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CESAREAN MYOMECTOMY TECHNIQUE: A CRITICAL REVIEW

Marina Vinciguerra [1], Radmila Sparic [2,3], Safak Hartinaz [4], Giuseppe Trojano [5], Andrea Tinelli [6,7,8]

[2] Clinic for Gynecology and Obstetrics, Clinical Centre of Serbia, Belgrade, Serbia;
[3] School of Medicine, University of Belgrade, Belgrade, Serbia
[4] Samsun Training and Research Hospital, Gynecology and Obstetrics Department, Samsun, Turkey
[5] Department of Obstetrics and Gynecology, "Madonna delle Grazie Hospital, Matera, Italy
[6] Department of Obstetrics and Gynecology, "Veris delli Ponti" Hospital, Scorrano, Lecce, Italy;
[7] Division of Experimental, Endoscopic Surgery, Imaging, Technology and Minimally Invasive Therapy, Vito Fazzi Hospital, Lecce, Italy.
[8] Laboratory of Human Physiology, Phystech BioMed School, Faculty of Biological and Medical Physics, Moscow Institute of Physics and Technology (State University), Dolgoprudny, Moscow Region, Russia

Corresponding author: Andrea Tinelli
andreatinelli@gmail.com

Background: Cesarean myomectomy (CM) is, for many gynecologists, a discussed surgical procedure characterized by fibroid's removal during cesarean section (CS) followed by possible complications. For a long time, it has been common and shared thinking that myoma should not be surgically treated in pregnant women at the time of birth through CS in order to avoid complications for the patient. Nowadays, many studies reconsidered the feasibility of CM. The aim of this investigation is to summarize the scientific evidences on this procedure, highlighting when and how it can be performed safely.
Methods: This review has realized basing on evidences reported in scientific database, as PubMed, Scopus, Cochrane Library, Medline and EMBASE databases, found using key words of reference to the main topic, the cesarean myomectomy. All the observational studies and meta-analysis published in the current century has been considered and results were critically evaluated by the authors, experts on CM.
Results: According to the findings reported, the CM could be a valid and feasible treatment option for patients, especially when there are specific conditions which are associated with a lower risk of complications, as perioperative blood loss and risk of hysterectomy. Authors' experience and judgment agree with the evidences about the importance of the surgeons' skill and experience, both to make safer the surgical procedure and to have intraoperative and post-surgical outcomes.
Conclusion: The applied surgical technique and the informative counselling and/or informed consent, still need standardization for a safer CM, both for the patients and for the operator, at the same time.

Keywords:
Cesarean Myomectomy, Cesarean Section, Myoma, Fibroids, Pregnancy, Complications.

1. Introduction

In the last decades epidemiological data have reported a growing rise of the average pregnant age: This phenomenon hits mostly industrialized countries, where the percentage of women giving birth to a child in their 40's has more than doubled to date (Bellieni 2016). Postponing pregnancy and delayed childbearing have brought to light problems of management of coexisting organic diseases. The incidence of such pathologies is directly linked to the age, therefore obstetricians have had to face new clinical questions on topics less frequent and less investigated in the past. This lead to reevaluate and subvert ancient axioms and preconceptions, bringing out an innovative obstruct point of view: the caesarean myomectomy. This surgical procedure is currently discussed for the risk of complications during and after surgery. Myomas or leiomyoma, also known as uterine fibroids, are the most common benign lesions

in women, prevalently consisting of monoclonal smooth muscle cell. Fibroids' presence during pregnancy is often associated with a high risk of cesarean section, as well as peripartum hemorrhage (Laughlin, Schroeder, and Baird 2010; Sparić 2014; Klatsky et al. 2008). The prevalence of myomas ranges between 20% and 25%, while their incidence can be up to 70% in women of reproductive age ('Myomas and Reproductive Function' 2004; 'Myomas and Reproductive Function' 2006).

2. Epidemiology of fibroids' in pregnancy

According to increase of maternal age mentioned above, the prevalence of fibroids during pregnancy has been increasing too during these years, shifting from 0.1%-3.9%, as reported in the initial reports, up to 10.7% in the most recent evidences (Cooper and Okolo 2005; Exacoustòs and Rosati 1993; Hartmann et al. 2009). Considering that these data are based on ultrasound assessment during pregnancy, it could be considered underestimated, because only 4% of myomas in pregnant women are diagnosed by ultrasound (Svigos, Robinson, and Vigneswaran 2006) and so many of them are detected mostly during cesarean delivery (Exacoustòs and Rosati 1993; Hartmann et al. 2009). This is also the reason why the choice of removing of myomas during cesarean delivery is not always an elective and premeditated one, but often it is made impromptu at operating table. Therefore, it is important to have good scientific evidences that can correctly guide the management of these lesions during pregnancy and mostly at the time of childbirth in order to guarantee the best outcomes for the patient. Nevertheless, cesarean myomectomy seems to be not yet sufficiently studied, this surgical procedure has its roots in the past.

3. History of cesarean myomectomy

It was reported in literature for the first time at the beginning of the twentieth century, when Bonney successfully removed up to six fibroids without any complications for the patient, who had three subsequent uncomplicated vaginal deliveries (Jauniaux and Khan 2014). Several other attempts followed in subsequent years, many of which were uneventful, but at the same time emerges a series of complications which apparently have a higher incidence in this type of procedure rather than cesarean section only (Lolis, Zikopoulos, and Paraskevaidis 1994). Finally, cesarean myomectomy was strongly discouraged also by worthy textbooks (Park and Kim 2009; Sparic et al. 2014), as Te Linde's too ('Te Linde's Operative Gynecology; Mattingly RF 1977).

Despite of this, the choice to avoid fibroid removal in pregnant women at the time of childbirth is not altogether a safer choice (Davis et al. 1990; Kwawukume 2002). In fact several studies are trying to attest the feasibility of cesarean myomectomy, because, as well as supported by many obstetricians, performing this apparently hazardous procedure through a safer way allows, on the other hand, in a single surgical time, to reduce other risks related to myoma in pregnancy and delivery (Klatsky et al. 2008; Park and Kim 2009), like:

-fertility impairment, miscarriage, placental insertion anomalies, alteration of fetal growth, fetal malpresentation, preterm birth and dystocia for subsequent pregnancy;

-peri-partum hemorrhage at the time of delivery with persistence of fibroid in situ;

-uterine rupture during pregnancy, in case of previous myomectomy.

Especially the latter represents two severe conditions burdened by a high rate of morbidity and mortality. In cases of previous myomectomy, the onset of a uterine rupture at the site of the scar during pregnancy or in labor is an occurrence which happens 0.2%-3.7% in an unpredictable way. According to some authors, uterine rupture is not always related to the length of interval between the fibroid removal and conception, as a matter of fact there is not an ideal interval which completely reset this risk (Gambacorti-Passerini et al. 2016). Moreover, the presence of one or more myomas, especially when they are large and/or intramural located, can hinder myometrium contractility mostly immediately after delivery and afterbirth, facilitating the onset of a life-threatening condition, like postpartum hemorrhage (Davis et al. 1990; Park and Kim 2009).

4. Fibroids' management during delivery

Fibroid removal during cesarean delivery could be an option to promote the physiological hemostatic effect of uterine contractions, making postpartum safer as far as possible, on the basis of modifiable etiological factors. Paradoxically, the most feared complication mentioned for cesarean myomectomy is just massive blood loss, which can happen intra and post-partum and which can be sometimes the reason for a hysterectomy. What lead many obstetricians to opt for fibroids removal during cesarean delivery, rather than leaving myomas in place, is that the recent experience on this surgical procedure has even more shown the possibility to reduce the hemorrhage risk, after taking specific precautions and techniques (Qidwai, Caughey, and Jacoby 2006; Cunningham et al. 2001). Furthermore, a really relevant benefit of cesarean myomectomy rather than myomectomy following pregnancy or the other way around is that a single surgical time significantly reduce costs and anesthetic complications, resulting more feasible in terms of cost and benefits (Awoleke 2013; Lolis, Zikopoulos, and Paraskevaidis 1994)).

According to recent studies performing a myomectomy during a cesarean section instead of on non-pregnant woman should be more suitable and advantageous for the surgeon as well as for the patient herself for several reason (Sparić et al. 2019; Hatırnaz et al. 2020; Tinelli et al. 2014). First of all, considering both that, contrary to what was thought in the past, myoma's dimension does not significantly varies during pregnancy (Muram, Gillieson, and Walters 1980). The volume of the uterine mass growths proportionally to amenorrhea (Shynlova et al. 2009) and fibroid is however relatively smaller than pregnant uterus. Therefore, the uterine incision needed to remove fibroid will be respectively always smaller during cesarean myomectomy rather than on a non-pregnant uterus, favoring wound healing with a smaller scar and so a lower risk of subsequent dehiscence or uterine rupture (Sparić et al. 2017). Moreover, during pregnancy, the gradual hypertrophy and hyperplasia of uterine smooth muscle cells, which develops also around myoma, facilitate the distinction between the lesion and the muscular layer, being more visible the cleavage plane. The easier removal of myoma reflects also the possibility to apply easier specific technique of myomectomy associated with lower risk of blood loss, like intracapsular myoma removing (Tinelli et al. 2014).

So that all this modification inevitably, contrary of what sustained in the past, can be considered the basis to reduce the risk of complications, making easier for the surgeon to use specific technique in order to limit the blood loss and other complications related to cesarean myomectomy.

5. Safety of cesarean myomectomy

The studies reported in literature on cesarean myomectomy are not yet enough satisfactory by a statistical point of view in term of quantity and quality of the evidences in order to definitively establish the safety and feasibility of the procedure. As a matter of fact, scientific databases reported less than thirty observational studies on the subject in question and, to date, no randomized controlled trial. Moreover most of them are retrospective studies and in the current century only six are the prospective studies mentioned in literature, which were respectively conducted by Kwawukume, first, in 2002 (40), Li et al in 2009 (41), Lin et al in 2010 (42), Tinelli et al in 2013 (43) and the two published in 2017 respectively by Valson et al (44) and by Rai and Mishra (45). No further and more recent prospective studies on cesarean myomectomy are reported in literature. With the sole exception of the Li's study, for which a total of 1387 patients were enrolled, 1242 cases and 145 controls, the other prospective studies are characterized by a small sample, well below hundreds (Kwawukume 2002; Li et al. 2009; Lin et al. 2010; Tinelli et al. 2014), mostly the two more recent ones (Rai and Mishra 2017; Valson, Nazer, and Mukerjee 2017). Retrospective studies on cesarean myomectomy, although more numerous, are almost burdened by the same limitation (Pergialiotis et al. 2017) and, for this reason, the latest study conducted by Zhao et al in 2019 stands out among them, having so far the biggest sample of patients, 2565 women all in all, whom 2344 underwent cesarean myomectomy and 221 cesarean delivery alone

(Zhao et al. 2019). The dimension of sample and the nature of the studies are the most strong limitations which allows to let many obstetricians still doubt quality of the study results, although the common findings of all the them seems to direct towards rather than against cesarean myomectomy (Zhao et al. 2019; Pergialiotis et al. 2017; Guler et al. 2020; Nargis, Karim, and Loverine 2019; Sparić et al. 2019, 2018; Senturk et al. 2017; Hatırnaz et al. 2020; Kwawukume 2002; Li et al. 2009; Lin et al. 2010; Tinelli et al. 2014; Rai and Mishra 2017; Valson, Nazer, and Mukerjee 2017).

6. Complications of cesarean myomectomy

Among the most feared intraoperative and/or postoperative complication related to cesarean myomectomy, the massive hemorrhage represents a common condition investigated by researchers. In several studies, obstetrics tried to investigated the real incidence and relevance of intra and post-surgical hemorrage, referring to different variables as: absolute value of blood loss, point of hemoglobin lost, anemia, need of transfusion and number of units transfused, need of hysterectomy. Therefore, the heterogeneous meaning attributed to the concept of massive blood loss represented an interpretational limit in order to have a global view from available of literature. About that highly useful and interesting is the statistical meta-analysis conducted in 2017 by Pergiaolitis et al., who selected all observational studies on cesarean myomectomy published until then, which amounted to only nineteen, in order to highlight the most frequent and significant complications associated (Pergialiotis et al. 2017). They surprisingly reported that, although the 2,301 patients undergoing cesarean myomectomy compared to the cesarean delivery group, 1,599 women, had been exposed to a longer intraoperative duration and to a greater mean hemoglobin drop, this statistically relevant data did not necessarily translate into a greater and significant clinical risk for the patient. In fact, the mean difference of hemoglobin drop reported between the two groups only amounted to 0.25 mg/dL (95% CI 0.06–0.45) and on the other hand the mean difference of duration of the operation was 13.87 minutes (95% CI 4.78–22.95). It could be considered a reasonable unreached of surgical time if compared with the possible benefits deriving from the procedure, without any significant impact on the rapidity of postoperative patient recovery. Moreover, no difference on haemorrhage, transfusion rates, or postoperative fever was reported between the two groups and the prolonged hospitalization recorded in cesarean myomectomy group, though statistically significant, was minimum and scarcely relevant in clinical terms and for patient health all in all (Pergialiotis et al. 2017). This reconfirmed the safety and feasibility of the myomectomy during cesarean delivery already suggested by the findings of a previous meta-analysis conducted in 2013 by Song et al, who reported a longer surgical time and a greater hemoglobin drop, while not achieving statistical significance (Song et al. 2013). Two observational studies conducted in the same year of Pergiaolitis' meta-analysis (Rai and Mishra 2017; Valson, Nazer, and Mukerjee 2017) and further observational studies published in the following years, all retrospective and none prospective as mentioned above, have remarked the relatively safety of the procedure, not reporting a significant increase of blood loss and massive haemorrhage as intra e postoperative complication for caesarean myomectomy. Mostly, not evidenced a considerable worsening of clinical outcomes for this set of patients (Guler et al. 2020; Nargis, Karim, and Loverine 2019; Sparić et al. 2019, 2018; Senturk et al. 2017). As a matter of fact, a common finding is a very low rate of incidence of so-called major complications, as blood transfusion or hysterectomy, this latter almost null (Pergialiotis et al. 2017; Nargis, Karim, and Loverine 2019; Sparić et al. 2019, 2018; Senturk et al. 2017; Hatırnaz et al. 2020). For example Valson et al in their recent prospective study reported on a total of twelve women with fibroids underwent lower segment cesarean section with myomectomy following delivery only three cases, who needed blood transfusion after surgery. Although the several patient-myoma and procedure variables investigated, the authors did not find an exact reason to explain the onset of this complication (Valson, Nazer, and Mukerjee 2017). Instead Pergiaolitis et al, as mentioned above, on the basis of the analysed studies, detected an hemorrhage incidence, as a blood loss major than 1000mL, and rate of

blood transfusion as independent variables, which do not achieve a statistically significance p-value between the cesarean myomectomy group and the cesarean delivery group (Pergialiotis et al. 2017).

7. Blood loss during cesarean myomectomy: clinical strategy to contain hemoglobin drop

Despite its clinical relevance, the greater hemoglobin drop as in fact a constant findings in women underwent myomectomy removal after cesarean delivery, therefore a common trend, mostly in the recent studies, is to focus on possible strategies available during procedure in order to prevent and contain blood loss with the aim to test their real effectiveness. One of the most investigated is the pharmacological strategy, based on the employment of uterotonics, administrated in different ways and in different moments of the surgical procedure, favoring myometrium, especially the perilesional one, contraction in order to avoid atony and so massive bleeding. Already in 1999 Brown et al in his case-controlled study chose to resort to diluted oxytocin, which was directly injected in pseudocapsule of intramural and subserosal myomas of 16 women undergoing cesarean myomectomy and compared the results with a same sample cesarean delivery control group. Although the interesting idea proposed neither mean blood loss, hemoglobin levels and transfusion rate nor other surgical outcomes, as length of hospitalization and febrile illness were significantly different between the two groups (Brown et al. 1999). Later Ehigiegba et al on a sample of 25 pregnant women underwent cesarean myomectomy, experienced the use of intravenous oxytocin administrated in high dose immediately after delivery of the baby. They reported only five patients required blood transfusion and no one needed hysterectomy, therefore the authors concluded that high dose of oxytocin infusion intra and post-operatively could be a safe and wise choice Ehigiegba (Ehigiegba, Ande, and Ojobo 2001). On the contrary Dedes et al claimed that the use of uterotonics does not significantly modify the outcome following cesarean myomectomy rather than cesarean delivery alone, shifting the focus on other variables possibly related to peri-operative complications, as myoma and patients' characteristics (Dedes et al. 2017). In the more recent prospective study conducted by Rai and Mishra a possible solution used to prevent or minimize bleeding at myoma bed immediately after myoma removal during cesarean delivery is the local infiltration of dilute adrenaline, managing to achieving good results with a 20% of incidence of hemorrhage in the study group and no hysterectomy required at all. The data reported has been affected by the three cases of atonic peripartum hemorrhage in cesarean myomectomy group, treated with stepwise devascularization until adequate bleeding control (Rai and Mishra 2017). Considering this eventuality it is advisable to perform myomectomy always after baby extraction and afterbirth, even when the myoma is located anterior at the lower uterine segment, even if this let surgeon to opt for an unusual uterine incision as the longitudinal and/or corporal one, because in case of massive hemorrhage is fundamental to have clearly visible anatomical landmarks for proper and safe devascularization. About that several surgical techniques have been described recently for blood loss sparing during cesarean myomectomy. When a case on the basis of patient's and myoma's characteristics could be more exposed to massive blood loss is possible temporary block the uterine arteries bilaterally both using tourniquet and ligating or clamping them with a soft-ended instrument. Sapmaz et al published a randomized prospective study on a sample of 70 women in order to compare the effectiveness of the two methods mentioned above during cesarean section. They showed no statistically significant differences in term of perioperative blood loss between the use of tourniquet and the bilateral ascending uterine artery ligation, however it emerged that only this latter strategy ensured a good blood loss control even in the postoperative period, so that in the view of the authors it should be prefer (Sapmaz, Celik, and Altungul 2003). Instead Kwawukume did not evidence statistically proved benefit in the use of tourniquet tied both around the uterine arteries and ovarian vessels during cesarean myomectomy in comparison with cesarean alone in terms of blood sparing (Kwawukume

2002). Another possible choice is the electrocautery of myoma at the time of cesarean myomectomy as successfully experimented by Cobellis et al in 2002 on two cases of multiple fibroids of little or middle size (Cobellis et al. 2002). Moreover Incebyik et al. proposed the use of electro surgery associated to tourniquet and oxytocin infusion as bleeding prevent strategy for cesarean myomectomy. According to this approach first tourniquet is temporary applied at the cervico-istmic level, passing through the broad ligament, so electrocautery is employed for myoma removal and at the end of the uterine suture tourniquet is removed; postoperatively intravenous oxytocin is administered up to reach adequate uterine contraction. The results were encouraging and only two out of 16 patients required blood transfusion (Incebiyik et al. 2014).

8. Cesarean myomectomy outcomes

Assessing the intra and post-operative complication of cesarean myomectomy led many authors to explore the possible variables of each cases, which could affect the outcome of the procedure in order to have a clearly and wise evaluation of the case preoperatively, eventually guiding the choice to do or not myoma removal at the time of cesarean delivery. In these terms a really interesting study is the retrospective one conducted by Dedes et al in 2017, in which emerges that the significant increase of blood loss, meant as ≥500mL (p=0.02), rather that associated with the cesarean myomectomy procedure itself is related to large myoma size of ≥5cm, which, according to the results reported, is linked to this complication independent of a concomitant myomectomy or not (Dedes et al. 2017). This overturns at the same time both the idea to avoid cesarean section anyway and the idea of the absolute safety to not treat myoma during cesarean section. Maybe in this case removing myoma with a correct and wise technique could be the safer choice in spite of the risk? And if Zhao et al remarks the augmentation of risk of bleeding with myoma larger than 5cm maximum of diameter (Zhao et al. 2019), on the other hand Ehigiegba et al concluded that, employing the right technical precautions, even in case of big myoma cesarean myomectomy could be a safe option for the patient and for the surgeon (Ehigiegba, Ande, and Ojobo 2001). The question of the impact of the size of myoma on safety of cesarean myomectomy has been also well investigated by Kwon et al in their retrospective study of 2014, in which enrolled 65 patients underwent myomectomy versus 96 controls and, using the threshold of 5cm to differentiate the myoma labelled as large or not, did not find any statistically significant differences in consideration of the mean hemoglobin change, operative time and length of hospitalization (Kwon et al. 2014). Another ancient doubt is about the possible affection of the position of myoma on a greater incidence of bleeding, as a matter of fact in the past, while pedunculated or subserosal myoma removal was considered relatively safe during cesarean delivery, not the same point of view there was for the intramural lesions because of the feared relationship hypotized between the larger myometrium wound following removal and the incidence of atony and so massive blood loss. Actually, all the observational study up to nowadays do not report a statistical correlation between this complication and myoma location (Pergialiotis et al. 2017). On the other hand, is not well explored the real risk linked to a multiple myomectomy during cesarean section, mostly because almost the totality of the observational study excluded patients affected by more than one myoma, especially large and with different position, in order to prevent worst outcome. Dedes et al tried to dissipate this doubt and effectively found a greater incidence of massive blood loss in multiple cesarean myomectomies rather than the removal of single pedunculated or subserosal and intramural leiomyomas during cesarean section (OR respectively of 4.7 and 1.1.-1.4, 95% CI 0.8-26.3) (Dedes et al. 2017). The interpretation of these results could debatable in relation to the too much low threshold employed to define hemorrhage, 500mL, but to date are still one of the studies of reference on this question. None of the observational studies published evidence a significant relationship between the augmentation of intra and postoperative surgical and clinical risk and characteristics of the patient, with the exception of Dedes et al, who registered a significant postoperative drop in hemoglobin in women ≥40 years of age (OR 2.4 CI 95% 1.0–5.4, p=0.04) (Dedes et al. 2017). However, this

remains a controversial data which is not supported by other studies and so it could be considered not useful for practical implications.
Since the first attempt of cesarean myomectomy a technical constant, as reported above, is the need to postpone the myoma removing after baby extraction and placental expulsion not only for the anatomical reason already exposed, but also to ensure good neonatal outcomes, which in every study published are not affected in any way by the procedure, and at the same time to eventually manage first placenta related complications without getting worse maternal outcomes.

9. Surgical techniques to remove fibroids during cesarean section

On the other hand, contrary to Bonney's time, when gravid uterus used to be incised longitudinally (Jauniaux and Khan 2014), the recent attempts of cesarean myomectomy have been done in line with the more current and safer indications for cesarean section, according to which it should be preferable, when it is possible, a transverse incision of the inferior segment of the uterus to access to the uterine cavity for baby extraction. This consideration is fundamental for a preliminary evaluation, because the aim of the surgeon should be to try to limit the incision sites for myoma or myomas removing, using in all case is possible the incision just done. So that the myoma location predict the eventual necessity of further uterine incision over the extraction one and so, because of the number of the scars it could be needed, it could be a predictor of major risk of blood loss. Considering that anterior isthmic myomas could be the most eligible to cesarean myomectomy. Instead when additional incisions are needed different approach can be considered. In particular many of the different studies mentioned above do not the type of procedure employed to removal myoma and, when the incision of the uterine segment is not used, the conventional choice is a serosal myomectomy, which is performed through an incision over the site of myoma by the external face of the uterine wall, from which myoma is enucleated and then the dead space is closed. On the contrary recently a new and controversial technique has been proposed in a retrospective single institution study by Hatırnaz et al, the so called "endometrial myomectomy", which would be a less invasive and safer rather than the conventional fashion. As a matter of fact it is characterized by a small trans-endometrial incision at the site of myoma, performed after a quick and accurate visual and palpatory evaluation of location of the lesion, through which myoma is removed within the pseudocapsule; uterine breach is sutured only when the defect site is larger than 3cm with absorbable suture (Hatırnaz et al. 2020). The two main benefits of this procedure are: the absence of further scar on uterine surface and so the reduced risk of adhesion onset; the very small incision on the inner uterine surface which should be associated with a statistical significant lower intraoperative bleeding rather than serosal myomectomy (209mL versus 375mL, p=0.001) without at the same time the concrete remotely risk of intracavity adhesions or Ashermann syndrome (Hatırnaz et al. 2020). In spite of these considerations the endometrial approach has been criticized for several reason, like the possible affection of endometrial role in reproductive process (52) or the consequently higher risk of abnormal placentation (Sparić et al. 2017), but no evidences are available to date. Much more distinctive is the disagreement of Tinelli about the fibroid removal during cesarean myomectomy (Sparić et al. 2017), remarking the fundamental role of a "myoma pseudocapsule sparing" approach, described first by himself in 2014 (Tinelli et al. 2014). In fact, according to the biological mechanism that guide a correct wound healing in order to have better outcome especially in a so controversial procedure like cesarean myomectomy should be fundamental opting for the safest and optimal surgical strategy. Actually, scientific community has discovered the fundamental role of pseudocapsule in the management of fibroids, demonstrating that a preservation of the latter represents a way to preserve all the structure fundamental for a correct healing, like vessels, neurotransmitters, and neuropeptides, involved in inter-intracellular signalling. In order to correctly perform an intracapsular myoma removing during cesarean section according to Tinelli et al. it

is essential to do a sharp and exact dissection of the pseudocapsule and then to do an accurate approximation of the edges of the myometrium with a complete closure of all dead space (Tinelli et al. 2014). Applying this approach interesting really good outcomes has been registered in literature, in fact the 2014 prospective study conducted by Tinelli reported a mean hemoglobin decline lower in intracapsular cesarean myomectomy group rather than in cesarean delivery without myomectomy group (respectively 1.5 versus 1.6) (Tinelli et al. 2014), a result which is totally against the trend of the remaining observational study, with the only exception of Kwon et al (Kwon et al. 2014). Huang S.Y. et al fused the novel trans endometrial cesarean myomectomy technique proposed by Hatırnaz et al with the pseudocapsule sparing approach of Tinelli et al, demonstrating that it could be a safe treatment option without long-term adverse surgical outcomes and with better obstetric outcomes of subsequent pregnancy (Huang et al. 2018).

Another variable of cesarean myomectomy technique affecting clinical and surgical outcomes is the way chosen to obliterate the myometrium breach after myoma removal. As a matter of fact, mostly when an additional incision is needed to do or complete myomectomy, all the dead space have to be completely closed, otherwise that site can become full of blood and seat of hematoma with all the complications related. To date, we are not studies which investigated the best technique, instead each author reported several ways to closure according to the surgeon's experience. As can be seen from the various studies in the literature, fibroid bed can be sutured, beginning from the bottom, with one or more layers of interrupted Vicryl suture, generally choosing the size of needle on the basis of the myoma bed, up to a complete myometrial wall closure and with the aim to achieve haemostasis. For the superficial layer the surgeon can opt for continuous suture, introflexing or not, or simply for X stiches (36,39,43,44).(Sparić et al. 2018; Hatırnaz et al. 2020; Tinelli et al. 2014; Rai and Mishra 2017).

10. Conclusions

For a long time, it has been common and shared thinking that myoma should not be surgically treated in pregnant women at the time of birth through cesarean section in order to avoid complications for the patient. Nowadays the increasingly evidences reported in literature are gradually subvert the obstetrician point of view, leading to a concrete revaluation of this procedure.

Currently, the lack of randomized control trials make difficult to absolutely state the safety of the procedure and at the same time to definitively standardize the indications, but the several conclusions of all the observational studies available up to now surely give us elements to guide the choice to do cesarean myomectomy in specific set of women. Moreover, besides the clinical feasibility of the procedure itself, authors' experience and judgment agree with the evidences about the importance of the experience of the operator both to make safer the surgical procedure and to have intra-operative and after-surgery outcomes. However, the type technique should be preferred and then informative counselling and/or consensus complete of higher quality data than those currently available are topics that need standardization to make cesarean myomectomy safer for the patients and for the operator at the same time.

Therefore, we can conclude that a knowledge of all the aspects of this apparently controversial surgical procedure plus a consolidated surgical experience can give the instrument to offer an additional safe option of treatment, which to date cannot longer be avoided a priori, aiming to a tailored treatment for each patient.

11. References

- Awoleke, JO. 2013. 'Myomectomy During Caesarean Birth in Fibroid-Endemic, Low-Resource Settings - PubMed'. Obstet Gynecol Int, 520834.
- Bellieni, Carlo. 2016. 'The Best Age for Pregnancy and Undue Pressures.' Journal of Family & Reproductive Health 10 (3): 104–7.
- Brown, D., H. M. Fletcher, M. O. Myrie, and M. Reid. 1999. 'Caesarean Myomectomy - A Safe Procedure. A Retrospective Case Controlled Study'. Journal of Obstetrics and Gynaecology 19 (2): 139–41. https://doi.org/10.1080/01443619965435.
- Cobellis, Luigi, Pasquale Florio, Luigi Stradella, Eugenio De Lucia, Enrico M. Messalli, Felice Petraglia, and Giovanni Cobellis. 2002. 'Electro-Cautery

of Myomas during Caesarean Section - Two Case Reports'. European Journal of Obstetrics and Gynecology and Reproductive Biology 102 (1): 98–99. https://doi.org/10.1016/S0301-2115(01)00572-3.

- Cooper, Natalie Paloma, and Stanley Okolo. 2005. 'Fibroids in Pregnancy - Common but Poorly Understood'. Obstetrical and Gynecological Survey. Obstet Gynecol Surv. https://doi.org/10.1097/01.ogx.0000154688.02423.68.
- Cunningham, FG, NF Gant, KJ Levenok, LC Gilstrap, JC Hauth, and Wenstrom KD. 2001. Abnormalities of the Reproductive Tract. Edited by Williams Obstetrics. 21st ed. Vol. 930. New York: McGraw Hill;
- Davis, Jane L., Shibani Ray-Mazumder, Calvin J. Hobel, Karin Baley, and Deborah Sassoon. 1990. 'Uterine Leiomyomas in Pregnancy: A Prospective Study'. Obstetrics and Gynecology 75 (1): 41–44.
- Dedes, I., L. Schäffer, R. Zimmermann, T. Burkhardt, and C. Haslinger. 2017. 'Outcome and Risk Factors of Cesarean Delivery with and without Cesarean Myomectomy in Women with Uterine Myomatas'. Archives of Gynecology and Obstetrics 295 (1): 27–32. https://doi.org/10.1007/s00404-016-4177-8.
- Ehigiegba, A. E., A. B. Ande, and S. I. Ojobo. 2001. 'Myomectomy during Cesarean Section'. International Journal of Gynecology and Obstetrics 75 (1): 21–25. https://doi.org/10.1016/S0020-7292(01)00452-0.
- Exacoustòs, Caterina, and Paolo Rosati. 1993. 'Ultrasound Diagnosis of Uterine Myomas and Complications in Pregnancy'. Obstetrics and Gynecology 82 (1): 97–101. https://doi.org/10.1016/0020-7292(94)90784-6.
- Gambacorti-Passerini, Zita, Alexis C. Gimovsky, Anna Locatelli, and Vincenzo Berghella. 2016. 'Trial of Labor after Myomectomy and Uterine Rupture: A Systematic Review'. Acta Obstetricia et Gynecologica Scandinavica. Taylor and Francis Ltd. https://doi.org/10.1111/aogs.12920.
- Guler, Askın Evren, Zeliha Çiğdem Demirel Guler, Mehmet Ferdi Kinci, and Muhittin Tamer Mungan. 2020. 'Myomectomy During Cesarean Section: Why Do We Abstain From?' Journal of Obstetrics and Gynecology of India 70 (2). https://doi.org/10.1007/s13224-019-01303-6.
- Hartmann, Katherine E., Shannon K. Laughlin, Donna D. Baird, David A. Savitz, and Amy H. Herring. 2009. 'Prevalence of Uterine Leiomyomas in the First Trimester of Pregnancy: An Ultrasound-Screening Study'. Obstetrics and Gynecology 113 (3): 630–35. https://doi.org/10.1097/AOG.0b013e318197bbaf.
- Hatırnaz, Şafak, Oğuz Güler, Alper Başbuğ, Mehmet Bilge Çetinkaya, Mine Kanat-Pektaş, Kadir Bakay, Samettin Çelik, et al. 2020. 'A Comparative Multicentric Study on Serosal and Endometrial Myomectomy During Cesarean Section: Surgical Outcomes'. Journal of Investigative Surgery. https://doi.org/10.1080/08941939.2020.1725188.
- Huang, S. Y., S. W. Shaw, S. Y. Su, W. F. Li, H. H. Peng, and P. J. Cheng. 2018. 'The Impact of a Novel Transendometrial Approach for Caesarean Myomectomy on Obstetric Outcomes of Subsequent Pregnancy: A Longitudinal Panel Study'. BJOG: An International Journal of Obstetrics and Gynaecology 125 (4): 495–500. https://doi.org/10.1111/1471-0528.14798.
- Incebiyik, Adnan, Neşe Gul Hilali, Aysun Camuzcuoglu, Mehmet Vural, and Hakan Camuzcuoglu. 2014. 'Myomectomy during Caesarean: A Retrospective Evaluation of 16 Cases'. Archives of Gynecology and Obstetrics 289 (3): 569–73. https://doi.org/10.1007/s00404-013-3019-1.
- Jauniaux, Eric, and Khalid S Khan. 2014. 'Caesarean Myomectomy: Victor Bonney Reports the First Case in 1913'. BJOG: An International Journal of Obstetrics & Gynaecology 121 (2): 193–193. https://doi.org/10.1111/1471-0528.12548.
- Klatsky, Peter C., Nam D. Tran, Aaron B. Caughey, and Victor Y. Fujimoto. 2008. 'Fibroids and Reproductive Outcomes: A Systematic Literature Review from Conception to Delivery'. American Journal of Obstetrics and Gynecology. Am J Obstet Gynecol. https://doi.org/10.1016/j.ajog.2007.12.039.
- Kwawukume, E. Y. 2002. 'Myomectomy during Cesarean Section'. International Journal of Gynecology and Obstetrics 76 (2): 183–84. https://doi.org/10.1016/S0020-7292(01)00586-0.
- Kwon, Dam Hye, Ji Eun Song, Kyung Ran Yoon, and Keun Young Lee. 2014. 'The Safety of Cesarean Myomectomy in Women with Large Myomas'. Obstetrics & Gynecology Science 57 (5): 367. https://doi.org/10.5468/ogs.2014.57.5.367.
- Laughlin, Shannon K., Jane C. Schroeder, and Donna Day Baird. 2010. 'New Directions in the Ep-

idemiology of Uterine Fibroids'. Seminars in Reproductive Medicine. Semin Reprod Med. https://doi.org/10.1055/s-0030-1251477.

- Li, Hui, Juan Du, Liangyi Jin, Zhan Shi, and Mingying Liu. 2009. 'Myomectomy during Cesarean Section'. Acta Obstetricia et Gynecologica Scandinavica 88 (2): 183–86. https://doi.org/10.1080/00016340802635526.
- Lin, Jui Yu, Wen Ling Lee, Peng Hui Wang, Man Jung Lai, Wen Hsun Chang, and Wei Min Liu. 2010. 'Uterine Artery Occlusion and Myomectomy for Treatment of Pregnant Women with Uterine Leiomyomas Who Are Undergoing Cesarean Section'. Journal of Obstetrics and Gynaecology Research 36 (2): 284–90. https://doi.org/10.1111/j.1447-0756.2009.01158.x.
- Lolis, D., K. Zikopoulos, and E. Paraskevaidis. 1994. 'Surgical Management of Leiomyomata during Pregnancy'. International Journal of Gynecology and Obstetrics. Int J Gynaecol Obstet. https://doi.org/10.1016/0020-7292(94)90026-4.
- Muram, David, Martin Gillieson, and Jack H. Walters. 1980. 'Myomas of the Uterus in Pregnancy: Ultrasonographic Follow-Up'. American Journal of Obstetrics and Gynecology 138 (1): 16–19. https://doi.org/10.1016/0002-9378(80)90005-8.
- 'Myomas and Reproductive Function'. 2004. Fertility and Sterility 82 (SUPPL. 1). https://doi.org/10.1016/j.fertnstert.2004.05.061.
- 'Myomas and Reproductive Function'. 2006. Fertility and Sterility 86 (5 SUPPL.). https://doi.org/10.1016/j.fertnstert.2006.08.026.
- Nargis, Nazlima, Md Iqbal Karim, and Salma Loverine. 2019. 'Evaluation of Safety of Caesarean Myomectomy: A Prospective Study'. Bangladesh Critical Care Journal 7 (1): 40–43. https://doi.org/10.3329/bccj.v7i1.40765.
- Park, Byung Joon, and Yong Wook Kim. 2009. 'Safety of Cesarean Myomectomy'. Journal of Obstetrics and Gynaecology Research 35 (5): 906–11. https://doi.org/10.1111/j.1447-0756.2009.01121.x.
- Pergialiotis, Vasilios, Ilias Sinanidis, Ioannis Evangelos Louloudis, Theodoros Vichos, Despina N. Perrea, and Stergios K. Doumouchtsis. 2017. 'Perioperative Complications of Cesarean Delivery Myomectomy: A Meta-Analysis'. Obstetrics and Gynecology. Lippincott Williams and Wilkins. https://doi.org/10.1097/AOG.0000000000002342.
- Qidwai, G. Iram, Aaron B. Caughey, and Alison F. Jacoby. 2006. 'Obstetric Outcomes in Women with Sonographically Identified Uterine Leiomyomata'. Obstetrics and Gynecology 107 (2): 376–82. https://doi.org/10.1097/01.AOG.0000196806.25897.7c.
- Rai, A, and MG Mishra. 2017. 'A Study on Safety and Feasibility of Caesarean Myomectomy: At a Private Institute'. Int J Reprod Contracept Obstet Gynecol, 2765–70.
- Sapmaz, E, H Celik, and A Altungul. 2003. 'Bilateral Ascending Uterine Artery Ligation vs. Tourniquet Use for Hemostasis in Cesarean Myomectomy. A Comparison'. J Reprod Med 48: 950–54.
- Senturk, Mehmet Baki, Mesut Polat, Ozan Doğan, Çiğdem Pulatoğlu, Oğuz Devrim Yardlmcl, Resul Karakuś, and Ahter Tanay Tayyar. 2017. 'Outcome of Cesarean Myomectomy: Is It a Safe Procedure?' Geburtshilfe Und Frauenheilkunde 77 (11): 1200–1206. https://doi.org/10.1055/s-0043-120918.
- Shynlova, Oksana, Prudence Tsui, Shabana Jaffer, and Stephen J. Lye. 2009. 'Integration of Endocrine and Mechanical Signals in the Regulation of Myometrial Functions during Pregnancy and Labour'. European Journal of Obstetrics and Gynecology and Reproductive Biology 144 (SUPPL 1): S2. https://doi.org/10.1016/j.ejogrb.2009.02.044.
- Song, Dianrong, Wei Zhang, Mark C. Chames, and Jie Guo. 2013. 'Myomectomy during Cesarean Delivery'. International Journal of Gynecology and Obstetrics. John Wiley and Sons Ltd. https://doi.org/10.1016/j.ijgo.2013.01.021.
- Sparic, R, L Nejkovic, D Mutavdzic, A Malvasi, and A Tinelli. 2014. 'Conservative Surgical Treatment of Fibroids'. Acta Chir Iugosl 61: 11–66.
- Sparić, Radmila. 2014. 'Uterine Myomas in Pregnancy, Childbirth and Puerperium'. Srpski Arhiv Za Celokupno Lekarstvo 142 (1–2): 118–24. https://doi.org/10.2298/SARH1402118S.
- Sparić, Radmila, Saša Kadija, Aleksandar Stefanović, Svetlana Spremović Radjenović, Ivana Likić Ladjević, Jela Popović, and Andrea Tinelli. 2017. 'Cesarean Myomectomy in Modern Obstetrics: More Light and Fewer Shadows'. Journal of Obstetrics and Gynaecology Research. Blackwell Publishing. https://doi.org/10.1111/jog.13294.
- Sparić, Radmila, Antonio Malvasi, Saša Kadija, Aleksandar Stefanović, Svetlana Spremović Radjenović, Jela Popović, Aleksandra Pavić, and Andrea Tinelli. 2018. 'Safety of Cesarean Myomectomy in Women with Single Anterior Wall and Lower Uterine Segment Myomas'. Journal of Maternal-Fetal and Neonatal Medicine 31 (15): 1972–

75.
https://doi.org/10.1080/14767058.2017.1333096.

- Sparić, Radmila, Dimitrios Papoutsis, Zoran Bukumirić, Saša Kadija, Svetlana Spremović Radjenović, Antonio Malvasi, Milan Lacković, and Andrea Tinelli. 2019. 'The Incidence of and Risk Factors for Complications When Removing a Single Uterine Fibroid during Cesarean Section: A Retrospective Study with Use of Two Comparison Groups'. Journal of Maternal-Fetal and Neonatal Medicine.
https://doi.org/10.1080/14767058.2019.1570124.
- Svigos, JM, JS Robinson, and R Vigneswaran. 2006. 'High Risk Pregnancy: Management Options'.
- 'Te Linde's Operative Gynecology; Mattingly RF 1977 - Google Scholar'. n.d. Accessed 10 July 2020. https://scholar.google.com/scholar?hl=it&as_sdt=0%2C5&q=Te+Linde's+Operative+Gynecology%3B+Mattingly+RF+1977&btnG=.
- Tinelli, Andrea, Malvasi, Antonio, Mynbaev, Ospan A, Barbera, Antonio, Perrone, Emanuele, Guido, Marcello, Kosmas, Ioannis and Stark, Michael. 2014. 'The Surgical Outcome of Intracapsular Cesarean Myomectomy. A Match Control Study'. Journal of Maternal-Fetal and Neonatal Medicine 27 (1): 66–71. https://doi.org/10.3109/14767058.2013.804052.
- Valson, H, T Nazer, and S Mukerjee. 2017. 'Myoma in Pregnancy and Outcome after Cesarean Myomectomy'. Int J Reprod Contracept Obstet Gynecol 6: 2267–71.
- Zhao, R, X Wang, L Zou, and W Zhang. 2019. 'Outcomes of Myomectomy at the Time of Cesarean Section Among Pregnant Women With Uterine Fibroids: A Retrospective Cohort Study'. BioMed Research International 2019. https://doi.org/10.1155/2019/7576934.