QOL).	6
<u>Methods:</u>	We conducted a retrospective cohort study In an Endometriosis referral	7
	center at a tertiary care university affiliated medical center. Patients diagnosed with	8
	endometriosis that underwent laparoscopic neurolysis for chronic pain were	9
	included. Patients rated their pain before and after surgery and differentiated	10
	between chronic pain and acute crises. Patients were requested to maintain a record	11
	of analgesic consumption and to evaluate their quality-of-life (QOL).	12
<u>Results:</u>	Of the 21 patients in our study 15 (71.5%) had obturator nerve involvement,	13
	2 (9.5%) had pudendal nerve involvement and 4 (19%) had other pelvic nerve	14
	involvement. Median postoperative follow – up was of 8 months. All but 2 patients	15
	(9.6%) had significant chronic pain improvement with a mean decrease of VAS of	16
	3.05 (± 2.5). Analgesic habits changed postoperatively with a significant decrease of	17
	66% of patients' daily consumption of any analgesics. Surgery improved QOL in 12	18
	cases (57.1%) and two patients (9.6%) completely recovered with a high QOL.	19
<u>Conclusion:</u>	Neurolysis and excision of endometriosis of pelvic nerves could results in	20
	significant improvement of quality of life.	21
Keywords:	Deep endometriosis; nerve lysis; complex surgery; chronic pain; acute	22
	pain.	23
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Endometriosis is a benign condition that may affect up to 10% of women of reproductive age [1,2]. Exact prevalence is hard to determine since many patients are asymptomatic, including even cases with severe disease [3]. It has been demonstrated that endometriosis might have a huge impact on the lives of affected women, their partners and their families [4]. In a previous retrospective study, 50% of women with surgically confirmed endometriosis reported a significant effect on education, work ability, relationship and social life [5].

Extrapelvic localization is reported to represent 5 % of lesions in patients with endometriosis, this rate is probably underestimated [6]. Several authors focused on clinical and pathological evidence on the involvement of pelvic nerves in women with endometriosis in recent years[7–11]. De Sousa et al. in their recent literature review reported 365 cases of patients with endometriosis and nerve infiltration, including involvement of the lumbosacral trunk in 57% and of the sciatic nerve [12] in 39% of cases. Further spread of the endometriotic lesions into the spinal nerves and even the dura of the spinal cord has been proposed to be a possible etiology of DIE [12,13].

The management of excessive endometriosis – related pain remains a medical challenge [14,15]. The benefit of surgery in endometriosis patients with pain and / or infertility has been extensively reported[16,17]. Currently, various surgical procedures may be required from uterosacral ligament resection to complex excision of nodules from bowel, urinary tract, nerves or blood vessels. These procedures

carry a relative increased risk of complications, which correlate to the extent of the 50
lesions and their tissue penetrance [18]. 51

Little data exist on endometriosis patients with pelvic nerve infiltration. The 52
ESHRE guidelines recently underlined that evidence to predict endometriosis based 53
on clinical symptoms alone is weak and incomplete and women may present to their 54
practitioners with a variety of non-specific symptoms [15]. This statement seems 55
particularly relevant in patients who have nervous lesions and are often under 56
diagnosed, despite having more frequently specific neurologic complains. Possover 57
et al. reported several cases as well as cohorts of patients that underwent 58
laparoscopic neurolysis for severe endometriosis, and demonstrated feasibility of 59
improvement in terms of pain scale intensity [10,19]. However, such procedures are 60
considered to be highly advanced laparoscopic procedures and carry significant 61
surgical risks, even in the hands of experienced surgeons[18].So far, the most 62
appropriate treatment for patients with proven pelvic nerve infiltration is unclear, 63
with only few authors focusing on this unique site. 64

The aim of our study was to assess the benefit of surgical management of 65
patients with endometriosis infiltrating pelvic nerves in terms of pain, analgesic 66
consumption and quality of life. (QOL) 67

68

	Methods	69
	<u>Study design</u>	70
A single center retrospective study that was performed in the Endometriosis and		71
Chronic pelvic pain clinic of the Sheba Medical Center, Tel Hashomer (Israel). All		72
patients surgically treated for deep infiltration endometriosis with nerves infiltration		73
between 1/2020 and 1/2022 were included. The study was approved by the ethic		74
committee of the hospital (number SMC – 8107 – 21) and all patients gave their		75
consent for their data to be included.		76
Indications for surgery were based on the European Society of Human Reproduction		77
and Embryology (ESHRE) guidelines and included medical treatment failure or		78
intolerance in symptomatic patients[15]. All decisions for surgery were		79
systematically validated by a multidisciplinary committee and cautiously discussed		80
with the patients, especially balancing the risk and potential benefits of the		81
procedure.		82
Confirmation of endometriosis diagnosis was histological if patients had lesion		83
excision during the surgical procedure and visual if they underwent only nerve lysis.		84
Preoperative workup included physical examination, transvaginal ultrasonography,		85
and pelvic neurographic MRI. The MRI protocol included 3D T2, 3D T1 sequences		86
with and without fat saturation and gadolinium injection [20].		87
Selection criteria included patients who presented to our service with chronic pelvic pain of		88
at least 6 months and signs and symptoms attributed to the affected nerve, for example in		89
case of obturator nerve involvement, limping, and aggravation of pain in abduction of the		90

knee insinuating involvement of the nerve. In some cases, we had an MRI scan that revealed	91
fibrosis or endometriosis nodules at the nerve level.	92
	93
<u>Outcomes evaluation</u>	94
Patients were followed for a minimum 8 months postoperatively. A Visual	95
Analog Scale (VAS) of 0—no pain to 10—worst pain imaginable was used for	96
standard quantification of the pain level. Patients rated their pain before and after	97
surgery and differentiated between chronic pain and acute episodes. Patients were	98
requested to maintain a record of analgesic consumption before and following	99
surgery.	100
The main socio-demographic characteristics of the patients were collected.	101
Two questionnaires were handed out to patients before and after surgery: (a) a	102
general one to assess pain localization and type of painful symptoms associated with	103
endometriosis and (b) a specific questionnaire to assess neurological symptoms. All	104
symptoms investigated in patients are detailed in the corresponding tables of the	105
results.	106
<u>Surgical procedure</u>	107
All operations were performed by a senior surgeon experienced with	108
endometriosis (S.C). The surgical method has been previously described by Possover	109
et al. [21]. Briefly, the lumbosacral space was developed to permit exposure of the	110
sacral plexus ventral to the level of the cardinal ligament, (also known as the	111
Mackenrodt ligament) - a paired, dense band of connective tissue that	112

supports the uterus and upper vagina.. This space was opened laterally to the 113
external iliac vessels and the exposure of the obturator nerve as well as the 114
lumbosacral trunk is systematically performed in the depth of this space. By 115
following the lumbosacral trunk distally, the superior gluteal nerve could be exposed 116
in the supra-piriform part of the sciatic foramen as well as the upper border of the 117
sciatic nerve itself. Suprapiriformis is located above the piriformis muscle, a flat, 118
pear-shaped muscle deep in the buttock Elective dissection of the different 119
branches of the internal iliac vessels and proximal transection of the obturator 120
vessels permits good exposure of the distal part of the sacral plexus, the sciatic nerve 121
and its endopelvic distal branches, making the further dissection of the 122
endometriosis safe [21]. The involved nerves, obturator and pudendal (S2-3), 123
are somatic in origin and function. Patients most frequently reported pain and 124
limited motor function in these nerves. Consequently, laparoscopic dissection 125
and release of endometriosis or fibrosis were performed after all other 126
treatment modalities failed. 127

Surgical technique for the Sacral Nerve roots and fo the Pudendal nerve: 128

Sacral Nerve Root Dissection: Dissection to expose the sacral nerve roots 129
(S1-S4) begins with a pararectal peritoneal incision medial to the ureter. The 130
anatomic pararectal space is bluntly dissected downwards to the coccyx. This 131
dissection is then carefully extended laterally, reaching the hypogastric fascia, 132
which is then transected to expose the space beyond. 133

Pudendal Nerve Decompression: Laparoscopic decompression of the right 134
pudendal nerve involves dissecting the ischiorectal fossa along the right 135
internal obturator muscle. After visualizing the obturator vessels and 136
identifying the pudendal nerve, the right sacrospinous ligament is sectioned 137
and removed entirely. The nerve is then repositioned in its natural course and 138
followed until it freely passes through Alcock's canal. 139

A standard follow-up visit was made between 4 and 6 weeks postoperatively.	140
Following this visit, additional evaluations were determined based on symptoms	141
reported by the patients.	142
<u>Statistical analysis</u>	143
Categorical variables were described as frequency and percentage and continuous	144
variables as median and interquartile range (IQR). Wilcoxon signed-rank test and	145
McNemar's test were used to compare pre- and post-surgical parameters. Since the	146
sample size was limited, we also calculated the standardized difference and	147
employed 0.2, 0.5 and 0.8 as cutoff values for small, medium, and large effect,	148
respectively. All statistical tests were two-sided and $p < 0.05$ was considered as	149
statistically significant, although calculated in a restrained number of cases due to	150
the size of our cohort. Statistical analysis was performed using SPSS statistical	151
software (IBM SPSS Statistics for Windows, version 27, IBM Corp., Armonk, NY, USA,	152
2020).	153
	154
	155
	156

	Results	157
	<u>Study population</u>	158
Over the last 2 years, 21 patients underwent neurolysis for deep infiltrating		159
endometriosis in Sheba medical center. The main characteristics of the patients are		160
displayed in table 1. Median age was 36 (IQR 27-41) and 81.0% (n = 17) of patients		161
had undergone previous surgery for endometriosis. The non-specific symptoms of		162
endometriosis expressed by patients who underwent surgery are detailed in		163
supplementary Table 1. The 3 most often reported symptoms were pelvic pain (n =		164
14, 55.7%), dyspareunia (n = 10, 47.6%), dysuria (n = 9, 42.9%).		165
Neurological symptoms reported by patients are detailed in Table 2. Pain radiating to		166
lower back (n = 10, 47.6%), urinary frequency (n = 10, 47.6%) and pain radiating to		167
left lower limb (n = 9, 42.9%) were frequently reported by patients with neural		168
involvement of their endometriosis.		169
The nerve specific symptoms were as follows:		170
For obturator nerve involvement, Pain radiating to one leg, leg dragging, limping and		171
difficulty in locomotion.		172
For pudendal nerve, the specific symptoms were vaginal and urinary bladder pain, tenesmus		173
and burning sensation on the outer aspect of the groin and inner thigh, and dyspareunia.		174
	<u>Management prior to surgery</u>	175
All but 2 patients used alternative treatments including arvigo therapy (n = 1),		176
cupping (n = 2), occupational therapy (n = 1), dietary changes (n = 2), pilates (n = 1),		177
physical activity (n = 1), shiatsu (n = 2), osteotherapy (n = 2), reflexology (n = 3),		178

medical massage (n = 4), acupuncture (n = 11), hydrotherapy (n = 6), physiotherapy	179
	(n = 12). 180
Medical treatment including oral contraceptives improved symptoms in 28.6% (n =	181
6), 47.6% (n = 10) used them before and after surgery and 14.3% (n = 3) did not	182
	neither before nor after. 183
Among the 21 patients included, 17 had undergone surgery for endometriosis before	184
the current procedure (81.0%). Among those, 6 (28.6%) had hysterectomy, 1 (4.8%)	185
had a resection of rectovaginal endometriosis nodule, 2 (9.6%) had a lysis of	186
rectosigmoid adhesions, 1 (4.8%) had ovarian cyst surgery and 1 (4.8%) had	187
	ureteroscopy and ureteral catheterization. 188
	<u>Surgical management</u> 189
Fifteen patients (71.4%) underwent neurolysis of the obturator nerves, 2	190
(9.6%) lysis of proximal part of the pudendal nerves, 8 patients (38.1%) lysis of other	191
pelvic nerves, one (4.8%) laparoscopic excision of pelvic nerves endometriotic	192
	nodule. 193
Median operation time was 2.15 hours. Median length of hospitalization was 3 days	194
(IQR 3-5).The median duration of recovery was of 3 weeks (IQR 2-8). One patient	195
experienced a postoperative complication of reduced locomotor motion due to	196
possible nerve praxis which spontaneously waxed and waned till full recovery.	197
One case the patient had indwelling catheter infection and in one case we were	198
required to instruct the patient regarding self-catheterization for three weeks post	199
	op. 200
	<u>Impact of surgery on pain intensity</u> 201

Median follow up was 8 months (IQR 6-11). Acute and chronic pain intensity in the 21 202
patients included before and after surgery is displayed in Figures 1 and 2. 203

Among all patients operated, only one (4.8%) experienced no change in chronic or 204
acute pain scale. All except 2 patients (9.6%) had significant improvement in chronic 205
pain with a median decrease of VAS of 3 (IQR 2-4). Two patients (9.6%) had no 206
residual chronic pain following surgery. 207

Five patients (23.8%) had acute pain worsening following surgery, five patients 208
(23.8%) had no difference in acute pain intensity before and after surgery and 11 209
patients (52.4%) had pain decrease after surgery. Acute pain following surgery 210
decrease by a median of 1 (IQR 0-2). 211

Analgesic intake before and after surgery is displayed in table 3. Analgesics habits 212
changed postoperatively with significant decrease of 66% of patients consuming 213
such medications daily (n = 9 before versus n = 3 after, p=.031) with a tendency for 214
more patients using them only during pain episodes (n = 2 beforehand versus n = 8 215
afterwards). Following surgery there was a decrease in consumption of strong 216
opioids by 25% (n = 4 before versus n = 3 after), weak opioids by 22% (n = 9 before 217
versus n = 7 after) and NSAIDS by 19% (n = 16 before and n = 13 after). Furthermore, 218
intake of Gabapentin or Amitriptyline decreased by 37.5% (n = 8 before and n = 5 219
after). Medical cannabis consumption increased by 11% after surgery (n = 10 versus 220
9 before). Two patients (9.6%) had no improvement with analgesics (refractory pain) 221
after surgery. 222

Impact of surgery on quality of life 223

QOL details following surgery are displayed in Supplementary Table 2. 224

Surgery improved quality of life in 12 cases (57.1%) and two patients (9.6%) 225

completely recovered with high QOL. Five patients (23.8%) considered the surgery 226

had no impact on their QOL. After surgery, seven patients (33.3%) still reported 227

having a low QOL. 228

During the follow up period, three patients (14.3%) were free of residual 229

symptoms, nine (42.9%) experienced symptoms that were less severe, three (14.3%) 230

perceived more severe symptoms, three (14.3%) had no improvement of their 231

symptoms following surgery and three (14.3%) were indeterminate. Three patients 232

indicated that their symptoms relapsed after a period of improvement, one that only 233

some symptoms returned after a period of improvement and five patients stated 234

that episodes were less frequent and /or of shorter duration after surgery. 235

236

237

We report here a cohort of 21 patients deep nerve infiltrating endometriosis 239
who underwent laparoscopic management with neurolysis, mostly of the obturator 240
nerves (15 patients, 71.4%). In these subjects, medical treatment by oral 241
contraceptives had improved symptoms in only 28.6% cases. All except 2 patients 242
(9.6%) had significant chronic pain improvement with a mean decrease of VAS of 243
3.05 (± 2.5). Analgesics habits changed postoperatively with a significant decrease of 244
66% of patients consuming them daily. Surgery improved QOL in 12 cases (57.1%) 245
and two patients (9.6%) completely recovered. 246

The mechanism of neuropathic pain in patients with endometriosis is 247
complex. Proposed hypotheses [22,23] include: (a) real damage to a nerve trunk or 248
to peripheral nerves leading to pain in certain dermatomes, muscle weakness and 249
sensitivity disorders; (b) nerve irritation due to inflammation causing pain projection; 250
this pain is frequently less well characterized at the dermatome level. A potential 251
source of neuropathic symptoms is the infiltration of the parametrium by nodules 252
compressing or involving nerves of large diameter, inducing somatic and vegetative 253
symptoms [7]. In our cohort, sciatic pain radiating to the lower limb, urinary 254
frequency and pain radiating to the lower back were frequently reported. In order to 255
improve diagnostic strategy, clinicians should be aware of possible atypical 256
presentation of nerve infiltration. In a prospective study, Possover et al. [9] 257
published the findings of 213 laparoscopies performed for symptoms suggestive of 258
sciatic or sacral plexus involvement with obscure etiology. In their cohort, 27 cases of 259
isolated endometriosis of the sciatic nerve were found, principally in its proximal 260

suprapiriform part, and 148 cases of infiltration of the sacral plexus, especially at the 261
level of the S1 and S2 roots. Of note, these patients had undergone an average off 262
our “inconclusive” laparoscopies, highlighting the need for systematic opening of the 263
retroperitoneal space together with progressive and meticulous exploration of these 264
nerve trunks and nerves. Roman et al. published an educational video that could 265
help endometriosis surgeons improve their skills [24]. 266

There are no reports of a comparison of medical and surgical treatment in 267
appropriate prospective randomized study to treat endometriosis patients with 268
neural involvement. In our cohort, three out of four patients still complained of pain 269
when using hormonal treatment alone. There have been similar reports for other 270
deep infiltrating endometriosis locations such as urinary lesions [25]. In such 271
patients, surgery is a “last chance” procedure to ease the pain and again attain a 272
satisfying QOL, even though some patients will not experience significant enough 273
improvement of their QOL. In a national Australian survey that included a total of 274
484 responses, Armour et al. reported that 76% of the women with endometriosis 275
used general self-management strategies within the last 6 months. Self-reported 276
effectiveness in pain reduction was high (7.6 of 10), with 56% also able to reduce 277
pharmaceutical medications by at least half [26]. Among the 21 patients included in 278
our cohort, medical cannabis consumption increased by 11% after surgery (n = 10 279
versus 9 before): almost half patients were using cannabis following surgery. Several 280
preclinical studies have shown the potential role of CBD to decrease the secretion of 281
pro inflammatory cytokines such as IL-6 and TNF- α , and to increase the levels of 282
anti-inflammatory cytokines IL-10 [27]. The other positive aspect of CBD to treat 283

pain-related symptoms include its anxiolytic, antidepressant, sleep modulating effects etc. [28]

In patients with nerves infiltration of their endometriosis, the benefit of surgery to decrease post operative pain has been described in several reports [10,11,21,29]. Initial approaches focused on interrupting nerves transmission through neurotomy or neurectomy. Initial evidence of the safety and effectiveness of neurectomy of the superior hypogastric plexus was reported by Plancarte et al [30] in patients with pelvic cancer pain. Subsequently the indications were expanded to include benign pathologies [31]. In a recent Cochrane review and meta-analysis by Proctor et al. [32], the effectiveness of surgical interruption of pelvic nerves for treating dysmenorrhea was analyzed. They summarized the findings of 7 controlled studies, including 3 RCT on treatment failure and complications, concluding that the procedure could benefit patients with midline pain. This raises the issue of the origin of neurogenic symptoms in these patients, and especially question the role of nerve infiltration in chronic pain. In our cohort, a large majority of patients had significant improvement of their chronic pain following surgery. As it has been correctly asserted by Soysal et al. [33], it is very difficult from the literature to ascertain the precise modality that accomplished relief of endometriosis symptomatology, since presacral neurectomy is often performed in conjunction with other procedures such as fulguration and excision of endometriotic foci [34]. According to our experience neurolysis and complete removal of endometriosis lesions should be the preferred approach whenever possible to improve symptoms and QOL. Improvement of QOL was observed in most patients following surgery in our cohort. These results are consistent with those of Roman et al. in their 52 patient cohort [11]. After a follow

up of 5 years, M. Possover reported sciatic nerve function recovery, although normal 308
gait function may take at least 3 years including intensive physiotherapy [10]. 309

It is important to not the risk of such operations. Firstly, irreversible nerve 310
damage, by erroneously cutting or heating the nerve. Another injury to the nerve 311
might be praxis i.e. reversible injury to some sensory or temperature fibers. In our 312
series we had no such complications. 313

Several limits of our work should be mentioned. First, despite the 314
retrospective nature of our study, the extent of data collected, including analgesic 315
consumption and precise symptoms description, is rare in the previous literature. 316

While our cohort included solely 21 patients, very little data is currently available in 317
the literature as these high-risk procedures require specific expertise introducing a 318
center- bias reporting results. In addition, the questionnaires were given out at the 319
end and not prior to the surgery. Second, the post operative follow up was limited to 320
a few months in some patients which could have contributed to two forms of bias: 1. 321
Underestimation of the benefit of the surgery on pain evolution. Indeed, persistence 322
of immediate postoperative pain and analgesic consumption is difficult to interpret 323
because the surgery itself could be responsible for transient pain increase. 2. 324

Overestimation of the benefit of the surgery on disease management: one of the 325
main issues in patients undergoing surgery for endometriosis – associated pain is the 326
high – risk of recurrence almost reaching 25% in deep endometriosis infiltrating 327
patients [35]. Indeed, in our cohort, at the time of study, three patients reported 328
that their symptoms returned after transient relief., and a further subject stated that 329
only some symptoms recurred after a period of improvement. Similar results were 330
reported by Roman et al. in their 52 patient’s cohort [11]. Third, it is not precisely 331

clear how patients were chosen for surgery. It is possible that the selection process 332
for these complex procedures could lead to an overestimation of its benefit. 333
However, the process of patients' selection is central in the role of expert center 334
[18]. Eventually, around 25% of patients had worsening of their pain following 335
surgery without clear explanation and the use of standardized questionnaires such as 336
EHP-30, SF-36 could have improved the reporting of these patients' outcomes. 337

Conclusion 338

In our cohort, neurolysis and excision of endometriotic pelvic nerves resulted 339
in significant improvement of chronic pelvic pain VAS score analgesic agent 340
consumption and improvement in neurological insult. These complex procedures 341
require the expertise of senior surgeons specialized in endometriosis. 342

343

Author contributions:	344
Project administration, supervision, and resources: SBC, ANB, MGP, RM, YZB	345
Methodology: YD, EB, JB	346
Data acquisition: YB, NMam, NMan	347
Data analysis: SBC, YD, YZB	348
Writing original draft: YD, TM, JB, MGP	349
All authors reviewed the manuscript for critical intellectual content.	350
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- Giudice LC. Clinical practice. Endometriosis. *N Engl J Med* 2010;362:2389–98. [1] 354
<https://doi.org/10.1056/NEJMcp1000274>. 355
- Zondervan KT, Becker CM, Missmer SA. Endometriosis. *N Engl J Med* [2] 356
 2020;382:1244–56. <https://doi.org/10.1056/NEJMra1810764>. 357
- Meuleman C, Vandenabeele B, Fieuws S, Spiessens C, Timmerman D, D’Hooghe [3] 358
 T. High prevalence of endometriosis in infertile women with normal ovulation 359
 and normospermic partners. *Fertil Steril* 2009;92:68–74. 360
<https://doi.org/10.1016/j.fertnstert.2008.04.056>. 361
- Culley L, Law C, Hudson N, Denny E, Mitchell H, Baumgarten M, et al. The social [4] 362
 and psychological impact of endometriosis on women’s lives: a critical narrative 363
 review. *Hum Reprod Update* 2013;19:625–39. 364
<https://doi.org/10.1093/humupd/dmt027>. 365
- Ballard K, Lowton K, Wright J. What’s the delay? A qualitative study of women’s [5] 366
 experiences of reaching a diagnosis of endometriosis. *Fertil Steril* 367
 2006;86:1296–301. <https://doi.org/10.1016/j.fertnstert.2006.04.054>. 368
- Machairiotis N, Stylianaki A, Dryllis G, Zarogoulidis P, Kouroutou P, Tsiamis N, et [6] 369
 al. Extrapelvic endometriosis: a rare entity or an under diagnosed condition? 370
Diagn Pathol 2013;8:194. <https://doi.org/10.1186/1746-1596-8-194>. 371
- Lemos N, Souza C, Marques RM, Kamergorodsky G, Schor E, Girão MJBC. [7] 372
 Laparoscopic anatomy of the autonomic nerves of the pelvis and the concept of 373
 nerve-sparing surgery by direct visualization of autonomic nerve bundles. *Fertil* 374
Steril 2015;104:e11-12. <https://doi.org/10.1016/j.fertnstert.2015.07.1138>. 375
- Ceccaroni M, Clarizia R, Alboni C, Ruffo G, Bruni F, Roviglione G, et al. [8] 376
 Laparoscopic nerve-sparing transperitoneal approach for endometriosis 377
 infiltrating the pelvic wall and somatic nerves: anatomical considerations and 378
 surgical technique. *Surg Radiol Anat SRA* 2010;32:601–4. 379
<https://doi.org/10.1007/s00276-010-0624-6>. 380
- Possover M, Schneider T, Henle K-P. Laparoscopic therapy for endometriosis [9] 381
 and vascular entrapment of sacral plexus. *Fertil Steril* 2011;95:756–8. 382
<https://doi.org/10.1016/j.fertnstert.2010.08.048>. 383
- Possover M. Five-Year Follow-Up After Laparoscopic Large Nerve Resection for [10] 384
 Deep Infiltrating Sciatic Nerve Endometriosis. *J Minim Invasive Gynecol* 385
 2017;24:822–6. <https://doi.org/10.1016/j.jmig.2017.02.027>. 386
- Roman H, Dehan L, Merlot B, Berby B, Forestier D, Seyer-Hansen M, et al. [11] 387
 Postoperative Outcomes after Surgery for Deep Endometriosis of the Sacral 388
 Plexus and Sciatic Nerve: A 52-patient Consecutive Series. *J Minim Invasive* 389
Gynecol 2021;28:1375–83. <https://doi.org/10.1016/j.jmig.2020.10.018>. 390
- Siquara De Sousa AC, Capek S, Amrami KK, Spinner RJ. Neural involvement in [12] 391
 endometriosis: Review of anatomic distribution and mechanisms. *Clin Anat N Y* 392
N 2015;28:1029–38. <https://doi.org/10.1002/ca.22617>. 393
- Siquara de Sousa AC, Capek S, Howe BM, Jentoft ME, Amrami KK, Spinner RJ. [13] 394
 Magnetic resonance imaging evidence for perineural spread of endometriosis 395
 to the lumbosacral plexus: report of 2 cases. *Neurosurg Focus* 2015;39:E15. 396
<https://doi.org/10.3171/2015.6.FOCUS15208>. 397

Koninckx PR, Ussia A, Adamyan L, Wattiez A, Donnez J. Deep endometriosis: definition, diagnosis, and treatment. <i>Fertil Steril</i> 2012;98:564–71. https://doi.org/10.1016/j.fertnstert.2012.07.1061 .	[14]	398 399 400
Endometriosis guideline n.d. https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Endometriosis-guideline.aspx (accessed December 14, 2021).	[15]	401 402
Bafort C, Beebeejaun Y, Tomassetti C, Bosteels J, Duffy JM. Laparoscopic surgery for endometriosis. <i>Cochrane Database Syst Rev</i> 2020;10:CD011031. https://doi.org/10.1002/14651858.CD011031.pub3 .	[16]	403 404 405
Arcoverde FVL, Andres M de P, Borrelli GM, Barbosa P de A, Abrão MS, Kho RM. Surgery for Endometriosis Improves Major Domains of Quality of Life: A Systematic Review and Meta-Analysis. <i>J Minim Invasive Gynecol</i> 2019;26:266–78. https://doi.org/10.1016/j.jmig.2018.09.774 .	[17]	406 407 408 409
Bendifallah S, Roman H, Rubod C, Leguevaque P, Watrelot A, Bourdel N, et al. Impact of hospital and surgeon case volume on morbidity in colorectal endometriosis management: a plea to define criteria for expert centers. <i>Surg Endosc</i> 2018;32:2003–11. https://doi.org/10.1007/s00464-017-5896-z .	[18]	410 411 412 413
Possover M, Chiantera V. Isolated infiltrative endometriosis of the sciatic nerve: a report of three patients. <i>Fertil Steril</i> 2007;87:417.e17-19. https://doi.org/10.1016/j.fertnstert.2006.05.084 .	[19]	414 415 416
Thomassin-Naggara I, Lamrabet S, Crestani A, Bekhouche A, Wahab CA, Kermarrec E, et al. Magnetic resonance imaging classification of deep pelvic endometriosis: description and impact on surgical management. <i>Hum Reprod Oxf Engl</i> 2020;35:1589–600. https://doi.org/10.1093/humrep/deaa103 .	[20]	417 418 419 420
Possover M, Baekelandt J, Flaskamp C, Li D, Chiantera V. Laparoscopic neurolysis of the sacral plexus and the sciatic nerve for extensive endometriosis of the pelvic wall. <i>Minim Invasive Neurosurg MIN</i> 2007;50:33–6. https://doi.org/10.1055/s-2007-970075 .	[21]	421 422 423 424
Walch K, Kernstock T, Poschalko-Hammerle G, Gleiß A, Staudigl C, Wenzl R. Prevalence and severity of cyclic leg pain in women with endometriosis and in controls - effect of laparoscopic surgery. <i>Eur J Obstet Gynecol Reprod Biol</i> 2014;179:51–7. https://doi.org/10.1016/j.ejogrb.2014.05.027 .	[22]	425 426 427 428
Pacchiarotti A, Milazzo GN, Biasiotta A, Truini A, Antonini G, Frati P, et al. Pain in the upper anterior-lateral part of the thigh in women affected by endometriosis: study of sensitive neuropathy. <i>Fertil Steril</i> 2013;100:122–6. https://doi.org/10.1016/j.fertnstert.2013.02.045 .	[23]	429 430 431 432
Roman H, Seyer-Hansen M, Dennis T, Merlot B. Excision of Deep Endometriosis Nodules of the Sciatic Nerve in 10 Steps. <i>J Minim Invasive Gynecol</i> 2021;28:1685–6. https://doi.org/10.1016/j.jmig.2021.05.019 .	[24]	433 434 435
Barra F, Scala C, Biscaldi E, Vellone VG, Ceccaroni M, Terrone C, et al. Ureteral endometriosis: a systematic review of epidemiology, pathogenesis, diagnosis, treatment, risk of malignant transformation and fertility. <i>Hum Reprod Update</i> 2018;24:710–30. https://doi.org/10.1093/humupd/dmy027 .	[25]	436 437 438 439
Armour M, Sinclair J, Chalmers KJ, Smith CA. Self-management strategies amongst Australian women with endometriosis: a national online survey. <i>BMC Complement Altern Med</i> 2019;19:17. https://doi.org/10.1186/s12906-019-2431-x .	[26]	440 441 442 443

Nichols JM, Kaplan BLF. Immune Responses Regulated by Cannabidiol. <i>Cannabis</i>	[27]	444
<i>Cannabinoid Res</i> 2020;5:12–31. https://doi.org/10.1089/can.2018.0073 .		445
Poli-Neto OB, Hallak JEC, Rosa-E-Silva JC, Crippa JA de S. Is it the Ideal Time to	[28]	446
Start Prescribing Cannabis Derivatives to Treat Endometriosis-associated Pain?		447
<i>Rev Bras Ginecol E Obstet Rev Fed Bras Soc Ginecol E Obstet</i> 2022;44:449–51.		448
https://doi.org/10.1055/s-0042-1749430 .		449
Possover M. Laparoscopic management of endopelvic etiologies of pudendal	[29]	450
pain in 134 consecutive patients. <i>J Urol</i> 2009;181:1732–6.		451
https://doi.org/10.1016/j.juro.2008.11.096 .		452
Plancarte R, Amescua C, Patt RB, Aldrete JA. Superior hypogastric plexus block	[30]	453
for pelvic cancer pain. <i>Anesthesiology</i> 1990;73:236–9.		454
https://doi.org/10.1097/00000542-199008000-00008 .		455
de Leon-Casasola OA, Kent E, Lema MJ. Neurolytic superior hypogastric plexus	[31]	456
block for chronic pelvic pain associated with cancer. <i>Pain</i> 1993;54:145–51.		457
https://doi.org/10.1016/0304-3959(93)90202-Z .		458
Proctor ML, Latthe PM, Farquhar CM, Khan KS, Johnson NP. Surgical	[32]	459
interruption of pelvic nerve pathways for primary and secondary		460
dysmenorrhoea. <i>Cochrane Database Syst Rev</i> 2005:CD001896.		461
https://doi.org/10.1002/14651858.CD001896.pub2 .		462
Soysal ME, Soysal S, Gurses E, Ozer S. Laparoscopic presacral neurolysis for	[33]	463
endometriosis-related pelvic pain. <i>Hum Reprod Oxf Engl</i> 2003;18:588–92.		464
https://doi.org/10.1093/humrep/deg127 .		465
Kwok A, Lam A, Ford R. Laparoscopic presacral neurectomy: a review. <i>Obstet</i>	[34]	466
<i>Gynecol Surv</i> 2001;56:99–104. https://doi.org/10.1097/00006254-200102000-		467
00023 .		468
De Cicco C, Corona R, Schonman R, Mailova K, Ussia A, Koninckx P. Bowel	[35]	469
resection for deep endometriosis: a systematic review. <i>BJOG Int J Obstet</i>		470
<i>Gynaecol</i> 2011;118:285–91. https://doi.org/10.1111/j.1471-		471
0528.2010.02744.x .		472
		473
		474

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Pat ien ts ID	Age (ye ars)	Number of years of symptoms evolution	Numbe r of Pregna ncies	Vagi nal deliv ery	Cesar ean Secti on	Previous surgery for endometri osis	Any history of other surgery	Chroni c morbi dities	Follow up (in month)
1	34	7	1	1	0	1	0	1	11
2	36	23	4	4	0	1	1	1	11
3	44	6	5	4	0	1	0	0	11
4	40	27	4	0	3	1	0	1	10
5	46	1	4	0	4	1	0	0	10
6	29	16	0	0	0	0	1	1	10
7	36	23	2	1	1	0	1	0	8
8	22	5	0	0	0	1	0	0	8
9	38	9	4	0	4	0	1	1	8
10	40	7	3	3	0	1	1	1	8
11	29	7	0	0	0	1	1	1	8
12	37	26	0	0	0	1	1	0	7
13	21	10	0	0	0	1	1	1	6
14	35	3	0	0	0	0	1	0	6
15	24	4	0	0	0	1	1	1	5
16	41	15	2	1	1	1	1	1	3
17	42	31	1	0	0	1	1	1	3
18	25	14	0	0	0	1	0	1	7
19	46	10	2	0	0	1	1	1	2,5
20	22	6	0	0	0	1	1	1	15
21	33	22	2	1	1	1	0	1	13

Table 1: Characteristics of the patients included.

Symptoms	Before surgery N = 21 (%)	After surgery N = 21 (%)	Number of patients with symptom "de novo" N = 21 (%)
Pain radiating to groin	8 (38.1)	4 (19.0)	0
Pain radiating to the vagina	4 (19.0)	2 (9.5)	1 (4.8)
Pain radiating to left lower limb	9 (42.9)	5 (23.8)	0
Pain radiating to the right lower limb	5 (23.8)	5 (23.8)	1 (4.8)
Pain radiating to lower digits	0	1 (4.8)	2 (9.5)
Pain radiating to lower back	10 (47.6)	7 (33.3)	1 (4.8)
Pain radiating to anus	6 (28.6)	2 (9.5)	0
Numbness in the right leg	4 (19.0)	1 (4.8)	0
Numbness in the left leg	6 (28.6)	4 (19.0)	0
Numbness in lower digits	1 (4.8)	1 (4.8)	0
Stabbing or burning sensation right leg	4 (19.0)	2 (9.5)	0
Stabbing or burning sensation left leg	3 (14.3)	3 (14.3)	1 (4.8)
Parashtesias in lower limbs	6 (28.6)	5 (23.8)	2 (9.5)
Anal and/or vaginal cramps	0	1 (4.8)	1 (4.8)
Dysesthesias in right leg	2 (9.5)	1 (4.8)	1 (4.8)
Dysesthesias in left leg	5 (23.8)	4 (19.0)	1 (4.8)
Dysesthesias in groin	0	0	0
Dragging left foot	5 (23.8)	2 (9.5)	0
Dragging right foot	2 (9.5)	0	0
Left leg tics	0	1 (4.8)	1 (4.8)

Right leg tics	0	0	0
Limping	2 (9.5)	1 (4.8)	0
Difficulty walking	8 (38.1)	4 (19.0)	0
Dorsiplantarflexion weakness	0	0	0
Weakness right leg	1 (4.8)	1 (4.8)	0
Weakness left leg	2 (9.5)	2 (9.5)	0
Urinary frequency	10 (47.6)	5 (23.8)	0
Urinary urgency	8 (38.1)	2 (9.5)	0
Urinary hesitancy	4 (19.0)	1 (4.8)	0
Urinary Incontinence	1 (4.8)	2 (9.5)	2 (9.5)
Stress Urinary Incontinence	0	0	0
Dyschezia	2 (9.5)	0	0
Fecal Incontinence	1 (4.8)	0	0
Sciatica	1 (4.8)	1 (4.8)	0
Loss of balance	0	1 (4.8)	1 (4.8)

Table 2 : Neurological symptoms before and after surgery in the patients included.

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Analgesics	Before surgery	After surgery	Standardized difference
Opiates	4 (19.0)	3 (14.3)	-25%
Semi opiates	9 (42.9)	7 (33.3)	-22%
NSAIDS	16 (76.2)	13 (61.9)	-18.7%
Lyrice (gabapentin)	7 (33.3)	5 (23.8)	-28.6%
Elatrol,Elatrolet (Amitrityline)	1 (4.8)	0	-100%
Medical cannabis	9 (42.9)	10 (47.6)	+11%
Takes them only during pain edisodes	2 (9.6)	8 (38.1)	+300%
Takes them daily	9 (42.9)	3 (14.3)	-66%
None	2 (9.6)	2 (9.6)	0
No improvement (Refractory) with analgesics	2 (9.6)	2 (9.6)	0

Table 3 : Analgesics consumption and habits before and after surgery in the patients 500
included. 501
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