

Original Research

Effect of Application of Dexmedetomidine in Perioperative Period on Postoperative Pain, Stress in Patients Undergoing Laparoscopic Uterine Fibroids Surgery: A Randomized Controlled Study

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Abstract

Background: This study aimed to evaluate whether dexmedetomidine (DEX) can relieve postoperative pain and reduce stress reaction after laparoscopic uterine fibroids (UF) surgery. **Methods:** This randomized controlled study included 100 patients age range of 40–60 years, American Society of Anesthesiologists (ASA) 1–2 grade, admitted for laparoscopic UF surgery from January 2020 to October 2023. The patients were randomly allocated to the DEX group (n = 50) and non-DEX group (n = 50). The visual analogue scale (VAS), Richmond Agitation-Sedation Scale (RASS) score, anesthesia time, spontaneous breathing recovery time, consciousness recovery time, extubation time, and recovery room time were recorded. **Results:** The VAS of the DEX group was smaller than that of the non-DEX group at half an hour, but there was no significant difference in VAS at 1 h, 12 h and 24 h. Dex group has a RASS value closer to zero than non-DEX group at half an hour. There was no significant difference in RASS at 1 h, 12 h, or 24 h. There were differences in spontaneous breathing recovery time, consciousness recovery time, extubation time, recovery room time, chills and nausea between the two groups. **Conclusion:** Application of DEX in perioperative period can relieve postoperative pain, reduce stress reaction after laparoscopic UF surgery. **Clinical Trial Registration:** The study has been registered on <https://classic.clinicaltrials.gov/> (registration number: NCT03524950).

Keywords: dexmedetomidine; laparoscopy; uterine fibroids; VAS; RASS

1. Introduction

Uterine fibroids are common benign tumors in women. Laparoscopic uterine fibroids (UF) surgery is currently the first choice for the treatment of uterine fibroids. However, abdominal pain and discomfort are common complications after UF surgery [1,2].

Dexmedetomidine (DEX) is a selective α_2 -adrenergic receptor agonist, which has been widely used to reduce stress response, maintain hemodynamic stability, and has played a very important role in the surgery [3]. Many studies have shown that dexmedetomidine can reduce pain and nausea in patients recovering from anesthesia, and has the effect of anti-anxiety after surgery [4–6].

In our study, 100 patients undergoing laparoscopic UF surgery were selected. The purpose of this study was to investigate whether dexmedetomidine can promote the recovery of patients with laparoscopic UF surgery and reduce the incidence of postoperative pain and complications.

2. Materials and Methods

2.1 Study Design and Participants

This was a pilot prospective interventional study from January 2020 to October 2023. This study was approved by the ethics review committee of Fuxing Hospital, Capital Medical University (Ethics approval num-

ber: 2020FXHEC-KY036). Trial registration number: NCT03524950. All patients signed the informed consent form. This study occurred 100 patients (The power of 0.9 and Alpha of 0.05 were calculated by PASS15 (NCSS Corp., Kaysville, UT, USA), and the sample size was 76, with 38 cases in each group. Considering a 10% increase in sample, a total of 100 patients were included. The two studies were divided into two groups with 50 cases in each group by random number table method). The inclusion criteria: patients aged 40–60 years, American Society of Anesthesiologists (ASA) class 1–2, and undergoing laparoscopic UF surgery under general anesthesia. The exclusion criteria: (1) hypertension; (2) thyroid disease; (3) adrenal disease; (4) acute or chronic renal disease; (5) impaired liver function; (6) obesity (body mass index (BMI) >30 kg/m²); (7) history of severe obstructive sleep apnea-hypopnea syndrome (OSAHS); (8) psychological disorders or mental disorders; (9) autonomic nervous diseases; (10) diabetes mellitus.

2.2 Randomization and Blinding

One hundred patients were randomly assigned to two groups by computer random number table method: dexmedetomidine group and non-dexmedetomidine group. Random numbers were sealed in envelopes. Prior to the operation, the nurse who did not participate in the study



opened the envelope and prepared the experimental drugs according to the grouping assignment in the envelope.

Dexmedetomidine group: study medication was: 0.2 mg of dexmedetomidine (Yangzijiang Pharmaceutical Company, Taizhou, Jiangsu, China) diluted with normal saline to 50 mL. The injection rate was 1 $\mu\text{g/kg/h}$ of dexmedetomidine and the injection time was 10 minutes before anesthesia induction. The injection rate was 0.7 $\mu\text{g/kg/h}$ of dexmedetomidine during the maintenance phase with discontinuation occurring 30 minutes before the end of the operation.

Non-dexmedetomidine group: study drug was: normal saline 50 mL. The dosage was calculated according to dexmedetomidine group.

2.3 Intervention

Prior to induction of anesthesia, the experimental drugs were injected into both groups by an intravenous infusion pump for 10 minutes (pump speed: 1.0 $\mu\text{g/kg/h}$ calculated according to dexmedetomidine). Patients in both groups received the experimental drug at a pump rate of 0.7 $\mu\text{g/kg/h}$ and the infusion was continued until half an hour before the end of surgery. Other induction drugs used in both groups were: sufentanil 0.5 $\mu\text{g/kg}$ (IDTBiologika GmbH, Beijing, China), propofol initiated at 6 $\mu\text{g/mL}$ via target-controlled infusion (TCI), and rocuronium 0.6 mg/kg.

During the maintenance phase of anesthesia, both groups received remifentanyl (0.1–0.3 $\mu\text{g/kg/min}$; Yichang Renfu Pharmaceutical Co., Ltd., Yichang, Hubei, China) and propofol (AstraZeneca, S.P.A, Milano, Lombardia, Italy) continuously. The injection speed of the propofol pump was adjusted according to the bispectral index (BIS) value, with BIS value maintained between 45–55. When blood pressure rises to 30% of baseline, 10–30 mg of urapidil hydrochloride is injected intravenously. When blood pressure is reduced by 30% from baseline, 6–10 mg of ephedrine hydrochloride (Northeast Pharmaceutical Group Company Shenyang first pharmaceutical factory, Shenyang, Liaoning, China) is injected intravenously. Vasoactive drugs could be reused after 10 minutes. There was no reduction in blood pressure in this study, therefore ephedrine hydrochloride was not used. After surgery: an intravenous analgesia pump was utilized (100 mL). Tropisetron Hydrochloride injection 5 mg and Flurbiprofen Axetil injection 50 mg were administered intravenously half an hour before the end of surgery to prevent postoperative nausea, vomiting and pain. When the postoperative visual analogue scale (VAS) of the patient was more than 5, Flurbiprofen Axetil injection 50 mg was injected intravenously.

The surgeon performs the operation through three small puncture sites made in the patient's abdomen. The surgeons were senior gynecologists who have performed more than 500 laparoscopic UF surgeries.

2.4 Observation Indexes

(1) General information of the patient, included: age, height, weight, uterine fibroids diameter, number of fibroids, anesthesia time, spontaneous breathing recovery time, consciousness recovery time, extubation time, and recovery room time.

(2) Post-operative pain: visual simulation scoring method (visual analogue scale, VAS) scores were recorded at 0.5 h, 1 h, 12 h and 24 h postoperatively. The VAS score was graded on a scale of 0–10. The score 0 was no pain and 10 was unbearable pain. The higher the score, the higher the pain level.

(3) Post operative stress response: Richmond Agitation-Sedation Scale (RASS) was recorded at 0.5 h, 1 h, 12 h and 24 h after the operation. The sedation score is on a 10-point scale, from –5 to 4.

A scale of –5 to 0 indicates coma to wakefulness, and the higher the score, the better the wakefulness. On a scale of 0 to 4, it ranges from wakefulness to agitation and violent behavior. The closer the score is to zero, the better the level of wakefulness.

(4) Postoperative chills (involuntary shaking of the whole body or part of the muscles occurs after surgery), nausea, and vomiting were recorded.

2.5 Statistical Analysis

SPSS 26.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The continuous variables conforming to the normal distribution (Kolmogorov-Smirnov test) were presented as means $\pm$ standard deviations and analyzed using the independent sample *t*-test. Categorical variables were expressed in frequency (%) and analyzed using Chi-square tests. RASS and VAS were expressed by *p*50 (*p*25, *p*75), and Mann-Whitney U test was used for data analysis. *p*-values < 0.05 were considered statistically significant.

3. Results

3.1 Characteristics

There were 50 patients in each group (Fig. 1). Their baseline characteristics are shown in Table 1. There were no significant differences in age, height, weight, diameter, or number of uterine fibroids between the two groups (Table 1).

3.2 Surgery-Related Parameters

There was no difference in anesthesia time. There were differences in spontaneous breathing recovery time, consciousness recovery time, extubation time, recovery room time (Table 2), chills and nausea between the two groups (Table 3).

Table 1. Patient basic information, expressed as: mean $\pm$ SD.

Characteristics	Group 1 (n = 50)	Group 2 (n = 50)	t/Z	p
Age (years)	40.12 $\pm$ 6.595	40.06 $\pm$ 6.498	0.046	0.964
Height (cm)	162.64 $\pm$ 4.294	162.06 $\pm$ 5.560	0.584	0.561
Weight (kg)	59.88 $\pm$ 8.743	59.60 $\pm$ 7.985	0.167	0.868
The number of uterine fibroids	1 (1, 2)	1 (1, 2)	0.373	0.709
The size of uterine fibroids (cm)	6.26 $\pm$ 1.445	6.24 $\pm$ 1.901	0.059	0.953

SD, standard deviation. The number of uterine fibroids expressed as: p50 (p25, p75).

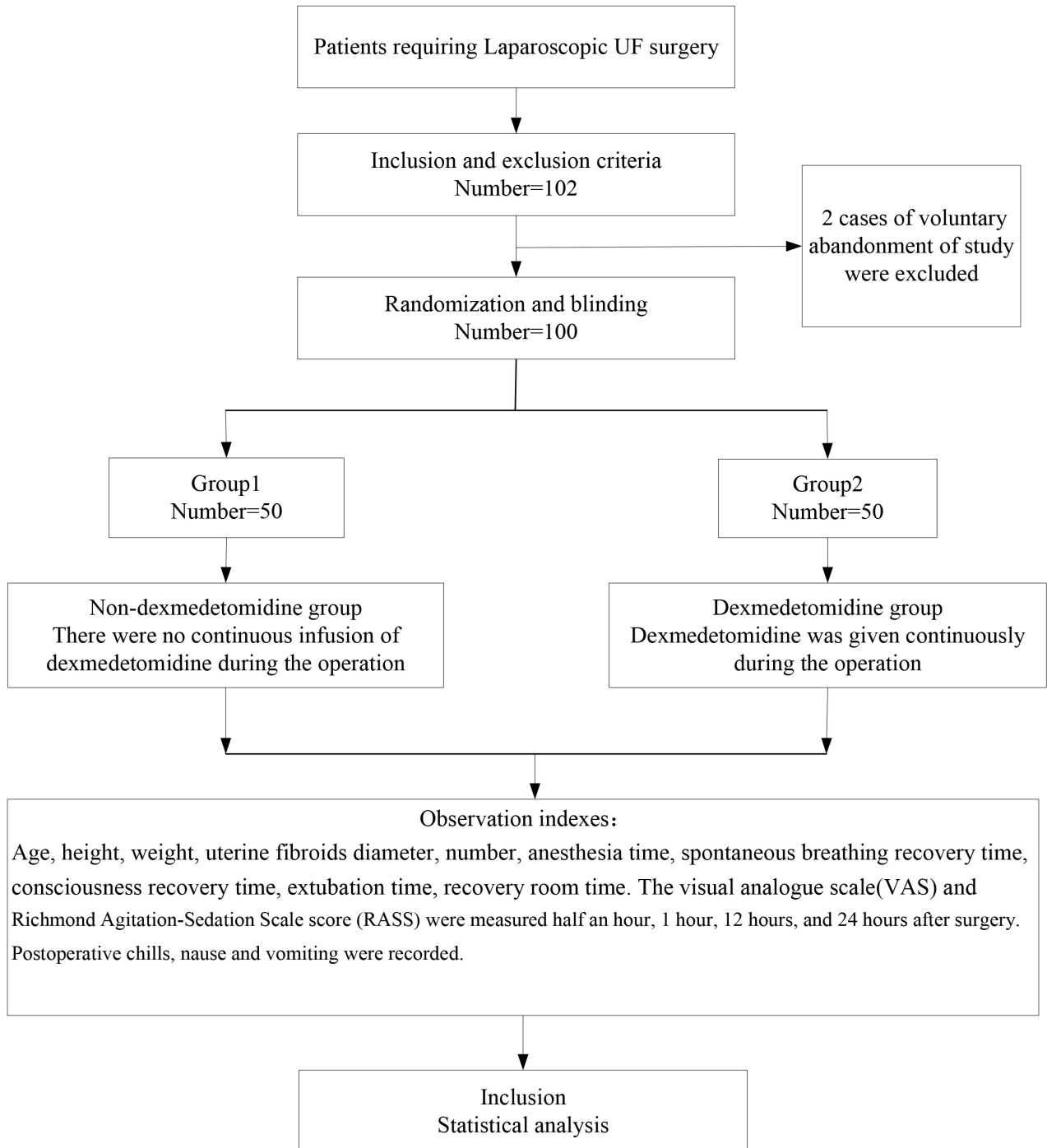


Fig. 1. Flow chart. UF, uterine fibroids.

Table 2. Surgery-related time parameters.

Characteristics (min)	Group 1 (n = 50)	Group 2 (n = 50)	<i>t</i>	<i>p</i>
Anesthesia time	115.26 ± 18.126	112.44 ± 18.326	0.774	0.441
Spontaneous breathing recovery time	6.48 ± 1.887	4.10 ± 1.313	7.320	0.000
Consciousness recovery time	16.98 ± 5.093	12.00 ± 2.814	6.052	0.000
Extubation time	18.98 ± 5.251	13.88 ± 2.890	6.017	0.000
Recovery room time	29.70 ± 5.346	26.06 ± 3.365	4.075	0.000

Table 3. Postoperative chills, nausea, vomiting parameters.

Characteristics n (%)	Group 1 (n = 50)	Group 2 (n = 50)	χ^2	<i>p</i>
Chills	10 (20.0%)	1 (2.0%)	8.274	0.004
Nausea	8 (16.0%)	1 (2.0%)	4.396	0.036
Vomiting	2 (4.0%)	1 (2.0%)	0.000	1.000

Table 4. Comparison of RASS of the two groups, expressed as: p50 (p25, p75).

Group	RASS			
	30 min	1 hour	12 hours	24 hours
Group 1	−1 (−3, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Group 2	−1 (−1, 0)	0 (−1, 0)	0 (0, 0)	0 (0, 0)
<i>F</i>	2.132	0.522	0.022	0.010
<i>p</i>	0.033	0.602	0.982	0.992

RASS, Richmond Agitation-Sedation Scale.

Table 5. Comparison of VAS of the two groups, expressed as: p50 (p25, p75).

Group	VAS			
	30 min	1 hour	12 hours	24 hours
Group 1	3 (2, 4)	2 (1, 3)	1 (1, 1)	0 (0, 0)
Group 2	3 (2, 3)	2 (1, 2)	1 (0, 1)	0 (0, 0)
<i>F</i>	2.471	0.451	1.283	0.348
<i>p</i>	0.013	0.652	0.199	0.728

VAS, visual analogue scale.

3.3 Comparison of RASS, VAS of the Two Groups

Dex group has a RASS value closer to zero than non-DEX group. There was no significant difference in RASS at 1 h, 12 h, 24 h (Table 4). The VAS of the DEX group was smaller than that of the non-DEX group at half an hour, but there was no significant difference in VAS at 1 h, 12 h and 24 h (Table 5).

4. Discussion

The incidence of uterine fibroids is common, and large fibroids are often accompanied by various symptoms [7–9]; which can reduce the quality of life of patients. Symptoms include: excessive abnormal uterine bleeding, pain, intestinal dysfunction and bladder irritation.

Laparoscopic UF surgery is the first choice for the treatment of uterine fibroids. Because a large number of experimental studies have shown that laparoscopic UF

surgery has less blood loss during the operation, shorter operative time and shorter postoperative recovery time, and it results in a lower probability of intrauterine adhesions after surgery [7,8,10].

However, laparoscopic UF surgery can stimulate the neuroendocrine system due to artificial pneumoperitoneum, special posture, and the use of pituitrin during the operation, which increase the secretion level of catecholamines in the body, stimulating the systemic stress response. This leads to increased conduction of the body's nervous system [11], and increases the level of inflammatory cytokines and transmitters. For example, the increased secretion of dopamine, vasopressin, epinephrine, norepinephrine, angiotensin and cortisol [12–15] leads to the enhancement of the body's stress response. The enhancement of the stress response can cause circulation instability and a series of complications in the perioperative period.

Dexmedetomidine is a selective α_2 -adrenergic receptor agonist, which is less inhibitory to respiration, has analgesic properties, and can reduce the use of opioids. It has been widely used in clinical anesthesia [16–18].

In this study, spontaneous breathing recovery time, consciousness recovery time, extubation time, and recovery room time of patients in the dexmedetomidine group were lower than those in the non-dexmedetomidine group. Portelli *et al.* [19] study showed that the use of dexmedetomidine could shorten extubation time and reduced mechanical ventilation time. This may occur because dexmedetomidine provides analgesia, reduces the use of opioids during surgery and simulates natural sleep with maintenance of spontaneous breathing and upper airway tone [20]. This is conducive to the recovery of patients' spontaneous breathing and consciousness after surgery.

In our study, postoperative VAS score at half an hour after surgery in the dexmedetomidine group were lower than that in the non-dexmedetomidine group. The dexmedetomidine group recovered better at half an hour after surgery (RASS score was closer to zero). This may occur because dexmedetomidine reduces the release of tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6),

interleukin-8 (IL-8) and other inflammatory factors, activates the cholinergic anti-inflammatory pathway, inhibits the expression of inflammatory factors in mononuclear macrophages and microglia, reduces stress response, reduces excessive cycle fluctuations, and maintains the stability of perioperative vital signs of patients [21,22]. Wu *et al.* [23] study showed that preoperative applications of DEX relieved postoperative pain in patients undergoing gynaecologic laparoscopic surgery, reduced stress responses and promoted rapid post-operative recovery. Their study compared the use of the same dose of dexmedetomidine pre-, intra- and post operation, and concluded that the use of dexmedetomidine pre- and intra- operation was more significant than that of postoperative use in reducing the stress response of patients. In our study, considering that there are many types of laparoscopic gynecological surgery, there are more patients undergoing laparoscopic UF surgery.

During laparoscopic UF surgery, the use of lithotomy, pneumoperitoneum, and pituitrin can greatly cause the body stress response [24]. Therefore, we selected patients for laparoscopic UF surgery. Our study is consistent with the results of the Wu *et al.* [23] study. In conclusion, dexmedetomidine can relieve postoperative pain and reduce stress reaction after laparoscopic UF surgery.

This study has limitations as it was a single center study. Additional studies are necessary with expansion of sample size and utilization of other surgical centers.

5. Conclusion

Application of DEX in perioperative period can relieve postoperative pain, reduce stress reaction after laparoscopic UF surgery.

Availability of Data and Materials

The data sets used in this article are available through the corresponding author upon reasonable request.

Author Contributions

XC—data collection, extraction, drafting of the manuscript, analysis of data, manuscript revision; XD—data collection; HHS—data collection; LHZ—data collection; XL—analysis of data. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. This study was approved by the ethics review committee of Fu Xing Hospital, Capital Medical University. Ethics approval number: 2020FXHEC-KY036. Trial registration: NCT03524950.

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Conflict of Interest

The authors declare no conflict of interest.

References

- [1] van der Meulen JF, Fisch C, Dreessen JRJ, Coppus SFPJ, Kok HS, Bongers MY. Procedural sedation and analgesia with propofol (PSA) for gynecologic surgery: A systematic review of the literature. *European Journal of Obstetrics, Gynecology, and Reproductive Biology*. 2023; 287: 137–146.
- [2] van der Meulen JF, Bongers MY, van der Zee LG, Leemans JC, Duijnhoven RG, de Leeuw RA, *et al.* Procedural sedation and analgesia versus general anesthesia for hysteroscopic myomectomy (PROSECCO trial): A multicenter randomized controlled trial. *PLoS Medicine*. 2023; 20: e1004323.
- [3] Ke HH, Liou JY, Teng WN, Hsu PK, Tsou MY, Chang WK, *et al.* Opioid-sparing anesthesia with dexmedetomidine provides stable hemodynamic and short hospital stay in non-intubated video-assisted thoracoscopic surgery: a propensity score matching cohort study. *BMC Anesthesiology*. 2023; 23: 110.
- [4] Labafchi A, Shoostari Z, Grillo R, Sharifian Attar A, Esghpour M, Samieirad S. The Beneficial Effect of Preoperative Dexmedetomidine in Controlling Postoperative Pain, Nausea, and Vomiting After Orthognathic Surgery: A Triple-blind Randomized Clinical Trial. *Journal of Oral and Maxillofacial Surgery*. 2023; 81: 941–949.
- [5] Yu Y, Li Y, Han D, Gong C, Wang L, Li B, *et al.* Effect of Dexmedetomidine on Posttraumatic Stress Disorder in Patients Undergoing Emergency Trauma Surgery: A Randomized Clinical Trial. *JAMA Network Open*. 2023; 6: e2318611.
- [6] Chen Y, Li M, Zheng Y, Chen A, Li C. The preventive effect of dexmedetomidine on anesthesia complications in strabismus surgery: a systematic review and meta-analysis. *BMC Anesthesiology*. 2023; 23: 253.
- [7] Capezzuoli T, Aslan B, Vannuccini S, Orlandi G, La Torre F, Sorbi F, *et al.* Recurrence of Uterine Fibroids After Conservative Surgery or Radiological Procedures: a Narrative Review. *Reproductive Sciences*. 2024; 31: 1171–1178.
- [8] Carugno J, Fatehi M. Abdominal Hysterectomy. *StatPearls Publishing: Treasure Island (FL)*. 2023.
- [9] Mercurio A, Della Corte L, Boccia D, Palumbo M, Reppucci S, Buonfantino C, *et al.* Myomectomy in infertile women: More harm than good? *Frontiers in Surgery*. 2023; 10: 1151901.
- [10] Morales HSG, López RR, López GGP, Mondragón PJC, Cortés DV, Hernández HS, *et al.* Surgical approach to uterine myomatosis in patients with infertility: open, laparoscopic, and robotic surgery; results according to the quantity of fibroids. *JBRA Assisted Reproduction*. 2022; 26: 44–49.
- [11] Stewart EA, Nowak RA. Uterine Fibroids: Hiding in Plain Sight. *Physiology*. 2022; 37: 16–27.
- [12] Sparić R. Uterine myomas in pregnancy, childbirth and puerperium. *Srpski Arhiv Za Celokupno Lekarstvo*. 2014; 142: 118–124. (In Serbian)
- [13] Stewart EA, Cookson CL, Gandolfo RA, Schulze-Rath R. Epidemiology of uterine fibroids: a systematic review. *BJOG: An*

International Journal of Obstetrics and Gynaecology. 2017; 124: 1501–1512.

- [14] Levast F, Legendre G, Bouet PE, Sentilhes L. Management of uterine myomas during pregnancy. *Gynecologie, Obstetrique & Fertilité*. 2016; 44: 350–354.
- [15] Gil-Moreno A, Carbonell-Socias M, Salicrú S, Bradbury M, García Á, Vergés R, *et al*. Nerve-sparing versus non-nerve-sparing radical hysterectomy: surgical and long-term oncological outcomes. *Oncotarget*. 2019; 10: 4598–4608.
- [16] Reel B, Maani CV. Dexmedetomidine. In: StatPearls [Internet]. StatPearls Publishing: Treasure Island (FL). 2023.
- [17] Mano A, Murata T, Date K, Kawata M, Sato M, Yamashita N, *et al*. Dexmedetomidine for dyspnoea. *BMJ Supportive & Palliative Care*. 2023; 13: e84–e85.
- [18] Strickley T, Smith K, Ericksen AM. Dexmedetomidine - An Alternative to Midazolam in the Treatment of Ketamine-Induced Emergence Delirium: A Systematic Review. *Journal of Peri-anesthesia Nursing*. 2024; 39: 311–318.
- [19] Portelli K, Kandiraju H, Ryu M, Shah PS. Efficacy and safety of dexmedetomidine for analgesia and sedation in neonates: a systematic review. *Journal of Perinatology*. 2024; 44: 164–172.
- [20] Ojha S, Abramson J, Dorling J. Sedation and analgesia from prolonged pain and stress during mechanical ventilation in preterm infants: is dexmedetomidine an alternative to current practice? *BMJ Paediatrics Open*. 2022; 6: e001460.
- [21] Xiao W, Chen S, Chen J, Huang J. Dexmedetomidine alleviates propofol-induced neural injury in developing rats. *International Journal of Developmental Neuroscience*. 2023; 83: 631–640.
- [22] Otonkoski S, Sainio T, Komar G, Suomi V, Saunavaara J, Blanco Sequeiros R, *et al*. Oxytocin selectively reduces blood flow in uterine fibroids without an effect on myometrial blood flow: a dynamic contrast enhanced MRI evaluation. *International Journal of Hyperthermia*. 2020; 37: 1293–1300.
- [23] Wu X, Xing Y, Pan L, Chai M. Effect of perioperative application of dexmedetomidine on post-operative stress reaction, pain and prognostic adverse effects in patients undergoing gynaecological laparoscopy. *Journal of Minimal Access Surgery*. 2023. (online ahead of print)
- [24] Cao X, Ma J. A Safety Study of Local Injection of Two Concentrations of Pituirin in Laparoscopic Uterine Fibroid Surgery: a Randomized Clinical Trial. *Clinical and Experimental Obstetrics & Gynecology*. 2022; 49: 103.