# Adenomyosis and Its Variance: Adenomyoma and Female Fertility

Peng-Hui Wang*, Wen-Hsiang Su[1], Bor-Ching Sheu[2], Wei-Min Liu[3]

*Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, National Yang-Ming University Hospital and National Yang-Ming University School of Medicine, Taipei, [1]Department of Obstetrics and Gynecology, Yee-Zen Hospital, and Institute of Systems Biology and Bioinformatics, National Central University, Tao-Yuan, [2]Department of Obstetrics and Gynecology, National Taiwan University, National Taiwan University Hospital, and [3]Department of Obstetrics and Gynecology, Taipei Medical University and Taipei Medical University Hospital, Taipei, Taiwan.*

**SUMMARY**

Extensive adenomyosis (adenomyosis) or its variance, localized adenomyosis (adenomyoma) of the uterus, is often described as scattered, widely-distributed endometrial glands or stromal tissue found throughout the myometrium layer of the uterus. By definition, adenomyosis consists of epithelial as well as stromal elements, and is situated at least 2.5 mm below the endometrial–myometrial junction. However, the diagnosis and clinical significance of uterine adenomyosis and/or adenomyoma remain somewhat enigmatic. The relationship between infertility and uterine adenomyosis and/or adenomyoma is still uncertain, but severe endometriosis impairs the chances of successful pregnancy when using artificial reproductive techniques. To date, there is no uniform agreement on the most appropriate therapeutic methods for managing women with uterine adenomyosis and/or adenomyoma who want to preserve their fertility. Fertility has been restored after successful treatment of adenomyosis using multiple modalities, including hormonal therapy and conservative surgical therapy via laparoscopy or exploratory laparotomy, uterine artery embolization, and other methods, including a potential but under-investigated procedure, magnetic resonance-guided focused ultrasound. This review will explore recent publications that have addressed the use of different approaches in the management of subfertile women with uterine adenomyosis and adenomyoma. [*Taiwan J Obstet Gynecol* 2009;48(3):232–238]

**Key Words:** adenomyoma, adenomyosis, infertility, subfertility

*This paper was presented at the 96th Annual Meeting of the Taiwan Association of Obstetrics and Gynecology, Taipei, Taiwan, March 24–25, 2007*

## Introduction

Adenomyosis is a disorder characterized by the presence of heterotopic endometrial glands and stroma in the myometrium with adjacent myometrial hyperplasia [1]. By definition, it consists of epithelial as well stromal elements, and is situated at least 2.5 mm below the endometrial–myometrial junction [2]. The disease appears in two forms, the diffuse type, known as adenomyosis, and the focal type, known as adenomyoma [3–5]. Any site in the uterus may be involved, but the posterior wall is affected the most [6]. In the past, the diagnosis relied on clinical manifestations, with the most frequently cited profile composed of the triad of abnormal uterine bleeding (50%), secondary dysmenorrhea (30%), and an enlarged, tender uterus [7].

Remarkable developments in imaging modalities, including high-resolution ultrasound and magnetic resonance imaging (MRI), have enhanced diagnostic accuracy, as proven by several studies [3–6,8–10].

*Correspondence to: Dr Peng-Hui Wang, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, National Yang-Ming University Hospital and National Yang-Ming University, 201, Shih-Pai Road, Section 2, Taipei 112, Taiwan.
E-mail: phwang@vghtpe.gov.tw
Accepted: March 12, 2009

The characteristics of transabdominal ultrasound include a honeycomb pattern, sonolucent 5–7 mm spaces, myometrial cysts, wide posterior wall, eccentric endometrial cavity, diffuse uterine enlargement but with no leiomyomas, and diminished uterine echogenicity [6]. However, the sensitivity and specificity of transabdominal ultrasound for the diagnosis of uterine adenomyosis is around 50% [11]. Transvaginal ultrasound may be superior to transabdominal ultrasound for the diagnosis of uterine adenomyosis since the diagnostic sensitivity and specificity are over 50%, ranging from 50% to 100% for both [6]. The characteristic findings of uterine adenomyosis using transvaginal ultrasound include (1) increased size, asymmetry, retroversion, globular or spherical shape, and uterosacral ligament nodularity for uterine body examination; (2) focal honeycomb, scattered, irregular, cystic, anechoic lacunae, asymmetrical thickening of the anterior or posterior uterine wall, heterogeneous increased or decreased myometrial echoes, mottled texture, lesions surrounded by anechoic shadows 1–3 mm in diameter, hyperechogenic or hypoechogenic striations, indistinct margins, nonencapsulated myometrial lesion, myometrial linear striation for the myometrium examination; and (3) a shaggy endometrial stripe, blurred endometrial–myometrial border, and thickened or distorted endometrium for the endometrium examination [6]. The presence of subendometrial echogenic linear striations, a globular configuration and myometrial cysts on transvaginal ultrasound supports the diagnosis of adenomyosis [3]. Among the transvaginal ultrasound diagnostic findings of adenomyosis, subendometrial linear striations have the highest diagnostic accuracy [3].

MRI is also an accurate, noninvasive modality for diagnosing adenomyosis and may be more helpful than transvaginal ultrasound in distinguishing adenomyosis from a leiomyoma, which is perhaps the most clinically important distinction [12]. In addition, MRI may be more effective for both diffuse and focal adenomyosis, with sensitivity and specificity comparable to or even better than those of ultrasound, as it depicts contrasts between low-intensity lesions and surrounding tissue [6]. The characteristic findings of MRI in uterine adenomyosis include a minimum width of the junction zone of 5 mm or 12 mm, a focal and uneven width of the junction zone, low intensity of the junction zone, high-intensity spots scattered in the junction zone, and indistinct junction zone margins for the myometrium examination [6]. Histologically, areas of low signal intensity correspond to smooth muscle hyperplasia, and bright foci on T2-weighted images correspond to islands of ectopic endometrial tissue and cystic dilatation of glands [12]. When menstrual hemorrhage occurs within these ectopic endometrial tissues, signal intensity on T1-weighted images may become high [12].

Even with advanced modern imaging technology, there is no definitive method to diagnose adenomyosis or its related diseases. The classical signs and clinical symptoms may suggest the diagnosis, but these signs and symptoms are, unfortunately, often misleading. In addition, without tissue proof, the diagnosis of uterine adenomyosis is controversial; therefore, of the minimally invasive diagnostic methods, myometrial biopsy has been used by several authors and seems promising [2,13,14].

Parallel to the development of improved diagnostic methods for adenomyosis, innovative modalities have been introduced as alternatives therapies, such as medical treatment, conservative surgical treatment, uterine artery embolization and laparoscopic uterine vessel occlusion, for those women for whom hysterectomy would not be considered an option [2,13–17]. The purpose of this review is to focus on the role of different therapies in managing subfertile women with symptomatic uterine adenomyosis and adenomyomas.

## Fertility and Adenomyosis and/or Adenomyomas

An association between adenomyosis and subfertility has not been fully established. Some believe that adenomyosis is not associated with subfertility, because it is widely held to be a condition associated with multiparity, and there have been several pathology-based studies published in which women with adenomyosis found at hysterectomy were often more parous than women in whom it was not found [18,19]. However, the possibility of an association between adenomyosis and subfertility has been raised in a few small case series and in a sole case report [1,7,8,17,20–34]. In this, fertility was restored after the successful treatment of adenomyosis with multiple modalities, including hormonal therapy and conservative surgical therapy via laparoscopy or exploratory laparotomy, uterine artery embolization (UAE) [17], and other methods, including a potential but under-investigated procedure, magnetic resonance-guided focused ultrasound (MRgFUS) [34].

## Medical Treatment

Gonadotropin-releasing hormone (GnRH) agonist may be the most popular and well-accepted therapy. In fact, this strategy has resulted in a few case reports of successful pregnancy and delivery [14,22–25,27]. The reason

for the improved reproductive performance in these patients is not well understood. It may be explained by the fact that GnRH agonist transiently suppresses the hypothalamus-pituitary gland-ovary axis and induces a hypoestrogenic effect with resultant shrinkage of the uterine adenomyosis (a reduced uterine size) and relief of the symptoms (a suppressed uterine adenomyosis). Furthermore, GnRH agonist is reported to possibly promote uterine and endometrial receptivity [2,24]. However, its effect is often transient and it is frequently used with a preoperative adjuvant therapy [1]. Rapid regrowth of adenomyosis and relapse of symptoms and signs always occurs after the treatment is stopped [14]. This phenomenon was similar to that in the use of GnRH agonist in the management of uterine myomas [35–40].

In a review of the use of GnRH agonist as conservative therapy for adenomyosis with successful pregnancy [14], nine women experienced spontaneous conception, and one had a successful term vaginal delivery with the use of surgical resection followed by 3 months of danazol delivery [1]. All pregnancies, indeed, occurred within 12 months after completing therapy or the return of the first menstruation, ranging from: immediately to 1 month [23–25], 2–4 months [24,30,31], 5 months [27], and 6 months [30], strongly suggesting that spontaneous pregnancy as a result of using GnRH agonist in these subfertile women with extensive uterine adenomyosis may be possible, but the effective period may be short if pregnancy is achieved. Previously, we studied 37 women with a clinic-pathologic diagnosis of uterine adenomyosis who were treated with GnRH agonist alone, and only three subfertile women had conception and finally a successful delivery [14]. Consistent with the above, all pregnancies in our study [14] also occurred within 12 months of completing medical therapy or the return of the first menstruation.

In summarizing the role of GnRH agonist for inducing spontaneous pregnancy in these subfertile women with extensive adenomyosis, nearly all spontaneous pregnancies occurred within 6 months after treatment or the return of the first menstruation (Table), so we suggest that further active management is highly recommended if pregnancy does not occur within the first year or 6 months after completing therapy or the return of menstruation.

**Table.** Summary of outcomes of subfertile women with adenomyosis and/or adenomyoma after different therapeutic strategies

| Authors | Treatment | Interval between spontaneous pregnancy and completed treatment (mo) |
|---|---|---|
| Wang et al [14] | GnRH agonist | <12 |
| Grow and Filer [23] | GnRH agonist | ~1 |
| Hirata et al [24] | GnRH agonist | ~1 |
| | | 2–4 |
| Nelson and Corson [25] | GnRH agonist | ~1 |
| Silva et al [27] | GnRH agonist | ~5 |
| Huang et al [30] | GnRH agonist | 2–4 |
| | | ~6 |
| Lin et al [31] | GnRH agonist | 2–4 |
| Rabinovici and Stewart [42] | MRgFUS | 2–4 |
| Wang et al [14] | Conservative surgery | 4–24 |
| Wang et al [33] | Conservative surgery | ~30 |
| Wang et al [53] | Conservative surgery | 3–19 |
| Fujishita et al [56] | Conservative surgery | ~4 |
| | | ~6 |
| Strizhakov et al [57] | Conservative surgery | <12 |
| Wang et al [14] | Combined therapy | 3–34 |
| Wood [20] | Combination therapy* | ? |
| Huang et al [29] | Combined therapy | ~7 |
| Wang et al [32] | Combined therapy | ~3 |
| | | ~12 |
| Wang et al [33] | Combined therapy (with danazol) | ~21 |
| Wang et al [53] | Combined therapy | 3–22 |

**Combination of any type of conservative surgery and medical treatment (gonadotropin-releasing hormone agonist). GnRH = gonadotropin-releasing hormone; MRgFUS = magnetic resonance-guided focused ultrasound.*

## Uterine Artery Embolization

UAE was first reported for the treatment of leiomyomata in 1995 [41]. Since that time, there has been rapid growth in the use of this treatment, and UAE has emerged in the past decade as a relatively safe, minimally invasive alternative therapy for uterine fibroids [42]. An increasing number of reports indicate that uterine fibroids can be successfully treated with UAE, and this technique seems to be a promising treatment for women who want to retain their uterus. The rationale for using laparoscopic uterine vessel occlusion in the management of symptomatic fibroids is found in the successful experience with UAE, Since then, it has become increasingly accepted as a minimally invasive, uterine-sparing procedure, and studies have reported relief of excessive menstrual bleeding or pressure in 80–90% of patients [43–47]. Laparoscopic uterine vessel occlusion provided similar relief of symptoms (89.4% with symptomatic improvement and 21.2% with complete resolution of symptoms) in 2001 in a 7- to 12-month follow-up of 87 patients [48].

Adenomyosis and uterine fibroids coexist in many uteri, and their symptoms are often similar [42]. Thus, performing UAE in women with symptomatic uterine fibroids will ultimately also include patients with adenomyosis. Because of the difficult differential diagnosis between the two entities, it can be assumed that if the embolization procedure is performed without a screening MRI examination, patients with undiagnosed adenomyosis are also being treated [49].

Pregnancies and vaginal deliveries seem to be possible after UAE for adenomyosis [42]. In a report on eight pregnancies in six patients after UAE, three women had adenomyosis and one woman had both uterine fibroids and adenomyosis [17]. One woman with adenomyosis delivered twice, once at 34 weeks' gestation and once at term. All neonates but one (premature rupture of membranes and 1,850 g birth weight at 34 weeks' gestation) were healthy and appropriate for their gestational age at delivery. Despite the small number of pregnancies, the authors argued that UAE with polyvinyl alcohol particles did not affect the fertility and pregnancy outcome [17].

Although it is reported that UAE has not shown an effect on fertility [2], a recent publication evaluating the midterm clinical and first reproductive results of the comparison between UAE and myomectomy is worthy of our attention. This study showed that myomectomy appears to have superior reproductive outcomes in the first 2 years after treatment compared with UAE in the management of uterine myomas [50]. Therefore, some papers suggested that myomectomy should be recommended as the treatment of choice over UAE in most patients desiring future fertility [51], even though most pregnancies following UAE have good outcomes [52]. In view of this, the policy of conservative surgery for adenomyosis and/or adenomyoma is similar to that of myomectomy for myoma, suggesting that conservative surgery may have been without detriment to reproductive performance [14,53].

## Magnetic Resonance-guided Focused Ultrasound

Since ultrasound waves carry energy, the ability of these waves to cause a rise in tissue temperature was recognized long ago, and if the pattern of the waves is modified so that they meet at a single point, one can achieve a localized high temperature rise at this focal point [42]. Using this technique, irreversible cell damage (60–90°C) can be generated within a few seconds at such a focal point [42]. Heating tissue to temperatures above 55°C leads to protein denaturation and irreversible cell death through coagulative necrosis [42]. Based on these characteristics, high-intensity focused ultrasound surgery has been proposed in the past as a noninvasive technique to treat soft tissue tumors deep in the body. Under the guidance of MRI, a brand-new tool, MRgFUS, has been used to treat uterine fibroids in more than 1,200 women who chose not to undergo hysterectomy, with promising results [42]. In a review by Rabinovici and Stewart [42], at least nine patients were treated with MRgFUS. One patient conceived spontaneously three menstrual cycles after MRgFUS, and the pregnancy course was uneventful; she gave birth to a full-term healthy baby girl weighing 3.050 kg, after an uneventful labor and vaginal delivery [34].

## Surgical Treatment

By contrast, and compared with the well-accepted GnRH agonist as a choice in the management of symptomatic and/or subfertile women with extensive adenomyosis, surgical intervention is seldom considered to play a role in managing such patients. The most important consideration is the difficulty of selecting a good candidate to undergo the surgical approach; for, how does one determine the extent of adenomyosis in a particular patient? Furthermore, adenomyosis is not cleared completely by conservative surgery, and postoperative sequelae, such as pelvic adhesion, future uterine deformities, intrauterine adhesions and reduced uterine capacity [2], cannot be completely avoided.

Yet another late complication is subsequent uterine scars which may conceal more adenomyotic foci and result in the reduction of tensile strength [2]. Therefore, the possible rupture of a pregnant uterus should be cause for alarm, because as mentioned above, adenomyosis is always mixed with the surrounding normal myometrium (which may impact on surgical treatment). Hence, conservative excision of extensive adenomyosis is very difficult to complete, with a resultant increasing frequency of entering the uterine cavity during the operation (e.g. nearly 30% of patients in one study [14]), as well as after removing the adenomyotic tissues. In addition, it is more difficult to repair the uterine defect, compared with excising a uterine leiomyoma [54]. Since rupture of a pregnant uterus has been observed after myomectomy [55], it is reasonable to expect the possibility of uterine rupture after excision of adenomyotic tissue. Therefore, the decision to use conservative surgery in the management of women with extensive adenomyosis should be taken safely. We reviewed the use of conservative surgery for the management of uterine adenomyosis with successful pregnancy, with nine spontaneous conceptions and one rupture of the uterus at 12 weeks of gestation [20]. The interval between the occurrence of the pregnancies and completed therapy or the return of the first menstruation varied from 3 to 30 months (Table) [2,29,32,33,56,57].

## Combination Therapy

Because of the transient effect of medical therapy and the only 50% effectiveness of surgical therapy in managing uterine adenomyoma-related diseases, the combination of conservative surgery and medical treatment with either GnRH agonist or danazol (surgical-medical treatment) has been developed [53]. The results are promising and welcome [14,29,32,33,53]. In a series of 165 patients with symptomatic adenomyoma who were treated with conservative surgery, regardless of GnRH agonist treatment or not, data showed that this treatment might be acceptable in the management of a selected population with severe symptomatic adenomyoma [53]. Combination therapy provided more effective symptom control (lower symptom relapse rate) than conservative surgery alone during the 2-year follow-up [53]. However, the reproductive outcomes seemed to be similar between conservative surgery with and without GnRH agonist treatment; there was no statistical significant difference in either the clinical pregnancy rate (79.5% in the combination therapy group versus 74.1% in the conservative surgery alone group) or the successful delivery rate (72.7% in the combination therapy group versus 63.0% in the conservative surgery alone group). Therefore, it was concluded that combination therapy might add some benefits in improvement of reproductive performance based on the findings of better symptom control and a lower relapse rate, although no evidence has supported this hypothesis yet.

## Conclusion

There is more evidence supporting the advantages of conservative surgery or UAE, in providing not only more effective symptom relief but also longer durable symptom control for symptomatic women with uterine adenomyosis and/or adenomyoma, compared with medical treatment alone, such as GnRH agonist alone. Furthermore, reproductive performance after conservative surgery seemed to be improved compared with that after GnRH agonist treatment; not only was there a longer cumulative pregnancy rate, but also a higher cumulative final successful delivery rate. Therefore, we recommend that subfertile women with the diagnosis of uterine adenomyosis or adenomyoma try GnRH agonist treatment first; then, these women should undergo an active therapy strategy to improve fecundity. Pregnancy frequently occurs within 6 months after completing medical treatment. If no pregnancy occurs, conservative surgery, regardless of GnRH agonist treatment or not, may be an alternative consideration in the management of severely symptomatic uterine adenomyosis and/or uterine adenomyoma, not only for symptom control, but also to increase reproductive performance. Future research addressing the relationship between adenomyosis/adenomyoma and fertility is worthwhile.

## Acknowledgments

This work was supported in part by grants from Taipei Veterans General Hospital (grant nos. V96ED1-003, V97ED1-008 and V98F-009) and the TVGH-NTUH Joint Research Program (grant no. 98VN-015), Taiwan.

## References

1. Ozaki T, Takahashi K, Okada M, Kurioka H, Miyazaki K. Live birth after conservative surgery for severe adenomyosis following magnetic resonance imaging and gonadotropin-releasing hormone agonist therapy. *Int J Fertil* 1999;44:260–4.
2. Levgur M. Therapeutic opinions for adenomyosis: a review. *Arch Gynecol Obstet* 2007;276:1–15.

3. Kepkep K, Tuncay YA, Göynümer G, Tutal E. Transvaginal sonography in the diagnosis of adenomyosis: which findings are most accurate? *Ultrasound Obstet Gynecol* 2007;30:341–5.
4. Fedele L, Bianchi S, Dorta M, Arcaini L, Zanotti F, Carinelli S. Transvaginal ultrasonography in the diagnosis of diffuse adenomyosis. *Fertil Steril* 1992;58:94–7.
5. Atzori E, Tronci C, Sionis L. Transvaginal ultrasound in the diagnosis of diffuse adenomyosis. *Gynecol Obstet Invest* 1996; 42:39–41.
6. Levgur M. Diagnosis of adenomyosis. *J Reprod Med* 2007; 52:177–93.
7. Matalliotakis IM, Katsikis IK, Panidis DK. Adenomyosis: what is the impact on fertility? *Curr Opin Obstet Gynecol* 2005; 17:261–4.
8. Reinhold C, McCarthy S, Bret PM, et al. Diffuse adenomyosis: comparison of endovaginal US and MR imaging with histopathologic correlation. *Radiology* 1996;199:151–8.
9. Chopra S, Lev-Toaff AS, Ors F, Bergin D. Adenomyosis: common and uncommon manifestations on sonography and magnetic resonance imaging. *J Ultrasound Med* 2006;25: 617–27.
10. Wu MH, Pan HA, Chang FM. Three-dimensional and power Doppler ultrasonography in infertility and reproductive endocrinology. *Taiwan J Obstet Gynecol* 2007;46:209–14.
11. Bazot M, Darai E, Rouger J, Detchev R, Cortez A, Uzan S. Limitations of transvaginal sonography for the diagnosis of adenomyosis with histopathological correlation. *Ultrasound Obstet Gynecol* 2002;20:605–11.
12. Tamai K, Togashi K, Ito T, Morisawa N, Fujiwara T, Koyama T. MR imaging findings of adenomyosis: correlation with histopathologic features and diagnostic pitfalls. *Radiographics* 2005;25:21–40.
13. Jeng CJ, Huang SH, Shen J, Chou CS, Tzeng CR. Laparoscopy-guided myometrial biopsy in the definite diagnosis of diffuse adenomyosis. *Hum Reprod* 2007;22:2016–9.
14. Wang PH, Fuh JL, Chao HT, Liu WM, Cheng MH, Chao KC. Is the surgical approach beneficial to subfertile women with symptomatic extensive adenomyosis? *J Obstet Gynaecol Res* 2009;35:495–502.
15. Wang PH, Lee WL, Cheng MH, Yen MS, Chao KC, Chao HT. Use of a gonadotropin-releasing hormone agonist to manage perimenopausal women with symptomatic uterine myomas. *Taiwan J Obstet Gynecol* 2009;48:133–7.
16. Liu WM, Wang PH, Tang WL, Wang IT, Tzeng CR. Uterine artery ligation for treatment of pregnant women with uterine leiomyomas who are undergoing cesarean section. *Fertil Steril* 2006;86:423–8.
17. Kim MD, Kim NK, Kim HJ, Lee MH. Pregnancy following uterine artery embolization with polyvinyl alcohol particles for patients with uterine fibroid or adenomyosis. *Cardiovasc Intervent Radiol* 2005;28:611–5.
18. Owolabi TO, Strickler RC. Adenomyosis: a neglected diagnosis. *Obstet Gynecol* 1977;50:424–7.
19. Siegler AM. Adenomyosis. *J Reprod Med* 1994;39:841–53.
20. Wood C. Surgical and medical treatment of adenomyosis. *Hum Reprod Update* 1998;4:323–36.
21. Devlieger R, D'Hooghe T, Timmerman D. Uterine adenomyosis in the infertility clinic. *Hum Reprod Update* 2003;9: 139–47.
22. Honore LH, Cumming DC, Dunlop DL, Scott JZ. Uterine adenomyoma associated with infertility: a report of three cases. *J Reprod Med* 1988;33:331–5.
23. Grow DR, Filer RB. Treatment of adenomyosis with long-term GnRH analogues: a case report. *Obstet Gynecol* 1991;78:538–9.
24. Hirata JD, Moghissi KS, Ginsburg KA. Pregnancy after medical therapy of adenomyosis with gonadotropin-releasing hormone agonist. *Fertil Steril* 1993;59:444–5.
25. Nelson JR, Corson SL. Long-term management of adenomyosis with a gonadotropin-releasing hormone agonist. *Fertil Steril* 1993;59:441–3.
26. Wood C, Maher P, Hill D. Biopsy diagnosis and conservative surgical treatment of adenomyosis. *Aust N Z J Obstet Gynaecol* 1993;33:319–21.
27. Silva PD, Perkins HE, Schauberger CW. Live birth after treatment of severe adenomyosis with a gonadotropin-releasing hormone agonist. *Fertil Steril* 1994;61:171–2.
28. Wood C, Maher P, Hill D. Biopsy diagnosis and conservative surgical treatment of adenomyosis. *J Am Assoc Gynecol Laparosc* 1994;1:313–6.
29. Huang WH, Yang TS, Yuan CC. Successful pregnancy after treatment of deep adenomyosis with cytoreductive surgery and subsequent gonadotropin-releasing hormone agonist: a case report. *Zhonghua Yi Xue Za Zhi (Taipei)* 1998;61:726–9.
30. Huang FJ, Kung FT, Chang SY, Hsu TY. Effects of short-course buserelin therapy on adenomyosis: a report of two cases. *J Reprod Med* 1999;44:741–4.
31. Lin J, Sun C, Zheng H. Gonadotropin-releasing hormone agonists and laparoscopy in the treatment of adenomyosis with infertility. *Chin Med J (Engl)* 2000;113:442–5.
32. Wang PH, Yang TS, Lee WL, Chao HT, Chang SP, Yuan CC. Treatment of infertile women with adenomyosis with a conservative microsurgical technique and a gonadotropin-releasing hormone agonist. *Fertil Steril* 2000;73:1061–2.
33. Wang CJ, Yuen LT, Chang SD, Lee CL, Soong YK. Use of laparoscopic cytoreductive surgery to treat infertile women with localized adenomyosis. *Fertil Steril* 2006;86:462.e5–8.
34. Rabinovici J, Inbar Y, Eylon SC, Schiff E, Hananel A, Freundlich D. Pregnancy and live birth after focused ultrasound surgery for symptomatic focal adenomyosis: a case report. *Hum Reprod* 2006;21:1255–9.
35. Cheng MH, Chao HT, Wang PH. Medical treatment for uterine myomas. *Taiwan J Obstet Gynecol* 2008;47:18–23.
36. Lee WL, Liu RS, Yuan CC, Chao HT, Wang PH. Relationship between gonadotropin-releasing hormone agonist and myoma cellular activity: preliminary findings on positron emission tomography. *Fertil Steril* 2001;75:638–9.
37. Chia CC, Huang SC, Chen SS, et al. Ultrasonographic evaluation of the uterine fibroids induced by treatment with a GnRH analog. *Taiwan J Obstet Gynecol* 2006;45:124–8.
38. Parsanezhad ME, Azmoon M, Alborzi S, et al. A randomized, controlled clinical trial comparing the effects of aromatase inhibitor (letrozole) and gonadotropin-releasing hormone agonist (triptorelin) on uterine leiomyoma volume and hormonal status. *Fertil Steril* doi: 10.1016/j.fertnstert.2008.09.064 (In press).
39. Wilson AC, Meethal SV, Bowen RL, Atwood CS. Leuprolide acetate: a drug of diverse clinical applications. *Expert Opin Investig Drugs* 2007;16:1851–63.

40. Cheng MH, Wang PH. Uterine myoma: a condition amendable to medical therapy? *Expert Opin Emerg Drugs* 2008;13: 119–33.
41. Ravina JH, Herbreteau D, Ciraru-Vigneron N, Bouret JM, Houdart E, Aymard A, Merland JJ. Arterial embolisation to treat uterine myomata. *Lancet* 1995;346:671–2.
42. Rabinovici J, Stewart EA. New interventional techniques for adenomyosis. *Best Pract Res Clin Obstet Gynaecol* 2006;20: 617–36.
43. Simsek M, Sadik S, Taskin O, et al. Role of laparoscopic uterine artery coagulation in management of symptomatic myomas: a prospective study using ultrasound and magnetic resonance imaging. *J Minim Invasive Gynecol* 2006; 13:315–9.
44. Liu WM, Wang PH, Chou CS, Tang WL, Wang IT, Tzeng CR. Efficacy of combined laparoscopic uterine artery occlusion and myomectomy via minilaparotomy in the treatment of recurrent uterine myomas. *Fertil Steril* 2007; 87:356–61.
45. Wang PH, Liu WM, Fuh JL, Chao HT, Chao KC, Yuan CC. Laparoscopic uterine vessel occlusion in the management of women with symptomatic uterine myomas with and without adding laparoscopic myomectomy: 4-year results. *J Minim Invasive Gynecol* 2008;15:712–8.
46. Holub Z, Mara M, Kuzel D, Jabor A, Maskova J, Eim J. Pregnancy outcomes after uterine artery occlusion: prospective multicentric study. *Fertil Steril* 2008;90:1886–91.
47. Wang PH, Liu WM, Fuh JL, Chao HT, Yuan CC, Chao KC. Symptomatic myoma treated with laparoscopic uterine vessel occlusion and subsequent immediate myomectomy: which is the optimal surgical approach? *Fertil Steril* 2009;92:762–9.
48. Liu WM, Tzeng CR, Yi-Jen C, Wang PH. Combining the uterine depletion procedure and myomectomy may be useful for treating symptomatic fibroids. *Fertil Steril* 2004;82:205–10.
49. Siskin GP, Tublin ME, Stainken BF, Dowling K, Dolen EG. Uterine artery embolization for the treatment of adenomyosis: clinical response and evaluation with MR imaging. *AJR Am J Roentgenol* 2001;177:297–302.
50. Mara M, Maskova J, Fucikova Z, Kuzel D, Belsan T, Sosna O. Midterm clinical and first reproductive results of a randomized controlled trial comparing uterine fibroid embolization and myomectomy. *Cardiovasc Intervent Radiol* 2008;31: 73–85.
51. American College of Obstetricians and Gynecologists. ACOG Committee Opinion no. 293: uterine artery embolization. *Obstet Gynecol* 2004;103:403–4.
52. Goldberg J, Pereira L. Pregnancy outcomes following treatment for fibroids: uterine fibroid embolization versus laparoscopic myomectomy. *Curr Opin Obstet Gynecol* 2006;18:402–6.
53. Wang PH, Liu WM, Fuh JL, Cheng MH, Chao HT. Comparison of surgery alone and combined surgical-medical treatment in the management of symptomatic uterine adenomyoma. *Fertil Steril* 2009;92:876–85.
54. Yen MS, Yang TS, Yu KJ, Wang PH. Comments on laparoscopic excision of myometrial adenomyomas in patients with adenomyosis uteri and main symptoms of severe dysmenorrhea and hypermenorrhea. *J Am Assoc Gynecol Laparosc* 2004;11:441–2.
55. Vercellini P, Maddalena S, De Giorgi O, Aimi G, Crosignani PG. Abdominal myomectomy for infertility: a comprehensive review. *Hum Reprod* 1998;13:873–79.
56. Fujishita A, Masuzaki H, Khan KN, Kitajima M, Ishimaru T. Modified reduction surgery for adenomyosis: a preliminary report of the transverse H incision technique. *Gynecol Obstet Invest* 2004;57:132–8.
57. Strizhakov AN, Davydov AI. Myometrectomy—a method of choice for the therapy of adenomyosis patients in the reproductive period. *Akush Ginekol (Mosk)* 1995;(5):31–3. [In Russian]