Myomectomy during cesarean section or non-caesarean myomectomy in reproductive surgery: this is the dilemma

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Nowadays it is quite common to encounter pregnant women over 35 years with uterine fibroids (UFs), requiring cesarean section (CS). Large UFs may cause severe complications during delivery, as bleeding and hemorrhage, during vaginal or cesarean delivery. Frequently, the cesarean myomectomy (CM) is recommended, but generally obstetricians are reluctant to perform CM, since literature data do not agree on its surgical recommendation. CM is jet particularly controversial, due to increased risk of perioperative hemorrhage and cesarean hysterectomy, and UFs are often left in situ during cesarean section (CS). CM investigations are generally directed to myomectomy associated issues, whereas CS complications without CM are largely underestimated. The risks of leaving UF for an interval myomectomy is underestimated and large UFs, left in uterus during CS, might cause significant early and late postoperative complications, even necessitating a relaparotomy and/or a subsequent hysterectomy. CM would be mandatory in some instances, whatever the UF diameter, to avoid further damage or complications. UFs management prior to CS should include a full counselling on pro and cons on the possible consequences of surgical decisioning. To illustrate what was discussed above, authors performed a narrative review with an expert opinion, reporting a case of a 31-year-old woman with a large UF who underwent a CS without myomectomy. Nine hours after CS, puerpera was submitted, for a massive postoperative hemorrhage and hemorrhagic shock, to an emergency relaparotomy with total hysterectomy without salpingo-oophorectomy.

Keywords
Uterine fibroids, Myoma, Pseudocapsule, Cesarean myomectomy, Complications, Hysterectomy, Cesarean section

1. Introduction

Uterine fibroids (UFs) or myomas represent the most common female benign tumors in reproductive age [1], consisting of smooth muscle cells, fibroblasts and extracellular matrix (ECM) [2]. UFs could have a negative impact on the reproductive system and might cause significant morbidity and quality of life impairment [3]. The presence of UFs is between 5.4 to 77% in female population, depending on the diagnostic techniques applied and study population [4]. Generally, overall prevalence of uterine UFs is underestimated because epidemiological studies are focusing mostly on symptomatic women [5]. Epidemiological risk factors associated with the onset and growth of uterine UFs are age, race, body mass index, sex hormones, heredity, lifestyle habits (including smoking, stress, physical activity, caffeine and alcohol consumption, diet rich in red meat and soy), environmental pollutants, as well as the chronic diseases, such as hypertension and diabetes [1]. Moreover, UFs represent a major public health issue because their follow-up and treatment, as well as perinatal and obstetric complications cause significant expense of resources and social expense [6]. UFs reach the...
largest sizes during women’s reproductive age and it has been found that incidence of UFs in pregnancy is about 0.05%–5% [7]. Since the incidence of UFs increases with the age and advancing maternal age during pregnancy, the obstetric chance to manage pregnant with UFs and to deal with their associated complications is worldwide rising [8]. UFs in pregnancy are significantly linked to higher rates of cesarean section (CS) [9].

2. Uterine fibroids in pregnancy

Incidence of UFs in pregnancy is estimated to be up to 10% [10], and there are controversial findings about UF size changes during pregnancy. While some authors reported increase of UF dimension in pregnancy, others didn’t show significant influence of pregnancy on UF growth [11]. Vitagliano et al. [12] analyzed of a total of 12 studies, investigating the effect of pregnancy on the size of UF. According to their results, there is a trend of increasing of UF dimension during the first trimester, while data on changes in UF’s size during the second and third trimester are conflicting. Additionally, it has been shown that 10 to 40% of women with UFs experience complications, such as first trimester bleeding, miscarriage, pain due to red degeneration, placental abruption, preterm delivery, placenta previa, preterm premature rupture of membranes, intruterine growth restriction, as well as increased rate of CS and postpartum hemorrhage [3].

3. Myomectomy during pregnancy

Uterine fibroid during pregnancy may be associated with pregnancy complications. Although myomectomy is preferably avoided antenatally, it has been reported in symptomatic cases that did not respond to conservative management. Syropoulou et al. [13] performed a recent meta-analysis including 54 relevant articles about myomectomy during pregnancy. Authors reported that median gestational age at diagnosis was 13 (range 6–26) weeks, while the median age at myomectomy was 16 (range 6–26) weeks. The most common indication for myomectomy during pregnancy was abdominal pain, not responding to medical treatment. The median number of fibroids removed per patient was one (range 1–5). Most of them were subserous pedunculated or subserous and fundal. The principal surgical approach was laparotomy, but laparoscopic and vaginal operations were also reported. The pregnancy outcome was favorable in most of the cases, with few complications reported. According to results reported in this meta-analysis, myomectomy during pregnancy appears as a safe procedure in cases of symptomatic uterine fibroids not responding to conservative management and, therefore, it may be considered, following appropriate counselling regarding the associated risks [13].

4. Cesarean myomectomy

Cesarean myomectomy (CM) is a long matter of debate among obstetricians since many years, as it carries high and effective risks of early and late complications, especially in case of large UFs [9]. Although the CM rate is currently increasing, many obstetricians are reluctant to perform CM, due to potential associated risks, particularly the perioperative hemorrhage [14]. It has been documented that a single CM is associated with a higher rate of hemorrhage when the UF diameter is more than 75 mm [15]. Nevertheless, the literature demonstrated that CM can be safely performed in cases of single anterior and lower uterine segment UFs [15, 16]. A large obstetrics’ consensus on UFs management, whether to be left or removed during CS, has not been yet reached [9]. Data on the CM safety and feasibility, especially in case of UFs which are difficult to enucleate for the position in pregnant uterus, are largely missing [9, 17]. Although obstetricians are mostly reluctant to perform CM when large and deep intramural UFs are encountered, a pregnant which will perform a CM in such cases, hardly she will undergo another myomectomy in the course of its life. Many patients can therefore benefit from two operations performed in one laparotomy: CS and contemporary myomectomy. Moreover, CM can reduce the overall cost and prevent the risk of UFs related complications in subsequent pregnancies, as anemia, infertility, pain and abnormal uterine bleeding [18]. Literature data show that CM represents a safe surgical procedure if several factors, as UFs localization, diameter and number, uterine contractility and UFs anatomic relationship with large vascular structures, are taken in account [19]. Anyway, many obstetricians are commonly skeptics on performing CM in case of large UFs, due to possible early perioperative complications, as massive bleeding or uncontrollable hemorrhage, or late complications, as cesarean hysterectomy, so they prefer to leave UFs in uterus during CS.

Basing on authors’ experience gained after years of researches on CM [9, 15] and on clinical and surgical reasoning, authors reviewed the pro and cons of CM, especially in case of large UFs encountered during CS. Furthermore, authors evaluated potential clinical and surgical risks of the non-removal of large UFs during CS.

5. Investigation setup

The authors used the PubMed (1966–2020) for the search on CM. Index words and the combinations used were as follows: (“pregnancy” AND “uterine fibroid OR uterine fibroids OR leiomyomas”), (“cesarean section OR caesarean section” AND “myomectomy”), (“cesarean section OR caesarean section” AND “uterine fibroid OR uterine fibroid OR leiomyomas”), (“cesarean myomectomy” OR “caesarean myomectomy”), (“delivery” AND “uterine fibroid OR uterine fibroid OR leiomyomas”), (“myomectomy in pregnancy”) and (“pregnancy OR delivery” AND “myomectomy”), (“cesarean myomectomy OR caesarean myomectomy” AND “complications”). The terms “leiomyomas”, “uterine fibroids”, “fibromyomas”, “leiomyofibromas” and “fibroleiomyomas” were also detected in literature describing UFs [20]. Authors identified articles reporting these key words, also evaluating
their references and selecting all available publications on this topic. Additional articles were identified from the references of relevant papers. In the narrative review performed, it was preferably used the term UF and neither approval from, nor communication with, the Ethics Committee was required. Authors realized the lack of quality of papers, in most cases only case reports on CM, without randomized controlled trials (RCT) on CM. Moreover, there is no evidence of papers on complications related to CM failure. After discussing the pro and cons of CM, authors illustrated, as an example, a case of uncontrollable postoperative hemorrhage after an elective CS without CM, performed in presence of a large single posterior UF, which required a relaparotomy and hysterectomy. The Ethics Committee of University Clinical Centre of Serbia approved data collection from patient in the reported case (N° 361/2).

6. Pro and cons of cesarean myomectomy

CM is a matter of debate among obstetric surgeons for over 100 years, since it is a surgical procedure combining two major operations into one, myomectomy and CS, both of which are potentially associated with complications, as heavy bleeding or hemorrhage, especially in the case of large size UFs [21]. Since a recent meta-analysis not yet defines conclusions on the feasibility and safety of CM [22], the decision to perform a CM, especially in the case of large UFs, is generally based on the patients’ preference, surgeon’ skill and intraoperative findings. Literature data provide reports on substantial early and late complication after CM, due to high risk of heavy bleeding or hemorrhage, owing to the increased uterine vascularization in pregnancy [3, 23]. The perioperative hemorrhage after CM, generally requires reoperation [3] for hysterectomy [3], arterial embolization or ligation [3, 14] and blood transfusion [24], as the most common CM complications. Obstetric intensive care unit (ICU) admissions, after CM, have been also described. Sparic et al. [25] have observed the relatively high rate of obstetric ICU admissions following CM and Seffah et al. [26] reported a case of disseminated intravascular coagulopathy after CM. Furthermore, authors reported ileus [14], significantly prolonged operative time [23] and prolonged hospital stay, as consequences of CM [27]. Significant differences in preoperative and postoperative hemoglobin values and postoperative fever [23] also were documented during and after CM. Simsek et al. [28] reported that postoperative hemoglobin and the mean difference in hemoglobin change were significantly different between women who have had CM and women who had CS without CM. The postpartum hysterectomy is one of the complications of CM, as well. Hassiakos et al. [29] reported that only disadvantages of CM were prolonged duration of surgery and hospitalization, without any other differences between women who have had CS and women with CM. They have also reported that none of the patients submitted to CM required blood transfusion [29]. Guler et al. [30] showed that changes of preoperative, postoperative, and mean hemoglobin values were not significantly different between patients with intramural or subserosal CM and only CS only. Kim et al. [14], investigated CM risk factors for major complications, reporting that patients with complications were older, with lower parity and bigger UFs [20]. Data from recent studies on CM outcomes are encouraging. The results reported by Zhao et al. [31] showed absence of significant differences in frequency of postpartum hemorrhage and neonatal outcomes (neonatal wight, fetal distress, and neonatal asphyxia) between patients with CM and patients with CS only. This study demonstrated that both birth weight ≥4000 g and presence of UFs larger than 50 mm were risk factors for postpartum hemorrhage. These results indicated that CM is safe and feasible when performed by skilled obstetricians. Despite a large number of CM cases included in the study, the question regarding management of large UFs during CS remained unsolved. Dedes et al. [32] evaluated the outcome of a CM versus a CS alone and the risk factors for adverse outcomes, concluding that CM is not associated with significant surgical adverse outcomes. The large UFs measuring ≥50 mm were associated with an increased blood loss of ≥500 mL, while women ≥40 years of age had a significant postoperative drop in hemoglobin, concluding that CM could be safe in selected pregnant without additional pre-existing risk factors. El-Refaie et al. [33] observed that CM can be performed safely without increase in the amount of blood transfusion and postoperative hemoglobin level drop, with the only addition of prolonged operative time and postoperative hospitalization. Results obtained from meta-analysis conducted by Huang et al. [34] showed that intramural UFs, when larger than 70 mm in diameter and multiple, were associated with more frequent intraoperative hemorrhage. These results suggest that CM performed by skilled surgeons and with appropriate hemostatic techniques represents safe and feasible procedure in selected patients. CM could be performed even for large UFs, regardless of size and locations, except if UFs are located close to large vessels or angular UFs. Similar results were obtained in a meta-analysis of Goyal et al. [35], who found there was not statistically significant incidence of hemorrhage between patients undergoing CM and CS alone. They reported a statistically significant, but clinically insignificant, hemorrhage drops, with a significant and more frequent need for blood transfusion in group of patients with CM compared with women with CS alone. The authors concluded that CM should be preferred over CS alone, especially in tertiary care centers, with staff expert in performing CM by appropriate hemostatic techniques. Sparic et al. [21] conducted retrospective study to analyze the incidence and risk factors for perioperative complications in women with a single UF submitted to CM. Study concluded with no significant differences on both minor and major complications in CM, laparotomic myomectomy and CS alone, highlighting the safety of CM without additional risks, when compared to CS alone and to laparotomic myomectomy in reproductive age women [15]. Kwon et al. [36] compared differ-
ences in maternal characteristics, UFs types, neonatal weight and operative outcomes between CS alone and CM. The subgroup analysis, according to UF size (>50 mm or not) in CM group, revealed that there were no significant differences in the mean hemoglobin change, operative time, and the length of hospital stay between two groups. These authors reported that there were no statistical significances in maternal characteristics, neonatal weight, and UF types between two groups. About CM complications, authors highlighted the literature bias on CM about uterine healing check, the scar quality at the hysterotomic site and the uterine myometrial integrity for subsequent pregnancy. Akkurt et al. [37] reported long-term outcomes of CM in study group, including 91 pregnancies and none of the participants, all women with subsequent pregnancy delivering by CS, had uterine rupture during pregnancy or delivery, and only one of these had uterine dehiscence and preterm delivery.

About placental complications in pregnant women with UFs, again Akkurt et al. [37] reported about 3.1% prevalence of placenta previa following CM, while a higher prevalence of placenta previa was reported by Adesiyun et al. [38]. Akkurt et al. [37] have also investigated adhesion formation as a late complication of CM, bearing in mind that postoperative adhesions are a well-known complication of conventional abdominal myomectomy. They observed postoperative adhesions in 25% of patients during subsequent CS.

Another bias is the data on UFs recurrence after CM, largely missing in the literature. Akkurt et al. [37] still reported a recurrence rate of 8.4% in women with CM, while 4.1% required additional major surgery for UFs (one abdominal myomectomy and two abdominal hysterectomies). As risk factors for UF recurrence after CM, the authors identified long follow-up (mean, 8.2 years), advanced age (>45 years), history of multiple UFs and larger UF size (>70 mm). None of the patients with UFs recurrence become pregnant during the follow-up period.

Literature also showed some advantages of CM either over CS without UF enucleation or over interval myomectomy. Incision on the uterus is smaller than in a non-pregnant uterus, because of the uterus/UF ratio is smaller for uterine grow, which is faster than CM growth in pregnancy [23]. The CM is technically easier to perform, the hysterotomory is easier in a pregnant uterus than in a non-pregnant one, for the uterine increased elasticity and stiffness in pregnancy [23]. Moreover, the hemorrhage is reduced by puerperal uterine contraction and physiological involution. The CM provides benefit of two operations in one, thus decreasing the risks and costs of reoperation. The CM improves quality of life and decreases UFs related symptoms, reducing risks of UFs related complications in puerperium and subsequent pregnancies [3].

Although there is no accurate diagnostic tool to assess the healing process at the myomectomy site and the quality of the scar, ultrasound assessment or intrasurgical visualization during subsequent CS, suggest better scar integrity after CM, than that following interval myomectomy [23]. Adesiyn et al. [38] reported that UF removal during CM increased the chances of vaginal delivery in subsequent pregnancies, observing that the total rate of vaginal delivery after CM was of 76.5%. According to the results of same study, the rate of spontaneous pregnancy after CM was 79.3%, indicating that future fertility and subsequent pregnancy outcome was not impaired by previous CM [38]. Authors summarized the data literature in Table 1 (Ref. [3, 9, 13, 14, 22, 23, 25–28, 32–34, 36, 37, 39]).

7. Cesarean section without myomectomy

Leaving UFs in pregnant uterus during CS has been also associated with severe complications. Hasan et al. [40] reported a high incidence of hysterectomy for the post-partum hemorrhage. Davis et al. [41] observed an increased incidence of post-partum sepsis in patients after CS without myomectomy. Price et al. [42] showed a rapid UF grow after elective CS, causing abdominal pain and hemoglobin drop, requiring a further surgical management after CS. Yel-lamreddygari et al. [43] reported the case of 35-years-old women who have had CS without UF removal. In postpartum period, she experienced persistent a smelling vaginal discharge for 3 weeks and urinary retention for 2 days. After an urgent ultrasound scan, patient underwent an emergency hysteromyectomy in early puerperium [43]. Murakami et al. [44] reported a case of UF prolapsed into vagina after elective CS, without contemporary myomectomy, required further surgery for a refractory infection [44]. A similar case reported by Zhang et al. [45], concerned a spontaneous expulsion of a huge cervical UF from the vagina after CS. Haskins et al. [46] reported case of 39-year-old primigravida, who underwent laparotomy for myomectomy of a 100 mm pedunculated UF, six months after CS. During CS obstetricians detected an intramural UF, located in the fundus and they decided to avoid CM [46]. Another case report showed a hypovolemic shock caused by edema of pedunculated UF, not removed during CS; a successive hysterectomy was performed to solve the hypovolemic shock [47]. Ergenoglu et al. [48] reported case of pulmonary embolism at 38-year-old women, submitted to emergency CS, without contemporary removing of a 150 mm intramural UF from uterus. The puerpera come back to the hospital on the 40th day from dismissal, with sepsis and pulmonary embolism, caused by obstruction of lochia drainage by the unremoved UF during CS. Puerpera required urgent hysterectomy, in association to medical therapy for pulmonary embolism [48]. Authors summarized the literature data in Table 2 (Ref. [3, 22, 23, 26, 28, 32, 40, 42–47]).

8. Descriptive case on the possible complications of non-cesarean myomectomy

Authors reported an example of what can happen if a large UF is left in situ during a CS, presented as an unusual complication of UF in the late postpartum after CS. A 31-years-
old woman (G4, P2) was referred to a University-affiliated hospital, at 35 weeks of gestation, for threatened preterm birth. Patient’ history showed the presence of an intramural UF diagnosed one year prior the pregnancy, two vaginal deliveries at term (nine and six years before hospital admission), and a missed abortion (one year before). At hospital admission, the ultrasound (US) scan showed a breech presentation and a missed abortion (one year before). At hospital admission, the ultrasound (US) scan showed a breech presentation and a missed abortion (one year before).

During laparotomy, obstetricians detected a very large and palpable through the posterior uterine wall, without the possibility of applying either a hemostatic suture of B-Lunch, or a uterine compression, with the UF left in uterus. They considered very unstable and in life threatening condition. A hysterectomy, since the patient, for anesthesiologists, was dynamically unstable by anesthesiologist, with a blood pressure of 95/58 mm/Hg and tachycardia (≥110 bpm). Clinicians decided for an immediate emergency re-laparotomy. The UF was fused the option of CM, preferring a successive interval myomectomy. The elective CS was scheduled at term, with the possibility of applying either a hemostatic suture of B-Lunch, or a uterine compression, with the UF left in uterus. They were urgently forced to choose between a myomectomy or a hysterectomy, since the patient, for anesthesiologists, was considered very unstable and in life threatening condition. A hysterectomy without salpingo-oophorectomy was performed, as the only option to achieve prompt and effective surgical hemostasis. The patient received, during surgery, a total of 845 mL of autologous blood and 1 gr of tranex-

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<td>Smaller incision of uterus</td>
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<td>Improving quality of life, reduce risk of myoma complication during puerperium and next pregnancy</td>
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<td>Better scar integrity</td>
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<td>Increased chance of vaginal delivery in next pregnancy</td>
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<td>Decrease risk for perioperative hemorrhage</td>
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amic acid. The immediate postoperative recovery required the transfusion of further six units of packed RBC (1.555 mL), plus three units of fresh frozen plasma and 10 units of cryoprecipitate, and patient has been transferred in the intensive care unit (ICU) for two days and her further recovery was uneventful. The patient was discharged nine days after hysterectomy. The histopathology report revealed a 165 × 130 × 125 mm uterus, weighing 1.570 g, with one large single posterior wall UF measuring 110 mm in diameter and two smaller UFs measuring 5 and 15 mm (Fig. 2). Discussing and criticizing as mentioned above, it is possible to affirm that this is a near-miss case, which could have ended tragically, for the choice of avoid the UF removal during CS. This approach however led to uterine atony and to the subsequent urgent life-threatening post-CS hysterectomy. What dramatically happened should be also evaluated by the analysis of the scientific literature on this topic, underlining the importance of surgical experience and intraoperative findings in case of large UFs during CS [9].

9. Analysis of the literature on the effects of failure to remove fibroids during a cesarean section

Sparic et al. [39] documented a case of multiple myomectomies performed by an experienced surgeon with the adjunct of intraoperative cell salvage without any perioperative complications. The largest UF diameter was 210 mm, and the total weight of enucleated UFs was 3300 g. Ma et al. [40] reported a CM of a 400 mm (3645 gr) large intramural UF, with the bilateral ligation of uterine arteries without any perioperative complications. In case of large intramural UFs greater than 50 cm³, CM can be associated with an increased rate of bleeding or hemorrhage [17]. Even if it is believed that, in case of UF encountered during CS, an interval myomectomy would be a safer option, however, large UFs could also cause excessive bleeding, uterine atony and massive PPH, up to even need emergency intra or post-CS hysterectomy, to control PPH, as reported in our case. Although UFs are frequently encountered during CS, especially in women of no younger age with UFs, the exact indications and contraindications for CM have not been agreed in obstetricians [49]. Generally, it is not recommended to remove UFs located in the fundal and cornual uterine areas, or as those located in proximity of major blood vessels, to avoid massive bleeding, even if most studies were not stratified according to the location and type of the myomas which affect the risk of hemorrhage. Additionally, the only contraindications for CM largely reported in literature concern uterine atony following fetal extraction and pre-existing maternal coagulopathies [49]. In the authors' reported case, uterine atony was assessed during the elective CS after the fetal delivery, due to the uterine inability to properly contract for the UF localization and large size. In fact, the uterotonics given intraoperatively and those given in the immediate postoperative period were rela-
Fig. 2. The histopathology specimen of the uterus that has been sectioned and reveals the large sized UF.

Nyflot et al. [50] conducted a large case-control study in Norway, including a total of 43,105 deliveries, out of which the severe PPH was recorded in 1064 cases. The most frequent cause of PPH was pure uterine muscular atony, present in 60.4% of cases, after excluding cases with atony due to retention of placental tissue. Authors showed that severe PPH was more likely to occur in women with UFs (4.9% of cases with severe PPH) and that the presence of UFs increased almost three-fold the risk of severe PPH.

Finally, even though the UF size and type are the most important features determining the perioperative risks of CM, the possible intra and post-operative complications of UF during CS, should be exposed during pre-surgical counselling with pregnant, when deciding “whether or not” performing a CM [49]. Although immediate abdominal myomectomy can be safely performed in cases of PPH, this approach seems to be recommended only in patients who have had a successful vaginal delivery. If the choice of delivery is a CS, perhaps a CM is an option to recommend in such patients with a previous vaginal delivery [51]. Large size UFs have also been described in association to retained placental products, both leading to PPH; however, this association was excluded in the above case, after the uterine histopathological examination [44, 51]. The high probability of uterine atony and consequent PPH (as in our case), poses a question if CM in such cases would have led to a more favorable maternal outcome, such as fertility preservation instead of hysterectomy, but it is not really possible to provide an answer due to lack of clinical data. Hence, from what was discussed, CM could represent an alternative option for the uterine atony prevention and of subsequent PPH in selected cases.

10. The most common complications after cesarean myomectomy

CM is a surgical procedure generally feared by obstetricians as it can lead to a number of short and long-term complications, such as perioperative hemorrhage [3, 14], diffuse intravascular coagulopathy (DIC) [26], ileus [14], postoperative fever [23]. If postoperative hemorrhage [3, 14] is a pathology to be taken into account in all surgical interventions, therefore easily treatable, another story is DIC [26], which has a high rate of mortality, morbidity and morbidity. On the other hand [14], and postoperative fever [23] are complications that can be easily dealt with in any postoperative course, so they do not cause major concerns among surgeons.

11. Conclusions

The CM has always been a controversial topic since risk factors for CM complications have been established, without assessing the risks associated to avoid a CM. It is still necessary to assess which UFs can increase the probability of complications if they are not removed during CS, so as the CS complications in the presence of UFs are largely under-reported. This manuscript discusses on how a CM can, in some narrow circumstances, prevent massive PPH and subsequent hysterectomy. However, obstetricians should also con-
sider novel techniques and their effects on the decision for CM, in addition to the use of minimally invasive surgery that makes use of instruments with energy (ligature, harmonic scalpel) can modify surgical times and blood loss. Moreover, the CM could be also valuable in resource limited settings by traditional techniques, for its advantages and limited risks. Anyway, there is a lack of prospective randomized clinical trials (RCTs) on the CM safety and feasibility and the available data, just refer to case-control and descriptive retrospective studies with low quality, due to large biased and scant conclusions. Therefore, further large multicenter prospective trials about CM are needed.

Author contributions

RSP, ILL, DP and AT designed the article. RSP MA, DT and AT wrote the manuscript, RST performed histopathological analysis. CN reviewed and edit the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The Ethic Committee of University Clinical Centre of Serbia approved data collection from patient in the reported case (No 361/2). The patient has given his consent in the file to anonymous participation in the publication of his clinical case.

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Conflict of interest

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