Review Article

Likelihood of Accomplishing an In-Patient Hysteroscopic Myomectomy in a One-Step Procedure: A Systematic Review and Meta-Analysis

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Purpose. To assess the feasibility rate of one-step hysteroscopic myomectomy according to the technique adopted. Methods. In July 2016, PubMed, ClinicalTrials.gov, SCOPUS, Scielo, and AJOL databases were used for searching references. Series of in-patient hysteroscopic myomectomies reporting success rate in only one-step procedure, categorization of submucous fibroids, explanation of the surgical technique, and description of patients were considered eligible for meta-analysis (retrospective, prospective randomized studies). Two authors extracted the data. Rate of myomectomies accomplished in only a surgical step and rate of intraoperative complications were extracted per protocol. A modified GRADE score was used for quality assessment. Random-effect models were already assumed. Mean rates were compared among subgroups. Results. One thousand two hundred and fifty-seven studies were screened and 241 of these were read for eligibility. Seventy-eight series were included in qualitative synthesis and 24 series were included in quantitative synthesis. Wide heterogeneity was found. In series with <50% of G2 myomas treated, the slicing technique feasibility rate was 86.5% while techniques for enucleating the deep portion of the myomas showed a feasibility rate of 92.3% (p < 0.001). In series with ≥50% of G2 myomas treated, the slicing technique feasibility rate was 70.6% while techniques for enucleating the deep portion of myomas showed a feasibility rate of 88.4% (p < 0.001). Complications were significantly lower for alternative techniques to the classical slicing. Conclusion. In case of submucous myomas with intramural development, the slicing technique was correlated with a lower rate of in-patient hysteroscopic myomectomies accomplished in a one-step procedure and a higher complications rate.

1. Introduction

Uterine myomas, also called leiomyomas or fibroids, are benign, monoclonal tumours developing from the smooth muscle cells of the myometrium. Myomas represent the most common pathology of the female genital tract causing abnormal uterine bleeding, pelvic pain, and infertility [1–3]. Although it has been estimated that the majority of uterine fibroids is asymptomatic, submucous myomas account for 5–10% of all fibroids and are correlated with the most severe symptomatology [4, 5].

The advent of endoscopic surgery has revolutionized the treatment of submucous myomas, offering a valid alternative to hysterotomy or hysterectomy. Nowadays, the resectoscopic myomectomy is considered the gold standard in the treatment of submucous myomas [6]. Neuwirth in 1976 described the first “excision of submucous fibroids with hysteroscopic control,” performed by classical slicing technique. Although this new surgical approach was a breakthrough in the treatment of submucous myomas, the authors recommended resectoscopic myomectomy be performed only by expert endoscopic surgeons [7, 8]. Indeed, the main limit in performing hysteroscopic myomectomy has always been represented by the intramural component of submucous myomas, as it is responsible for unsatisfactory surgical outcomes, intraoperative complications, and need
for repeated procedures [9, 10]. The difficulty to manage submucous myomas with a deep myometrial development was well described and demonstrated by Wamsteker in 1993, conceiving a new classification—still used today—based on the amount of intramural component of submucous myomas. The authors suggested limiting the treatment of deeper submucous myomas only in selected cases because it correlated with high risk of repeated procedures [9].

Over the last decades, there has been a rapid evolution in the hysteroscopic approach for the treatment of submucous myomas, driven by the technological progress that has offered a wide range of performing instruments to the surgeons. At the same time, several techniques for in-patient hysteroscopic myomectomy have been proposed aimed at ensuring the safe and effective removal of submucous myomas. Among them, in order to minimize the need of repeated procedures, the authors conceived techniques to accomplish the treatment in only one surgical time [11], as multiple treatments can cause physical and mental stress for both surgeons and patients, along with a higher surgical risk [12]. To date, a comprehensive analysis on the success rate of in-patient hysteroscopic myomectomy in a single treatment, according to the technique applied, is lacking in scientific literature.

The aim of this systematic review and meta-analysis was to assess the feasibility of the one-step in-patient hysteroscopic myomectomy according to the technique adopted. Moreover, as a secondary outcome, the rate of intraoperative complications recorded in the selected clinical series, when reported, was also meta-analysed to assess the safety of each technique.

2. Methods

2.1. Protocol. The review was reported following the PRISMA guidelines for reporting systematic reviews and meta-analyses [13] and registered in the PROSPERO database (registration number: CRD42017067543).

Prospective or retrospective clinical series, cohorts and case control studies, and randomized controlled trials were considered eligible for the review. Medical papers reporting feasibility of the one-step procedure, the technique by which the in-patient hysteroscopic myomectomies were performed, as well as the characteristics of patients and myomas treated were considered for the meta-analysis. If available, additional information such as myoma size, number/rate of cases with multiple myomas in the series, administration of gonadotropin releasing hormone analogue (GnRHa), or other presurgical therapies and intraoperative complications were also recorded. In the absence of information, the corresponding authors, if available, were contacted to provide them.

2.2. Literature Search and Review. A scientific literature search was performed in July 2016 and was conducted in main databases including PubMed, ClinicalTrials.gov (http://www.clinicaltrials.gov), SCOPUS, Scielo, and AJOL (African Journals Online) search engines, using combinations of the following keywords: “operative hysteroscopy” AND “myomectomy,” “operative hysteroscopy” AND “complications,” “hysteroscopic myomectomy,” “hysteroscopic complication” AND “myomectomy.” No language limits were set. In order to better categorise and analyse the one-step feasibility rate according to the kind of myomas treated, only medical papers reporting submucous myomas categorized according to the Wamsteker Classification (G0, completely intracavitary, pedunculated myoma, with no intramural extension; G1, submucous myoma with ≤50% intramural extension; and G2, submucous myoma with at least 50% intramural extension) [9] were considered as eligible. Therefore, clinical series published before 1993 were excluded from the review.

Medical papers were assessed in a multistep procedure as follows. Titles and abstracts were evaluated, and duplicates were discarded. Case reports, reviews, overviews, letters, guidelines, meta-analyses, and surveys with questionnaires were not considered eligible for meta-analysis. Studies about in-office hysteroscopic myomectomy were also excluded due to the different settings which could bias the comparison with in-patient procedures. Additional articles incidentally found during the full-text research and references discovered by reading the selected medical papers were also introduced in the meta-analysis database. English, French, Spanish, Portuguese, and Italian full-text articles were read in original languages. Other medical papers were translated in English or Italian.

2.3. Data Extraction. Feasibility rate of one-step in-patient hysteroscopic myomectomy was the main effect size assessed and was defined as the rate of cases in which in-patient hysteroscopic myomectomy was accomplished in only one surgical procedure, entirely removing submucous myomas treated. As a secondary effect size, the rate of complications found during the hysteroscopic procedure or immediately after the surgery was calculated. Long-term complications were not considered.

Rates were calculated per protocol and the rate of the event was assessed as a binomial casual variable. Two authors (I. U. and F. A.) performed data extraction at the same time by reading the texts altogether. Any disagreement between them over the eligibility of specific studies was resolved through discussion with a third author (B. V.). In case of complications or feasibility rates of 0% or 100%, the rate of rare events was calculated applying the rule of Quigley et al. (i.e., 2/5n in case 0 events occur in order to estimate rare events, where n is the number of observations in the sample) [14].

Missing information was asked to corresponding authors by e-mail or phone call.

2.4. Quality Assessment. The quality assessment of the series was evaluated based on the feasibility reported in accomplishing the in-patient hysteroscopic myomectomy in only one-step procedure. Two authors (F. A. and I. U.) provided the quality assessment altogether, and disagreements were resolved by discussion with a third author (B. V.). A quality
score system in accordance with the GRADE approach [15] was used for assessing the quality of each series included in meta-analysis. Considering that studied effect size was expressed as a rate, the GRADE score was modified assuming additional sources of bias.

Clinical series were scored as follows:

(i) 4 for randomized controlled trial
(ii) 3 for prospective studies
(iii) 2 for retrospective studies
(iv) 1 for small series

Complications in operative hysteroscopy are rare [16–18] but when trying to avoid them, they can influence the one-step procedure feasibility [19]. Some small series could not report complications, while other small series could report complications, leading to underestimation or overestimation of the complications rate. Therefore, during the selection of the clinical series, it was considered that the minimal limit of cases for including a small series was the one with at least a complication. Nevertheless, if other small series with the same number of patients enrolled were found but with no complications reported, they also were included in meta-analysis. This choice was given to balance the overestimation or underestimation of complications rates in small series. Small series were considered if characterised by a total of 14 cases or less.

The quality assessment downgraded the small series even when they were a part of other kind of studies (i.e., arms of randomized controlled trials or observational studies).

Additional sources of biases were considered, and the score was downgraded or upgraded as follows:

(i) Surgical technique description was not clearly available (−1: poorly explained, +1 clearly explained).
(ii) Feasibility was not clearly reported (−1: poorly reported, +1 clearly reported).
(iii) The characteristics of patients were not clearly described (−1: poorly described, +1 clearly described).
(iv) Need of estimating missing data (−1: yes; +1: no) in the feasibility if the reported rate of success in one-step myomectomy was 100% or 0% (need to estimate rare events) or missing mean myoma size as mean diameter.
(v) Sample of ≤100 cases (−1: yes; +1: no).

To get the overall quality score, this bias score was added to the one given according to the type of study as previously described. A score of more than 4 was considered to assess good quality series.

2.5. Statistical Analysis. Data were extracted from selected studies and combined applying a random-effect model [20], which incorporates heterogeneity of effects. Heterogeneity of studies was evaluated by the Cochrane Q test and reported as $I^2$ statistics, which describe the percentage of total variation across studies which is due to heterogeneity rather than chance [21]. Heterogeneity was considered significant if $p < 0.10$ and $I^2$ was more than 50%. Begg and Egger’s tests [22, 23] were used to test for publication bias. In a sensitivity analysis, the influence of individual studies on pooled estimates was assessed using Tobias’ method [24]. If the point estimate with one study omitted lay outside the confidence interval (CI) of the overall estimate of all trials, the study was indicated as having excessive influence.

2.6. Subgroup Analyses. On the basis of the main aim of this meta-analysis and on what already reported by Wamsteker et al. about difficulties of treating the intramural component of submucous myomas [9], the series were arranged in subgroups taking into consideration the technique for removing the myomas and the proportion of the G2 myomas reported in the series (more or equal to 50% or less than 50%).

The z-statistic (one-tailed) was applied to compare the subgroups effect sizes (mean feasibility and mean rate of complications) in subgroups. A $p < 0.05$ was set as significant.

The calculations were made by using StatsDirect Software, version 2.7.2 (Cheshire, UK, 2008).

3. Results

The steps of study selection are reported in Figure 1 (PRISMA flow diagram). During the literature review, 2472 references were found. There were 1215 duplicate references, which were removed by using the EndNote tool. After removing duplicates, 1257 references were screened by reading the titles and abstracts, looking for clinical series of in-patient operative hysteroscopies. Additional duplicate references were removed manually. Five hundred and ninety-four studies were reassessed focusing on operative hysteroscopies, excluding out-patient procedures. Two hundred and seventy-nine studies were reassessed looking for hysteroscopic myomectomies even in subgroups. In this step, the surveys based on questionnaires were also excluded. Twelve studies were removed from the database because they were published before 1993. Full texts of 222 studies were searched. Looking for full-texts, 19 more studies were found and were added to the database. The studies in the database were carefully checked for eligibility. Ten studies were discarded because after the full-text reading, it was understood that they were not clinical series on hysteroscopic myomectomy, while 18 other studies were discarded because the full texts were not available. Of the 213 studies, 11 were discarded because 10 of them reported duplicate cases and 1 study reported a series with duplicate cases in one arm and insufficient information in the other arm. One hundred and thirty-nine studies were discarded because they did not meet the inclusion criteria. Sixty-three references were eligible for the review [10, 12, 17, 25–50, 51–84] (Table 1). Thirteen studies reported two or more arms. Each arm was able to be meta-analysed for feasibility. Therefore, 78 effect sizes were assessed. Instead, 73 series were adequate to be assessed for complications rate [10, 12, 17, 25–29, 31–39, 41–76, 79–84].
The 78 series came from 20 different countries: 26 from Italy (33.3%), followed by France (9 series, 11.5%), United States, China, Spain (5 series, 6.4%), Egypt (4 series, 5.1%), United Kingdom, Turkey, Japan (3 series, 3.8%), Tunisia, Poland, Greece, the Netherlands (2 series, 2.6%), Australia, Belgium, Brazil, Germany, Taiwan, Finland, and India (1 series, 1.3%).

Series of poor quality (≤4 in quality score) were 54 (69.2%). The characteristics of the selected study and the quality score given for each series are reported in Table 1.

With regard to the techniques applied, classical slicing was the most commonly used technique for removing submucous myomas (45 series, 57.7%). In 6 series (7.7%), morcellators (Truclear®, MyoSure®, and Bigatti shaver®) were used. In one series (1.3%), the YAG laser was used (Table 1). In the series of Smets et al. [77], morcellators, YAG laser, and classical slicing were all used.

The hysteroscopic myomectomy techniques conceived for treating the intramural component of fibroid in only one surgical step are summarized in Table 2.
| Author          | Country | Type of study | Patients treated | Mean age | Other surgeries | Rate of GnRh agonist | Technique       | Some multiple myomas | Rate of G2 | Mean myoma size reported as main diameter (cm) | Notes                      |
|-----------------|---------|---------------|------------------|----------|-----------------|----------------------|-------------------|----------------------|-----------|-----------------------------------------------|-----------------------------|
| Ahdad-Yata 2015 | France  | Retrospective | 71               | 38.4     | No              | 7.0%                 | Classical slicing | Yes                  | 59.0%     | 2.8                                           | Provided missing information |
| Arcaini 1994    | Italy   | Prospective   | 17               | 43.4     | No              | 100%                 | Classical slicing | Yes                  | 0         | 1.4                                           | Provided missing information |
| Arnold 2016     | Australia | Prospective  | 95               | 47.5     | No              | 0                    | MyoSure®         | Yes                  | 17.9%     | 4.0                                           |                             |
| Bernard 2000    | France  | Retrospective | 31               | 35       | Yes             | 0                    | Hydromassage      | Yes                  | 51.6%     | 2.0                                           | Provided missing information |
| Bigatti 2012    | Italy   | Randomized    |                  |          |                 |                      |                   |                      |           |                                               |                             |
| Group A         |         |               | 2                | 12       | 49.4            | No                   | 0                 | Bigatti Shaver®     | No        | 50%                                           | 2.0                        |
| Group B         |         |               | 0                | 3        | 47.7            | No                   | 0                 | Classical slicing  | No        | 1.8                                           | Provided missing information |
| Bigatti 2014    | Italy   | Retrospective |                  |          |                 |                      |                   |                      |           |                                               |                             |
| Group A         |         |               | 3                | 76       | 47.6            | Missing              | 0                 | Bigatti Shaver®     | Yes       | 36.4%                                        | 2.2                        |
| Group B         |         |               | 3                | 51       | 48              | Missing              | 0                 | Classical slicing  | Yes       | 35.8%                                        | 2.5                        |
| Bizzarri 2015   | Italy   | Prospective   |                  |          |                 |                      |                   |                      |           |                                               |                             |
| Group S         |         |               | 2                | 23       | 35              | No                   | 0                 | Classical slicing  | No        | 38.7%                                        | Missing                    |
| Group T         |         |               | 2                | 20       | 36.3            | No                   | 100%              | Classical slicing  | No        | 42.3%                                        | Missing                    |
| Group L         |         |               | 0                | 11       | 36.8            | No                   | 0                 | Classical slicing  | No        | 50.0%                                        | Missing                    |
| Group U         |         |               | 0                | 7        | 38.4            | No                   | 0                 | Classical slicing  | No        | 40.0%                                        | Missing                    |
| Blanc 1997      | France  | Prospective   | 196              | 41       | Yes             | 18.9%                | Classical slicing | Yes                  | 4.1%      | 2.3                                           |                             |
| Bori 2011       | Italy   | Retrospective | 80               | 41       | Yes             | 1.0%                 | “Cold loop”       | Yes                  | 13.0%     | 3.0                                           | Provided missing information |

Table 1: Description of series in each study.
| Author          | Country | Type of study | Quality score | Patients treated | Mean age | Other surgeries | Rate of GnRh agonist | Technique                  | Some multiple myomas | Rate of G2 | Mean myoma size reported as main diameter (cm) | Notes               |
|----------------|---------|---------------|---------------|------------------|---------|----------------|---------------------|--------------------------|------------------------|------------|---------------------------------------------|---------------------|
| Bourdel 2010   | France  | Retrospective 3 | 3 | 72 | 45.6 | Missing | 0 | Classical slicing | Yes | 12.5% | 2.3 |                                     |
| Camanni 2010   | Italy   | Prospective 4 | 4 | 33 | 41.3 | Yes | 9.1% | “Cold loop” | Yes | 60.2% | 5.5 | Provided missing information |
| Campo 2005     | Italy   | Prospective   | 3 | 42 | 38.8 | Yes | 0% | Classical slicing | Yes | 21.4% | 2.9 |                                     |
|                | Group A |            | 2 | 38 | 39   | Yes | 0% | Classical slicing | Yes | 18.4% | 3.0 |                                     |
| Camanni 2010   | Italy   | Prospective 4 | 4 | 33 | 41.3 | Yes | 9.1% | “Cold loop” | Yes | 60.2% | 5.5 | Provided missing information |
| Casadio 2011   | Italy   | Prospective 0 | 0 | 13 | 36.5 | No  | 0  | “Cold loop” | No  | 100%  | Missing |                                     |
| Chelli 2006    | Tunisia | Retrospective 3 | 3 | 125 | 40.2 | Yes | Missing | Classical slicing | Yes | 22.0% | 2.9 |
| Darwish 2003   | Egypt   | Prospective   | 3 | 65 | 21.7 | No  | 0  | Technique for deep portion | No  | 0  | Missing |                                     |
| De Blok 1995   | The Netherlands | Retrospective 5 | 5 | 109 | 40 | Missing | 100% | Classical slicing | Missing | 11.0% | 1.1 |
| Di Spiezo Sardo 2015 | Italy   | Prospective 6 | 6 | 72 | 38 | Yes | Missing | Classical slicing | Missing | 11.0% | 1.1 |
| Favilli [42]   | Italy   | Randomized    | 7 | 42 | 40.5 | No  | 100% | “Cold loop” | No  | 57.1% | 2.8 | Raw data available                  |
|                | GnRH group Controls | 7 | 42 | 40.9 | No  | 0  | “Cold loop” | No  | 57.1% | 2.5 |
| Fernandez 2001 | France  | Retrospective 5 | 5 | 177 | 42.2 | Missing | 13% | Classical slicing | Yes | 17.0% | 2.9 |                                     |
Table 1: Continued.

| Author                  | Country | Type of study quality score | Patients treated | Mean age | Other surgeries | Rate of GnRh agonist | Technique | Some multiple myomas | Rate of G2 | Mean myoma size reported as main diameter (cm) | Notes                                      |
|-------------------------|---------|-----------------------------|------------------|---------|----------------|----------------------|-----------|----------------------|-----------|-----------------------------------------------|--------------------------------------------|
| Goldrath 1997 [43]      | USA     | Small series 2              | 3                | 31      | Yes            | 0                    | YAG laser destruction | Yes       | 66.7%                                           | Missing                                   |
| Hallez 1995 [44]        | France  | Retrospective 6             | 274              | 45      | Yes            | Missing              | Manual massage       | Yes       | 34.7%                                           | Missing                                   |
| Hamerlynck 2011 [45]    | The Netherlands | Retrospective 1             | 37               | 41.3    | Missing        | 0                    | Trudear®              | Missing   | 8.1%                                           | 2.0                                     |
| Hamidouche 2015 [46]    | France  | Retrospective               | 5                | 34      | 40.8           | Yes                  | MyoSure®              | Yes       | 41.7% G0, G1, G2 mean diameters in both arms |                                           |
| Hart 1996 [47]          | United Kingdom | Prospective 6             | 122              | 43.2    | Yes            | Missing              | Classical slicing     | Yes       | 33.0%                                           | 3.4                                     |
| Imbesi 2008 [48]        | Italy   | Prospective 6               | 78               | 43.9    | Yes            | 65.4%                | “Cold loop”           | Yes       | 26.9%                                           | 2.8                                     |
| Ioannis 2006 [49]       | Greece  | Prospective 6               | 25               | 28.1    | Missing        | 33.3%                | Classical slicing and laparoscopy | Missing | 5.4% Missing                                    |                                           |
| Jayakrishnan 2013 [50]  | India   | Prospective 1               | 37               | 32      | Yes            | 5.4%                 | Classical slicing     | Missing   | 16.7% Missing                                    |                                           |
| Kim 1995 [51]           | USA     | Small series -2             | 6                | 42      | No             | 33.3%                | Classical slicing     | Yes       | 16.7% Missing                                    |                                           |
| Korkmazer 2016 [52]     | Turkey  | Prospective 4               | 64               | 43.9    | No             | 0                    | Technique for deep portion | No       | 28.1%                                           | 4.0                                     |
| Lasmar 2004 [53]        | Brazil  | Retrospective 3             | 44               | 43.5    | Missing        | 0                    | Technique for deep portion | Yes       | 34.1% Provided missing information            |                                           |
| Leone 2012 [54]         | Italy   | Prospective 6               | 159              | 44      | Yes            | 50.9%                | “Cold loop”           | Yes       | 54.1% Missing                                    |                                           |
| Lin 2012 [55]           | Japan   | Prospective 2               | 1569             | 38.6    | Missing        | Not reported          | Technique for deep portion | Yes       | 1.2% Missing                                    |                                           |
| Lin 1994 [56]           | Japan   | Prospective 4               | 25               | 38      | No             | 100%                 | Technique for deep portion | No       | 16.0% Missing                                    |                                           |
| Author                  | Country   | Type of study | Patients treated | Mean age | Other surgeries | Rate of GnRh agonist | Technique                          | Some multiple myomas | Rate of G2 | Mean myoma size reported as main diameter (cm) | Notes                      |
|-------------------------|-----------|---------------|------------------|----------|----------------|----------------------|------------------------------------|---------------------|------------|-----------------------------------------------|----------------------------|
| Litta 2014 [58]         | Italy     | Retrospective | 104              | 35.7     | No             | 19.2%                | Technique for deep portion         | Yes                  | 32.7%     | 2.8                                           |                            |
| Litta 2003 [57]         | Italy     | Prospective   | 41               | 42.1     | No             | 82.9%                | Technique for deep portion         | No                   | 100%      | 3.2                                           |                            |
| Loffer I 2005 [59]      | USA       | Retrospective | 20               | 63.3     | Yes            | 0                    | Classical slicing                 | Yes                  | 15.0%     | 2.4                                           |                            |
| Loffer II 2005 [60]     | USA       | Retrospective |                  |          |                |                      | Classical slicing                 | Yes                  | 20.5%     | 3.0                                           | EA: endometrial ablation  |
|                        |           | With EA       | 1                | 73       | 44             | 79.4%                | Classical slicing                 | Yes                  | 29.8%     | 3.4                                           |                            |
|                        |           | Without EA    | 3                | 104      | 37.6           | 21.2%                | Classical slicing                 | Yes                  | 29.8%     | 3.4                                           |                            |
| Ludwin 2013 [61]        | Poland    | Prospective   |                  |          |                |                      | Technique for deep portion         | No                   | 63.8%     | 2.4                                           |                            |
| Group 1                 |           |               | 6                | 58       | 37.2           | 17.2%                | Technique for deep portion         | No                   | 50.0%     | 2.4                                           |                            |
| Group 2                 |           |               | 6                | 62       | 37.3           | 21.0%                | Classical slicing                 | No                   | 50.0%     | 2.4                                           |                            |
| Lure 1999 [62]          | Spain     | Retrospective | 143              | 45       | Yes            | 62.3%                | Classical slicing                 | Yes                  | 16.9%     | 1.5                                           | Missing                   |
| Makris 2007 [63]        | Greece    | Prospective   | 59               | 34.6     | Missing        | 100%                  | Classical slicing                 | No                   | 16.9%     | 1.5                                           |                            |
| Malek-Mellouli 2012 [64]| Tunisia   | Retrospective | 105              | 41.4     | Missing        | Missing              | Classical slicing                 | Yes                  | 5.8%      | 3.1                                           | Provided missing information |
| Marziani 2005 [65]      | Italy     | Prospective   | 107              | 38       | Missing        | Not reported           | Classical slicing                 | Yes                  | 12.1%     | Missing                                       | Provided missing information |
| Mavrellos 2014 [66]     | United Kingdom | Randomized  | 5                | 19       | 44.5           | Missing              | Classical slicing                 | Yes                  | 0         | 2.9                                           | Provided missing information |
|                         | Placebo   | G2            | 5                | 21       | 38.8           | Missing              | Classical slicing                 | Yes                  | 0         | 2.9                                           | Provided missing information |
| Mazzon 2015 [17]        | Italy     | Retrospective | 1215             | 42       | Yes            | 60.4%                | “Cold loop”                       | Yes                  | 49.8%     | 2.0                                           |                            |
| Muñoz 2003 [67]         | Spain     | Retrospective | 120              | 44.8     | Yes            | 60.0%                | Classical slicing                 | Yes                  | 14.2%     | Missing                                       |                            |
| Murakami 2008 [12]      | Japan     | Prospective   | 28               | 35.1     | No             | Missing              | Technique for deep portion         | Yes                  | 78.6%     | Missing                                       | Provided missing information |
| Muzii 2010 [68]         | Italy     | Randomized    |                  |          |                |                      | Classical slicing                 | Yes                  | 0         | 1.9                                           |                            |
|                        | Group A   |               | 3                | 20       | 42             | 100%                 | Classical slicing                 | Yes                  | 0         | 1.9                                           |                            |
|                        | Group B   |               | 3                | 19       | 42             | 0                    | Classical slicing                 | Yes                  | 0         | 2.0                                           |                            |
| Author                  | Country      | Type of study | Patients treated | Mean age | Other surgeries | Rate of GnRh agonist | Technique                     | Some multiple myomas | Rate of G2 | Mean myoma size reported as main diameter (cm) | Notes |
|------------------------|--------------|---------------|------------------|----------|-----------------|----------------------|-------------------------------|----------------------|-----------|-----------------------------------------------|--------|
| Namazov 2015 [69]      | Turkey       | Retrospective | 98               | 35       | Missing         | 0                    | Classical slicing            | No                   | 4.1%      | Missing                                      |        |
| Polena 2007 [70]       | France       | Retrospective | 235              | 47.9     | Yes             | 3%                   | Classical slicing           | Yes                  | 70.0%     | Missing                                      |        |
| Romer 1997 [71]        | Germany      | Prospective   | 70               | 41       | Missing         | 28.6%                | Classical slicing           | No                   | 34.3%     | Missing                                      |        |
| Rovio 2009 [72]        | Finland      | Prospective   | 53               | 44.7     | Yes             | 0                    | Classical slicing           | Yes                  | 0         | 2.1                                           |        |
| Rovira Pampalona 2012 [73] | Spain     | Retrospective | 76               | 47       | Yes             | 0                    | Truclear®                    | No                   | 0         | Missing                                      |        |
| Sancho 2016 [74]       | Spain        | Retrospective | 1                | 26       | 44              | Missing              | 100% Classical slicing     | Yes                  | 50.0%     | 3.4                                          |        |
| Shendag 2013 [75]      | Turkey       | Retrospective | 40               | 35       | Missing         | Missing              | Classical slicing           | Yes                  | 20.0%     | 2.2                                          |        |
| Shokeir 2005 [76]      | Egypt        | Prospective   | 29               | 31.4     | Missing         | Missing              | Classical slicing           | No                   | 0         | 1.3                                          |        |
| Smets 1996 [77]        | Belgium      | Retrospective | 1                | 24       | 38              | Missing              | Classical slicing, morcellator, or YAG laser | Yes                  | 23.8      | Missing                                      |        |
| Vercellini 1999 [10]   | Italy        | Prospective   | 108              | 37.3     | Yes             | 82.4%                | Technique for deep portion  | Yes                  | 22.2%     | G0, G1, G2 mean diameters                    |        |
| Wang 2016 [78]         | China        | Retrospective | 40               | 32.6     | No              | 0                    | Technique for deep portion  | No                   | 100%      | 4.0                                          |        |
| Wong 2013 [79]         | China        | Small series  | 5                | 41.6     | Missing         | 0                    | Classical slicing           | Yes                  | 20.0%     | 2.9                                          |        |
| Wong 2014 [80]         | China        | Randomized    | 1                | 20       | 41.6            | Missing              | Classical slicing           | Yes                  | 15.0%     | Missing                                      |        |
| Xia [81] 2005          | China        | Retrospective | 877              | 44       | Yes             | 32.2%                | Classical slicing           | Yes                  | 32.2%     | 3.9                                          |        |
| Yen [82] 2007          | Taiwan       | Small series  | 5                | 28       | No              | 20.0%                | Classical slicing           | Yes                  | 40.0%     | 2.8                                          |        |
| Zayed [83] 2015        | Egypt        | Prospective   | 6                | 49       | 37.6            | Missing              | Technique for deep portion  | Yes                  | 46.9%     | 6.0                                          |        |

Studies are listed alphabetically on the first left column. The characteristics of the series are reported along with quality score given. The description of the techniques for treating the deep portion of the myoma is wider reported in Table 2.
Figure 2 shows in details the subgroup arrangement for qualitative and quantitative analysis. The good quality series (>4 quality score) were 25. In total, 3037 and 2888 patients were considered to study feasibility and complications rates, respectively. Of the 25 series of good quality, 10 used the slicing technique (7 with <50% of G2 myomas rate, while 3 with ≥50% of G2 myomas rate). One series reported the use of Myosure® [46]. Techniques for enucleating the deep portion of myomas were reported in 14 series (8 with <50% of G2 myomas rate, while 6 with ≥50% of G2 myomas rate). The “Cold loop” technique [17] was reported in 7 series (4 with <50% of G2 myomas rate and 3 with ≥50% of G2 myomas rate) (Table 1). Complications were not assessed in 2 [40, 78] of 25 series. Table 3 reports the quality score results in assessing bias risk, of the 24 series of good quality available for meta-analysis. The Myosure® arm series in Hamidouche et al. [46] is not reported in Table 3 because it was the only good quality series of the morcellators group. Therefore, it was not possible to meta-analyse data on the morcellators group.

Quantitative subgroup findings were reported in Table 4. The forest plots for the feasibility proportions are shown in Figures 3 to 8. Figures 3 and 4 report forest plots for the slicing technique. Figures 5 and 6 report forest plots for the techniques used for removing the deep portion of myomas. Figures 7 and 8 report forest plots for the “Cold loop” technique. The figures report data syntheses of series with less than 50% rates of G2 myomas and at least 50% rate of G2 myomas.

The Myosure® arm series in Hamidouche et al. study [46] (the only good quality series among morcellators group) reports 0.647 (95% CI 0.476–0.787) of feasibility, while complications cases were 5 to 34 patients (0.147; 95% CI 0.063–0.308). All complications reported in the study of Hamidouche et al. [46] were instances of bleeding.

Table 5 reports descriptive statistics of complications rates found in good quality studies. The comparison among groups of good quality series resulted in the following:

| Author                  | Short description of the technique for treating the deep portion                           |
|-------------------------|-------------------------------------------------------------------------------------------|
| Bernard [28]            | Inducing uterine contraction by changing intrauterine pressure (“hydromassage”)            |
| Darwish [39] Group A.   | Vertical linear incision of the myoma to facilitate the sliding into the endometrial cavity. Ergometrine administration to promote uterine contractions. The base was cut and the whole myoma extracted through the primed cervical canal using a ring forceps. |
| Hallez [44]             | Massage of the uterus manually, applying a pressure on the deep portion of myoma (so-called ”manual massage”) |
| Jayakrishnan, 2013 [50] | Classical slicing under laparoscopic check in 86.5% of patients. Laparoscopic removal of larger myomas with intramural portion |
| Korkmazer [52]          | Cavitation of the cleavage. The cleavage was detected by transabdominal ultrasonography. Then, slicing of the deep portion under transabdominal sonographic check. |
| Lasmar [53]             | Collins’ electrode was used to encircle the entire myoma and to reach the pseudocapsule. From this point, the fibroid was mobilized and the fibrous bundles were individualized and sectioned with electrical energy. |
| Lin [56]                | Cutting the pseudocapsule of the myoma. Lin’ grasper for pulling the deep portion into uterine cavity. Slicing under ultrasonographic check. |
| Litta [55]              | Elliptical incision of the mucosa that covers the myoma at the level of uterine wall and detection of the cleavage. Cutting of the fibrous bridges between myoma and uterine wall, thereby obtaining expulsion of the deep portion into uterine cavity. |
| Ludwin [61], Group I.   | Classic slicing and cut of pseudocapsule, under trans rectal ultrasonicographic check. |
| Murakami [12]           | Resection of the intrauterine dome of the myoma. Induction of strong contraction by using PGE2alpha within uterine body. Slicing or vaporization of the deep portion. Sometimes, mechanical detachment. Echographic check. |
| Vercellini [10]         | Deactivated electrode within the cleavage for pulling and detaching the deep portion from the uterine wall. |
| Wang [78]               | Exposing the myoma edges by cutting endometrium close to the myoma dome. Classic slicing. Oxytocin for inducing contractions in case of large myomas and forceps for pulling the residual portion of the deep myoma. Echographic check. |
| Zayed [83]              | Introducing the loop into the cleavage; traction of the deep portion into uterine cavity. Hydromassage. Manual massage. Echographic check. Multiple slicing session after each induced protrusion of the myoma into uterine cavity. |
| Mazzon [17]             | “Cold loop”: classic slicing of the intrauterine portion of the myoma. Exposure of the pseudocapsule. Change of the loop and use of the cold loop to mobilize the myoma from the uterine wall thereby pulling the deep portion into uterine cavity. |

The description of the techniques for treating the deep portion of the myomas is usually reported in the texts. Sometimes, the authors recall the papers where the techniques have been described.
4. Discussion

The main objective of the present systematic review and meta-analysis was to assess the feasibility rate of the one-step inpatient hysteroscopic myomectomy according to the technique adopted. Therefore, the results obtained from this meta-analysis should be considered with a descriptive value. To our knowledge, this is the first meta-analysis on this subject.

The high heterogeneity observed in inpatient hysteroscopic myomectomies in only one-step procedures, even after sub-groups analysis, was the main finding that emerged from the review of current literature. Therefore, it is difficult to provide the true rate of feasibility and complications according to techniques applied, based on the available literature. Indeed, a significant number of poor quality series—due to bias on collecting or reporting data—were found in the scientific literature available. Although myoma grading is reported in clinical series published after the advent of Wamsteker classification [9], the number of submucous myomas was missing at times and in the same way, the location of myomas was often not reported. The mean myoma size was also often not described in detail. Some authors reported the main diameter of myomas as mean or median with interquartile ranges, suggesting asymmetric distribution of myoma size. Additionally, in some cases, the authors provided the myomas' size as mean diameter using ultrasound investigation (transvaginal or trans-abdominal scans); in other ones, they used

Figure 2: Flow chart of the organization of subgroups.
radiological imaging techniques or subjective assessment during hysteroscopy. Moreover, all these methods might be imprecise in assessing myomas’ size, due to the irregular shape of fibroids. It should be underlined that with an increasing diameter, the volume of myoma grows to the third power. This issue greatly affects the complete removal of myomas in one-stepsurgical procedures [85].

Doubtless, the intramural extension of submucous fibroids influences the chance of achieving the complete resection of myomas in one surgical session [11]. As acknowledged by the authors [86, 87], the possibility to perform an in-patient hysteroscopic myomectomy with a low complications rate is also linked to several parameters related to the myomas (volume, number, grading, and location). Even in good quality series, all those factors related to the myoma characteristics may play a role in influencing the rate of incomplete removal of myomas, justifying the heterogeneity found.

The wide variability highlighted seems also to reflect the personal ability of surgeons to deal with submucous myomas, according to their skills and surgical background, as several techniques for removing deep submucous myomas have been reported (Table 2).

An additional source of variability may be the use of drugs before the hysteroscopic myomectomy or other concomitant surgeries in the same procedure. It is currently unclear if other surgeries or therapies could affect the one-step hysteroscopic myomectomy [42].

The use of alternative techniques for removing the intramural portion of the myomas seems to improve feasibility compared to the slicing technique, with less or equal rate of intraoperative complications. Nevertheless, none of

Table 3: Quality score results.

| Series | Modified GRADE score | Wide explanations on surgical techniques | Clearly reporting on feasibility | Characteristics of patients disclosed | Missing myoma diameter as mean | Sample size | Total |
|--------|-----------------------|----------------------------------------|----------------------------------|--------------------------------------|-------------------------------|-------------|-------|
| Arcaini [26] | 3 | 1 | 1 | 1 | 1 | −1 | 6 |
| De Blok [40] | 2 | −1 | 1 | 1 | 1 | 1 | 5 |
| Fernandez [84] | 2 | 1 | −1 | 1 | 1 | 1 | 5 |
| Hart [47] | 3 | −1 | 1 | 1 | 1 | 1 | 6 |
| Makris [63] | 3 | 1 | 1 | 1 | 1 | −1 | 6 |
| 2010, Placebo [66] | 4 | −1 | 1 | 1 | 1 | −1 | 5 |
| Mavrellos, GnRh [66] | 4 | −1 | 1 | 1 | 1 | −1 | 5 |
| Di Spieazio Srado [41] | 3 | 1 | 1 | 1 | 1 | −1 | 6 |
| Hallez [44] | 2 | 1 | 1 | 1 | 1 | −1 | 6 |
| Imbesi [48] | 3 | 1 | 1 | 1 | 1 | −1 | 6 |
| Ioannis [49] | 3 | 1 | 1 | 1 | 1 | −1 | 6 |
| Litta [58] | 2 | 1 | 1 | 1 | 1 | −1 | 6 |
| Mazzon [17] | 2 | 1 | 1 | −1 | 1 | 1 | 5 |
| Vercellini [10] | 3 | 1 | 1 | 1 | 1 | 1 | 7 |
| Zayed [83] | 3 | 1 | 1 | 1 | 1 | −1 | 6 |
| Ahdad-Yata [25] | 2 | 1 | 1 | 1 | 1 | −1 | 5 |
| Hamidouche [46] | 2 | 1 | 1 | 1 | 1 | −1 | 5 |
| Ludwin, Group 2 [61] | 3 | 1 | 1 | 1 | 1 | −1 | 6 |
| Bernard [28] | 2 | 1 | 1 | 1 | 1 | −1 | 5 |
| Favilli, GnRh group [42] | 4 | 1 | 1 | 1 | 1 | −1 | 7 |
| Favilli, Controls [42] | 4 | 1 | 1 | 1 | 1 | −1 | 7 |
| Leone [54] | 3 | 1 | 1 | 1 | −1 | 1 | 6 |
| Ludwin, Group 1 [61] | 3 | 1 | 1 | 1 | 1 | −1 | 6 |
| Wang [78] | 2 | 1 | 1 | 1 | 1 | −1 | 5 |

Quality score results for studies judged of good quality (quality score more than 4). None of the good quality series falls among the ones in which estimating the rare event has been needed. In the study of Leone et al. [54], the main myoma diameter was reported as median. Hallez et al. [44] provided intervals for diameters of myoma.
Table 4: Results of data syntheses.

|                              | Less than 50% of G2 myoma rate in clinical series | At least of 50% of G2 myoma rate in clinical series |
|------------------------------|--------------------------------------------------|--------------------------------------------------|
| **Slicing technique in clinical series** |                                                  |                                                  |
| Feasibility                  | 0.865 95% CI: 0.820–0.904 0.706 95% CI: 0.638–0.769 |                                                   |
| Feasibility                  | $I^2$: 41.8%, $p = 0.112$                        | $I^2$: 0%, $p = 0.928$                          |
| Begg’s risk of bias          | $-0.524, p = 0.069$                              | Begg and Egger’s risk of bias cannot be calculated |
| Egger’s risk of bias         | $-1.583, p = 0.083$                              | (too few strata)                                 |
| Complication rate            | 0.956 95% CI: 0.0301–0.0894                      | 0.0686 95% CI: 0.0092–0.1766                     |
| Begg’s risk of bias          | $0.467, p = 0.272$                               | Begg and Egger’s risk of bias cannot be calculated |
| Egger’s risk of bias         | $0.972, p = 0.336$.                              | (too few strata)                                 |
| **Techniques for enucleating the deep portion of myomas** |                                                  |                                                  |
| Feasibility                  | 0.923 95% CI: 0.836–0.978                        | 0.882 95% CI: 0.835–0.925                        |
| Feasibility                  | $I^2$: 96.1%, $p < 0.001$                        | $I^2$: 41.6%, $p = 0.128$                       |
| Begg’s risk of bias          | $-0.333, p = 0.239$                              | Begg’s risk of bias $-0.2, p = 0.719$           |
| Egger’s risk of bias         | $-3.913, p = 0.279$                              | Egger’s risk of bias $-0.627, p = 0.743$        |
| Complication rate            | 0.012 95% CI: 0.0062–0.0152                       | 0.0393 95% CI: 0.0204–0.0640                     |
| Begg’s risk of bias          | $0.357, p = 0.275$                               | Begg’s risk of bias $0.571, p = 0.173$          |
| Egger’s risk of bias         | $0.169, p = 0.627$                               | Egger’s risk of bias $0.787, p = 0.408$         |
| **“Cold loop” technique**   |                                                  |                                                  |
| Feasibility                  | 0.931 95% CI: 0.824–0.991                        | 0.854 95% CI: 0.754–0.932                        |
| Feasibility                  | $I^2$: 91.8%, $p < 0.001$                        | $I^2$: 68.6%, $p = 0.041$                       |
| Begg’s risk of bias          | $0, p = 0.750$                                   | Begg and Egger’s risk of bias cannot be calculated |
| Egger’s risk of bias         | $4.870, p = 0.435$                               | (too few strata)                                 |
| Complication rate            | 0.0156 95% CI: 0.0050–0.0318                      | 0.0285 95% CI: 0.0115–0.0530                     |
| Begg’s risk of bias          | $0.333, p = 0.218$                               | Begg and Egger’s risk of bias cannot be calculated |
| Egger’s risk of bias         | $0.434, p = 0.454$                               | (too few strata)                                 |

Sensitivity analyses confirmed the aforementioned overall proportions. The results are provided according to subgroups (Figure 2). The overall results in each subgroup are the weighted rate of feasibility and complications.

Figure 3: Forest plot of slicing technique feasibility in series with less than 50% of G2 myoma rate.
The techniques for treating the deep portion of myomas have been tested against the slicing technique or against other techniques in randomized controlled trials. Therefore, it is not possible to label a single technique as the best one. Among techniques for treating the intramural portion of the myomas, only the “Cold loop” technique has been reported by different authors, demonstrating a certain degree of reproducibility.

The use of morcellators seems to be limited to series with a low rate of or with no G2 myomas. In the present systematic review, only one good quality series describing morcellators was available for meta-analysis, it was therefore not possible to carry out data synthesis.

Finally, caution in interpreting the rate of complications should be used. It was decided to provide results of
complications as a secondary outcome because the effectiveness of a surgical technique cannot be assessed without taking into consideration intraoperative complications. As the quality assessment was only done on the feasibility rate, bias on the reports of complications could be found even in good quality studies. However, it has already been acknowledged that the complications of operative hysteroscopy are overall low [16–18], in agreement with the findings of the present study.

Based on the findings of this meta-analysis, it can be stated that it is hard to compare the feasibility and the complications rates of the resectoscopic myomectomy according to the technique adopted among available clinical series. The studies often do not report pivotal

**Figure 6:** Forest plot of the feasibility of techniques conceived to enucleate the deep portion of myomas in series with at least 50% of G2 myoma rate.

**Figure 7:** Forest plot of “Cold loop” feasibility in series with less than 50% of G2 myoma rate.
information to allow comparability. Future clinical series on in-patient hysteroscopic myomectomy should provide a detailed description of the myomas treated and of the characteristics of patients treated, along with information on additional hysteroscopic procedures needed to accomplish the treatment and any presurgical therapy administered.

5. Conclusions

In conclusion, it can be stated that there is still no single hysteroscopic technique proven to be unequivocally superior to the others for treating submucous fibroids with intramural development in one-surgical step. Nevertheless, despite the heterogeneity found among the clinical series analysed, it seems that all the techniques used to deal with the intramural portion of myomas work better than the slicing technique, achieving a higher rate of procedures accomplished in a single surgical time and a lower number of complications. Randomized controlled trials for testing which is the best technique for the one-step in-patient hysteroscopic myomectomy are needed. In absence of such evidence, it should be assumed that classical slicing is not the best surgical technique for treating the intramural portion of the myomas.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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References

[1] V. C. Buttram Jr. and R. C. Reiter, “Uterine leiomyomata: etiology, symptomatology, and management,” Fertility and Sterility, vol. 56, pp. 433–445, 1981.

[2] E. A. Stewart, “Uterine fibroids,” The Lancet, vol. 357, no. 9252, pp. 293–298, 2001.

[3] W. H. Parker, “Etiology, symptomatology, and diagnosis of uterine myomas,” Fertility and Sterility, vol. 87, no. 4, pp. 725–736, 2007.

[4] K. K. Roy, S. Singla, J. Baruah, J. B. Sharma, S. Kumar, and N. Singh, “Reproductive outcome following hysteroscopic myomectomy in patients with infertility and recurrent abortions,” Archives of Gynecology and Obstetrics, vol. 282, no. 5, pp. 553–560, 2010.

[5] T. Pakrashi, “New hysteroscopic techniques for submucosal uterine fibroids,” Current Opinion in Obstetrics and Gynecology, vol. 26, no. 4, pp. 308–313, 2014.

[6] American Association of Gynecologic Laparoscopists and Advancing Minimally Invasive Gynecology Worldwide, “AAGL practice report: practice guidelines for the diagnosis and management of submucous leiomyomas,” Journal of Minimally Invasive Gynecology, vol. 19, no. 2, pp. 152–171, 2012.

[7] R. S. Neuwirth and H. K. Amin, “Excision of submucous fibroids with hysteroscopic control,” American Journal of Obstetrics and Gynecology, vol. 126, no. 1, pp. 95–99, 1976.

[8] R. S. Neuwirth, “A new technique for and additional experience with hysteroscopic resection of submucous fibroids,” American Journal of Obstetrics and Gynecology, vol. 131, no. 1, pp. 91–94, 1978.

[9] K. Wamsteker, M. H. Emanuel, and J. H. de Kruijff, “Transcervical hysteroscopic resection of submucous fibroids for abnormal uterine bleeding: results regarding the degree of intramural extension,” Obstetrics and Gynecology, vol. 82, no. 5, pp. 736–740, 1993.

[10] P. Vercellini, B. Zaina, L. Yaylayan, A. Pisacreta, O. De Giorgi, and P. G. Crosignani, “Hysteroscopic myomectomy: long-term effects on menstrual pattern and fertility,” Obstetrics & Gynecology, vol. 94, no. 3, pp. 341–347, 1999.

[11] A. Di Spiezo Sardo, I. Mazzon, S. Bramante et al., “Hysteroscopic myomectomy: a comprehensive review of surgical techniques,” Human Reproduction Update, vol. 14, no. 2, pp. 101–119, 2008.

[12] T. Murakami, S. Hayasaka, Y. Terada et al., “Predicting outcome of one-step total hysteroscopic resection of sessile submucous myoma,” Journal of Minimally Invasive Gynecology, vol. 15, no. 1, pp. 74–77, 2008.

[13] A. Liberati, D. G. Altman, I. Tetzlaff et al., “The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration,” PLoS Medicine, vol. 6, no. 7, Article ID e1000100, 2009.

[14] J. Quigley, M. Revie, and J. Dawson, “Estimating risk when zero events have been observed,” BMJ Quality & Safety, vol. 22, no. 12, pp. 1042–1043, 2013.

[15] G. Guyatt, A. D. Oxman, E. A. Ald et al., “GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables,” Journal of Clinical Epidemiology, vol. 64, no. 4, pp. 383–394, 2011.

[16] L. D. Bradley, “Complications in hysteroscopy: prevention, treatment and legal risk,” Current Opinion in Obstetrics and Gynecology, vol. 14, no. 4, pp. 409–415, 2002.

[17] I. Mazzon, A. Favilli, M. Grasso, S. Horvath, G. C. Di Renzo, and S. Gerli, “Is cold loop hysteroscopic myomectomy a safe and effective technique for the treatment of submucous myomas with intramural development? A series of 1434 surgical procedures,” Journal of Minimally Invasive Gynecology, vol. 22, no. 5, pp. 792–798, 2015.

[18] M. G. Munro, “Complications of hysterectomy and uterine resectoscopic surgery,” Obstetrics and Gynecology Clinics of North America, vol. 37, no. 3, pp. 399–425, 2010.

[19] M. K. Aas-Eng, A. Langebrekke, and G. Hudeleit, “Complications in operative hysteroscopy—is prevention possible?,” Acta Obstetrica et Gynecologica Scandinavica, vol. 96, no. 12, pp. 1399–1403, 2017.

[20] R. DerSimonian and N. Laird, “Meta-analysis in clinical trials,” Controlled Clinical Trials, vol. 7, no. 3, pp. 177–188, 1986.

[21] J. P. T. Higgins, S. G. Thompson, J. J. Deeks, and D. G. Altman, “Measuring inconsistency in meta-analyses,” BMJ, vol. 327, pp. 1423–1427, 2003.

[22] C. B. Begg and M. Mazumdar, “Operating characteristics of a rank correlation test for publication bias,” Biometrics, vol. 50, no. 4, pp. 1088–1101, 1994.

[23] M. Egger, G. D. Smith, M. Schneider, and C. Minder, “Bias in meta-analysis detected by a simple, graphical test,” Biometrics, vol. 50, no. 4, pp. 919–926, 1994.

[24] L. Arcaìni, D. Federici, L. Muggiasca, G. Ghetti, B. Lacelli, and M. Conti, “Hysteroscopic myomectomy,” Minimally Invasive Therapy, vol. 3, no. 4, pp. 203–205, 1994.
morculation in the management of intrauterine pathologies,” Journal of Minimally Invasive Gynecology, vol. 23, no. 3, pp. 435–441, 2016.

[28] G. Bernard, E. Darai, C. Poncelet, J.-L. Benifla, and P. Madelelat, “Fertility after hysteroscopic myomectomy: effect of intramural myomas associated,” European Journal of Obstetrics & Gynecology and Reproductive Biology, vol. 88, no. 1, pp. 85–90, 2000.

[29] G. Bigatti, C. Ferrario, M. Rosales, A. Baglioni, and S. Bianchi, “IBS® Integrated Bigatti Shaver versus conventional bipolar resectoscopy: a randomised comparative study,” Gynecological Surgery, vol. 9, no. 1, pp. 63–72, 2012.

[30] G. Bigatti, S. Franchetti, M. Rosales, A. Baglioni, and S. Bianchi, “Hysteroscopic myomectomy with the IBS® Integrated Bigatti Shaver versus conventional bipolar resectoscope: a retrospective comparative study,” Gynecological Surgery, vol. 11, no. 1, pp. 9–18, 2014.

[31] N. Bizzarri, V. Ghirardi, V. Remorgida, P. L. Venturini, and S. Ferrero, “Three-month treatment with triptorelin, letrozole and ulipristal acetate before hysteroscopic resection of uterine myomas: prospective comparative pilot study,” European Journal of Obstetrics & Gynecology and Reproductive Biology, vol. 192, pp. 22–26, 2015.

[32] B. Blanc, L. Cravello, C. D’Ercole, V. Roger, and G. Porcu, “Role of endo-uterine resection using hysteroscopy in the treatment of sub-mucous hemorrhagic fibroma in the peri-menopausal period,” Bulletin de l’Académie nationale de médecine, vol. 181, no. 4, pp. 651–659, 1997.

[33] S. Bori, F. Lombardo, F. Servidio et al., “Operative hysteroscopy: our experience in hysteroscopic myomectomy and metroplasty,” International Journal of Gynecology & Obstetrics, vol. 23, pp. 97–100, 2011.

[34] N. Bourdel, C. Bonnefoy, K. Jardon et al., “Myometomie hystéroscopique: récitéve et enquête de satisfaction à court et long terme,” Journal de Gynécologie Obstétrique et Biologie de la Reproduction, vol. 40, no. 2, pp. 116–122, 2011.

[35] M. Camanni, L. Bonino, E. M. Delpiano, B. Ferrero, G. Migliaretti, and F. Delletto, “Hysteroscopic management of large symptomatic submucous uterine myomas,” Journal of Minimally Invasive Gynecology, vol. 17, no. 1, pp. 59–65, 2010.

[36] S. Campo, V. Campo, and P. Gambadaro, “Short-term and long-term results of resectoscopic myometomy with and without pretreatment with GnRH analogs in premenopausal women,” Acta Obstetricia et Gynaecologica Scandinavica, vol. 84, no. 8, pp. 756–760, 2005.

[37] P. Casadio, A. M. Youssef, E. Spagnolo et al., “Should the myometrial free margin still be considered a limiting factor for hysteroscopic resection of submucous fibroids? A possible answer to an old question,” Fertility and Sterility, vol. 95, no. 5, pp. 1764–1768, 2011.

[38] D. Chelli, M. Chanoufi, M. Mrad, H. Khoudhair, H. Chelli, and E. Sfar, “Résection hystéroscopique des myomes utérins, expérience tunisienne à propos de 130 cas,” La Lettre du Gynécologue, vol. 12-15, pp. 308–309, 2006.

[39] A. Darwish, “Modified hysteroscopic myomectomy of large submucous fibroids,” Gynecologic and Obstetric Investigation, vol. 56, no. 4, pp. 192–196, 2003.

[40] S. De Blok, A. Dijkman, and D. Hemrika, “Transcervical resection of fibroids (TCRM): results related to hysteroscopic classification,” Gynecological Endoscopy, vol. 4, pp. 243–246, 1995.

[41] A. Di Spiezo Sardo, G. Calagna, C. Di Carlo, M. Guida, A. Perino, and C. Nappi, “Cold loops applied to bipolar resectoscope: a safe “one-step” myomectomy for treatment of submucosal myomas with intramural development,” Journal of Obstetrics and Gynaecology Research, vol. 41, no. 12, pp. 1935–1941, 2015.

[42] A. Favilli, I. Mazzon, M. Grasso et al., “Intraoperative effect of preoperative gonadotropin-releasing hormone analogue administration in women undergoing cold loop hysteroscopic myomectomy: a randomized controlled trial,” Journal of Minimally Invasive Gynecology, vol. 25, no. 4, pp. 706–714, 2018.

[43] M. H. Goldrath and M. Husain, “The hysteroscopic management of endometrial leiomyomatosis,” The Journal of the American Association of Gynecologic Laparoscopists, vol. 4, no. 2, pp. 263–267, 1997.

[44] J. P. Hallez, “Single-stage total hysteroscopic myomectomies: indications, techniques, and results,” Fertility and Sterility, vol. 63, no. 4, pp. 703–708, 1995.

[45] T. W. O. Hamerlynck, V. Dietz, and B. C. Schoot, “Clinical implementation of the hysteroscopic morcellator for removal of intrauterine myomas and polyps. A retrospective descriptive study,” Gynecological Surgery, vol. 8, no. 2, pp. 193–196, 2011.

[46] A. Hamidouche, M. Vinciennne, T. Thubert et al., “Hystéroscope opérateur pour fibrome: morcellement versus résection à l’anse bipolaire,” Journal de Gynécologie Obstétrique et Biologie de la Reproduction, vol. 44, no. 7, pp. 658–664, 2015.

[47] R. Hart, B. G. Molnar, and A. Magos, “Long term follow up of hysteroscopic myomectomy assessed by survival analysis,” BJOG: An International Journal of Obstetrics and Gynaecology, vol. 106, no. 7, pp. 700–705, 1999.

[48] G. Imbesi, A. Azzerboni, S. Bonanno, G. Zoccali, and O. Triolo, “Hysteroscopic myomectomy: long-term results on menstrual patterns and reproductive outcome,” Giornale Italiano di ostetricia e ginecologia, vol. 30, pp. 217–223, 2008.

[49] S. Ioannis, A. Aristotelis, T. Antonios, S. Panagiotis, and B. John, “Fertility rates after hysteroscopic treatment of submucous myomas depending on their type,” Gynecological Surgery, vol. 3, no. 3, pp. 206–210, 2006.

[50] K. Jayakrishnan, V. Menon, and D. Nambiar, “Submucous fibroids and infertility: effect of hysteroscopic myomectomy and factors influencing outcome,” Journal of Human Reproductive Sciences, vol. 6, no. 1, pp. 35–39, 2013.

[51] A. H. Kim, M. D. Keltz, A. Arici, M. Rosenberg, and D. L. Olive, “Dilutional hyponatremia during hysteroscopic myomectomy using sorbitol-mannitol distention medium,” The Journal of the American Association of Gynecologic Laparoscopists, vol. 2, no. 2, pp. 237–242, 1995.

[52] E. Korkmazer, B. Tekin, and N. Solak, “Ultrasound guidance during hysteroscopic myomectomy in G1 and G2 Submucous Myomas: for a safer one step surgery,” European Journal of Obstetrics & Gynecology and Reproductive Biology, vol. 203, pp. 108–111, 2016.

[53] R. B. Lasmar, P. R. M. Barrozo, R. Dias, M. A. P. Oliveira, A. Pontes, and D. S. Dias, “Miomas submucosos: classificação pré-operatória para avaliação da viabilidade da cirurgia histeroscópica,” Revista Brasileira de Ginecologia e Obstetricia, vol. 26, no. 4, pp. 305–309, 2004.

[54] F. P. G. Leone, S. Calabrese, C. Marcianite, I. Cetin, and E. Ferrazzi, “Feasibility and long-term efficacy of hysteroscopic morcellation in women undergoing cold loop hysteroscopic myomectomy with sorbitol-mannitol distention medium,” The Journal of Minimally Invasive Gynecology Research, vol. 9, no. 2, pp. 155–161, 2012.

[55] B. L. Lin, T. Higuchi, A. Yabuno et al., “One-step hysteroscopic myomectomy using Lin dissecting loop and Lin
BioMed Research International

myoma graspers," *Gynecology and Minimally Invasive Therapy*, vol. 1, no. 1, pp. 27–33, 2012.

[56] B.-L. Lin, Y. Iwata, and K. H. Liu, "Removing a large submucous fibroid hysteroscopically with the two-resectoscope method," *The Journal of the American Association of Gynecologic Laparoscopists*, vol. 1, no. 3, pp. 259–263, 1994.

[57] P. Litta, C. Vasile, F. Merlin et al., "A new technique of hysteroscopic myomectomy with enucleation in toto," *The Journal of the American Association of Gynecologic Laparoscopists*, vol. 10, no. 2, pp. 263–270, 2003.

[58] P. Litta, L. Conte, F. De Marchi, C. Saccardi, and S. Angioni, "Pregnancy outcome after hysteroscopic myomectomy," *Gynecological Endocrinology*, vol. 30, no. 2, pp. 149–152, 2014.

[59] F. D. Loffer, "Improving results of hysteroscopic submucosal myomectomy for menorrhagia by concomitant endometrial ablation," *Journal of Minimally Invasive Gynecology*, vol. 12, no. 3, pp. 254–260, 2005.

[60] A. Ludwin, I. Ludwin, K. Pityński et al., "Transtectal ultrasound-guided hysteroscopic myomectomy of submucosal myomas with a varying degree of myometrial penetration," *Journal of Minimally Invasive Gynecology*, vol. 20, no. 5, pp. 672–685, 2013.

[61] M. Lure, N. Marin, J. Navarrina, A. Elorza, J. Cortabarría, and B. Rivero, "Resection of submucous myomas by hysteroscopy," *Progresos de Obstetricia y Ginecologia*, vol. 42, pp. 719–724, 1999.

[62] N. Makris, E. Vomvolaki, G. Mantzaris, K. Kalmantis, J. Hatzipappas, and A. Antsaklis, "Role of a bipolar resectoscope in subfertile women with submucous myomas and menstrual disorders," *Journal of Obstetrics and Gynaecology Research*, vol. 33, no. 6, pp. 849–854, 2007.

[63] M. Malek-Melloulí, F. Ben Amara, A. Yousef, M. Mbarki, and H. Reziga, "Hysteroscopic myomectomy," *Journal Medical Tunisie*, vol. 90, pp. 458–462, 2012.

[64] R. Marziani, B. Mossa, V. Ebano, G. Perniola, J. Melluso, and C. Napolitano, "Transcervical hysteroscopic myomectomy: long-term effects on abnormal uterine bleeding," *Clinical and Experimental Obstetrics & Gynecology*, vol. 32, no. 1, pp. 23–26, 2005.

[65] D. Mavrelos, J. Ben-Nagi, A. Davies, C. Lee, R. Salim, and D. Jurkovic, "The value of pre-operative treatment with GnRH analogues in women with submucous fibroids: a double-blind, placebo-controlled randomized trial," *Human Reproduction*, vol. 25, no. 9, pp. 2264–2269, 2010.

[66] J. L. Muñoz, J. S. Jimenez, C. Hernandez et al., "Hysteroscopic myomectomy: our experience and review," *JLS*, vol. 7, no. 1, pp. 39–48, 2003.

[67] L. Muzii, T. Boni, F. Bellati et al., "GnRH analogue treatment before hysteroscopic resection of submucous myomas: a prospective, randomized, multicenter study," *Fertility and Sterility*, vol. 94, no. 4, pp. 1496–1499, 2010.

[68] A. Namazov, R. Karakus, E. Gencer, H. Sozen, and L. Acar, "Do submucous myoma characteristics affect fertility and menstrual outcomes in patients underwent hysteroscopic myomectomy?" *Iranian Journal of Reproductive Medicine*, vol. 13, no. 6, pp. 367–372, 2015.

[69] V. Polena, J.-L. Mergui, N. Perrot, C. Poncelet, E. Barranger, and S. Uzan, "Long-term results of hysteroscopic myomectomy in 235 patients," *European Journal of Obstetrics & Gynecology and Reproductive Biology*, vol. 130, no. 2, pp. 232–237, 2007.

[70] T. Romer, "Hysteroscopic myoma resection of submucous myomas with largely intramural components," *Zentralbl Gynakol*, vol. 119, no. 8, pp. 374–377, 1997.

[71] P. H. Rovio, R. Helin, and P. K. Heinonen, "Long-term outcome of hysteroscopic endometrial resection with or without myomectomy in patients with menorrhagia," *Archives of Gynecology and Obstetrics*, vol. 279, no. 2, pp. 159–163, 2009.

[72] J. Rovira Pampalona, E. Raticia García, E. Muñoz Casas et al., "Morcellator hysteroscopy (trueclear system®): preliminary experience," *Progresos de Obstetricia y Ginecologia*, vol. 55, no. 9, pp. 459–463, 2012.

[73] J. M. Sancho, V. S. D. L. C. Delgado, M. J. N. Valero, M. G. Soteras, V. P. Amate, and A. A. Carrascosa, "Hysteroscopic myomectomy outcomes after 3-month treatment with either Ulipristal Acetate or GnRH analogues: a retrospective comparative study," *European Journal of Obstetrics & Gynecology and Reproductive Biology*, vol. 198, pp. 127–130, 2016.

[74] F. Şendağ, L. Akman, V. Turan, N. Karadaş, and K. Öztekin, "Hysteroscopic management of submucosal fibroids," *Türkiye Klinikerleri Jinekoloji Obstetrik*, vol. 23, pp. 23–26, 2013.

[75] T. A. Shokeir, "Hysteroscopic management in submucous fibroids to improve fertility," *Archives of Gynecology and Obstetrics*, vol. 273, no. 1, pp. 50–54, 2005.

[76] M. Smets, M. Nisolles, S. Bassil, and J. Donnez, "Expansive benign lesions: treatment by laser," *European Journal of Obstetrics & Gynecology and Reproductive Biology*, vol. 65, no. 1, pp. 101–105, 1996.

[77] H. Wang, J. Zhao, X. Li et al., "The indication and curative effect of hysteroscopic and laparoscopic myomectomy for type II submucous myomas," *BMC Surgery*, vol. 16, no. 1, pp. 9, 2016.

[78] A. S. W. Wong, E. C. W. Cheung, K.-T. Leung, S.-W. Yeung, T.-Y. Leung, and T.-Y. Fung, "Transcervical intrasional vasopressin injection in hysteroscopic myomectomy—description of a new technique," *Journal of Laparoscopic & Advanced Surgical Techniques*, vol. 23, no. 3, pp. 258–262, 2013.

[79] A. S. W. Wong, C. W. Cheung, S. W. Yeung, H. L. Fan, T. Y. Leung, and D. S. Sahota, "Transcervical Intrasional Vasopressin Injection Compared with Placebo in Hysteroscopic Myomectomy," *Obstetrics & Gynecology*, vol. 124, no. 5, pp. 897–903, 2014.

[80] E. L. Xia, H. Duan, X. W. Huang, J. Zheng, and D. Yu, "Transcervical resection of myoma in treatment of hystromyoma, experience in 962 xcases," *Zhonghua Yi Xue Za Zhi*, vol. 85, no. 3, pp. 173–176, 2005.

[81] C.-F. Yen, C.-L. Lee, C.-J. Wang, Y.-K. Soong, and A. Arici, "Successful pregnancies in women with diffuse uterine leiomyomatosi after hysteroscopic management," *Fertility and Sterility*, vol. 88, no. 6, pp. 1667–1673, 2007.

[82] M. Zayed, U. M. Fouda, S. M. Zayed, K. A. Elsetohy, and A. T. Hashem, "Hysteroscopic myomectomy of large submucous myomas in a 1-step procedure using multiple slicing sessions technique," *Journal of Minimally Invasive Gynecology*, vol. 22, no. 7, pp. 1196–1202, 2015.

[83] H. Fernandez, O. Kadoch, S. Capella-Allouc, A. Gervaise, S. Taylor, and R. Frydman, "Résection hystéroscopique des myomes sous muqueux: résultats à long terme," *Annales de Chirurgie*, vol. 126, no. 1, pp. 58–64, 2001.

[84] M. H. Emanuel, "Hysteroscopy and the treatment of uterine fibroids," *Best Practice & Research Clinical Obstetrics & Gynaecology*, vol. 29, no. 7, pp. 920–929, 2015.
[86] H. Xu, J. Lin, X. Z. Chen, and X. M. Zhang, “Evaluation of a self-defined classification of uterine submucous myomas for guiding transcervical hysteroscopic electric resection,” Zhonghua Yi Xue Za Zhi, vol. 88, no. 1, pp. 22–24, 2008.
[87] R. B. Lasmar, Z. Xinmei, P. D. Indman, R. K. Celeste, and A. Di Spiezio Sardo, “Feasibility of a new system of classification of submucous myomas: a multicenter study,” Fertility and Sterility, vol. 95, no. 6, pp. 2073–2077, 2011.