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Review

Uterine Fibroids-A Comprehensive Review On Symptoms, Diagnosis And Treatment

M. Yasmeen[1*], Dr. P. Amudha[2], V. K. Kishore[3], N. G. Lokeshwaran[4], K. S.Maheshwar[5], N. Kebinson[6], Harshita. M .Jain[7]

[1,3-7]Scholar, Department of Pharmacology, C.L.Baid Metha College of Pharmacy, Thoraipakkam, Chennai-6000097, TamilNadu, India.
[2] HOD, Department of Pharmacology, C.L.Baid Metha College of Pharmacy, Thoraipakkam, Chennai-6000097, TamilNadu, India.

*Author for Correspondence: Ms. M.Yasmeen
Email: hyasmeen856@gmail.com

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Abstract

Uterine fibroids, alternatively referred to as leiomyomas or myomas, constitute the most commonly observed benign gynecological disorder in individuals who exhibit symptoms such as atypical uterine hemorrhage, pelvic masses that generate sensations of pressure or discomfort, challenges related to infertility, and complications during pregnancy. It is observed that a specific subset of patients may display enduring pelvic pain and dyspareunia.The current strategies for managing symptomatic uterine fibroids include expectant observation, pharmacotherapy, surgical procedures, and interventions associated with interventional radiology. The intent of this careful and explanatory review is therefore to bring available information together on symptoms, diagnosis, and treatment of uterine fibroids, in particular, what has lately been achieved in the field of medicine and clinical practice, consequences for women's health, and effectiveness of the modalities of treatment including drugs, surgical interventions, and new minimally invasive procedures.In the end, their combination will provide a global picture on understanding and resolving the problems related to uterine fibroids so that better care of patients can be provided by taking a holistic approach.

Keywords: fibroids, imaging techniques, surgical options, hormonal treatment.

INTRODUCTION

One of the most prevalent benign tumors, uterine fibroids affect around 70% of women who are of reproductive age[1].These are brought on by the development of fibrous and muscle tissue, which can attach itself to the uterine wall or get entrenched in it. Depending on how deep they go, they are classified as submucosal, intramural, or subserous[2].These include irregularities in certain genes, disruptions in the normal function of growth-promoting substances, abnormalities within the blood vessels supplying the uterus, and the way uterine

tissue responds to injury or damage. Uterine fibroids, benign tumors in the uterus, are incredibly common, appearing in an estimated 80-90% of women by the time they reach 50. While more than half of premenopausal women with fibroids don't have any symptoms and just happen to find them by chance during regular pelvic exams, for others, these growths can result in a number of problems[3].A woman may experience serious effects from discomfort, heavy menstrual bleeding, or even infertility on her quality of life. The risk of fibroids varies among women and is impacted by age and ethnicity, among other things. While the exact cause remains unclear, research suggests that multiple factors likely contribute to their development. Key among these are hormonal influences, particularly the significant roles played by estrogens and progesterone.

Symptoms

Major indications comprise abnormal uterine bleeding [AUB], heavy menstrual bleeding [HMB], pelvic discomfort, voluminous symptoms, and infertility, all of which impact the quality of life [QoL] of individuals[4].

Abnormal uterine bleeding[aub]

Disorders of the uterine corpus constitute abnormal bleeding patterns if they differ from the norm in terms of regularity, volume, frequency or duration and are referred to as AUB. This makes them as presenting symptoms to those in which heavy menstrual bleeding, irregular menstrual bleeding and intermittent or intermenstrual bleed are the common occurrences seen among women of reproductive age affecting their quality of life significantly[5].Of particular interest is that abnormal uterine bleeding in women of reproductive age represents up to 30-40% of consultations at gynecological outpatient clinics[7].

The terminology associated with abnormal uterine bleeding was updated by the International Federation of Gynecology and Obstetrics [FIGO] in 2011, leading to its classification as PALM-COEIN [Polys, adenomyosis, leiomyoma, malignancy, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic and not yet classified]. Based on the timing and onset of symptoms, AUB can be divided into acute and chronic categories.When women of reproductive age experience acute bleeding, it is not associated with pregnancy and necessitates immediate medical attention. On the other hand, large, irregular, and prolonged bleeding that comes from the uterine corpus and lasts for at least six months is known as chronic bleeding[6].When managing women with abnormal uterine bleeding, the initial step involves conducting a comprehensive evaluation encompassing a detailed medical history, thorough physical examination, and appropriate imaging studies to rule out any significant structural abnormalities. Following the exclusion of structural causes, medical interventions are typically recommended as the primary line of treatment Notably, abnormal uterine bleeding linked to leiomyoma [AUB-L] and resultant iron deficiency anemia can be attributed to submucosal and intramural fibroids. Additionally, the presence of large fibroids may result in symptoms arising from pressure exerted on neighboring organs, often manifesting as issues like bowel or bladder dysfunction, or dyspareunia[8].

Heavy menstrual bleeding[hmb]

HMB, a subgroup of AUB, is defined as monthly blood loss exceeding 80 milliliters and is more strongly associated with myomas.There is still much to learn about the connection between HMB and fibroids, especially regarding endometrial function in women who have structural myometrial characteristics like leiomyomas[9].Heavy menstrual bleeding, a condition where women experience abnormally heavy or prolonged menstrual periods, is estimated to affect a significant portion of the female population during their reproductive years. HMB was officially recognized as a symptom in the 2018 FIGO revision, with the definition being "excessive menstrual blood loss, which interferes with a woman's physical, social, emotional, and/or material quality of life." It may manifest alone or in conjunction with other symptoms like infertility or both acute and chronic pelvic pain[4].

Pelvic pain and pressure related symptoms

Pelvic pain or pressure is a commonly observed symptom among women affected by leiomyomas, the likelihood of experiencing pain among women with myomas is only marginally higher compared to those without myomas. The discomfort felt in the pelvic and abdominal regions by women with myomas is frequently described as a sensation of pressure, akin to the discomfort associated with uterine growth during pregnancy[10].Pelvic pain may also arise from degenerative alterations, a phenomenon often encountered during pregnancy. Management typically involves conservative approaches such as analgesics and rest. Dyspareunia, on the other hand, is a less frequently reported symptom It should be acknowledged that a subgroup of individuals might display enduring pelvic discomfort and dyspareunia[11].

Fertility issues

Fibroids might be the primary factor contributing to infertility. An analysis of results in infertile women demonstrated that those with fibroids located in any area exhibited notably reduced rates of clinical pregnancy, implantation, ongoing pregnancy, and live birth rates in comparison to the control group.No disparity was

observed concerning rates of preterm delivery. Furthermore, a distorted endometrial cavity due to submucosal fibroids poses a heightened risk of infertility. The precise pathomechanism by which intramural fibroids impact the overlying endometrium and alter receptivity remains incompletely elucidated. Fibroids may impede implantation through various mechanisms, such as heightened uterine contractility, disrupted cytokine profile, abnormal vascularization, and chronic inflammation[12].

Diagnosis

Fibroids impact women's health and quality of life so early detection and accurate diagnosis are important. Though magnetic resonance imaging is considered the most accurate diagnostic tool, ultrasonography remains the cheapest and extensively used method. The primary method that has been acknowledged universally is ultrasonography because it is a widely accessible, non-invasive procedure and which successfully detects uterine fibroids[13].Magnetic resonance imaging can be useful when planning surgery and also used as supplementary method for assessing vascularity, degeneration, and the potential for malignant transformation [leiomyosarcoma][10].

Variety of diagnostic techniques are used to identify and differentiate uterine fibroids.Transvaginal ultrasound is the most widely used and conveniently accessible instrument. The following uterine region alterations can be visualized with it, and they are likely to indicate uterine myomatous changes. Regular tumor borders, peripheral and intralesional vascularization, non-homogeneous echogenicity, and endometrial visibility are a few of them. These characteristics aid in their differentiation from other diseased structures, such as malignant tumors like sarcomas. The patient's age should always be considered while comparing the aforementioned feature.[1,14]. Transvaginal ultrasonography is a recent discovery in the history of contemporary uterine disease detection techniques. uterus's structure can be seen the most detailed and clearly by transvaginal ultrasonography and is more frequently recommended by gynecologists. While there is no specific preparation needed for the examination, you should arrive at a transvaginal ultrasound empty-bladder, in contrast to a transabdominal ultrasound. An endovaginal sensor is used in this study even in cases when the nodes are extremely small, the TVUZI approach is the most sensitive, more informative, accessible, and has a greater resolution for the identification of nodular uterine fibroids utilizing a transvaginal sensor yields data regarding the existence of ultrasound indicators of uterine fibroids that have been histologically confirmed[15].The extent of submucosal fibroid tumors can be assessed using hysteroscopy and sonohysterography, however these procedures are quite painful[16].

Pharmacological treatment of uterine fibroids

Medical management is primarily focused on the reduction of heavy menstrual bleeding [HMB] and pain [dysmenorrhea, chronic pelvic pain] caused by uterine fibroids. The initial approach to symptomatic medical management involves the utilization of non-hormonal options such as non-steroidal anti-inflammatory drugs [NSAIDs] and tranexamic acid, given their widespread availability, cost-effectiveness, and minimal adverse effects[17].Estrogen has long been acknowledged as the primary hormone implicated in the formation and proliferation of uterine fibroids. Earlier research indicates that progesterone and its associated receptors also exert a notable influence on the development of fibroids. The dual proliferative and antiproliferative impacts of progesterone are subjects of ongoing investigation. Consequently, these hormones and their receptors represent the primary focus for pharmacological treatment of fibroids[18] Overall, the objective of long-term hormonal medical intervention is to alleviate symptoms associated with uterine fibroids in individuals who are not actively seeking pregnancy [due to the impact of these medications on ovulation] or in those who wish to postpone or avoid surgical interventions[17].

Medical therapy

Progestins

Progestins are typically used to address symptoms of uterine fibroids, such as excessive monthly flow. Progestins can diminish endometrial hyperplasia and induce endometrial shrinkage, perhaps alleviating fibroids-related excessive bleeding. However, there is scant evidence on tumor volume decrease and it has not been validated[20,21,22].They work by decreasing gonadotropin secretion and changing the hormonal milieu in the uterus. Progestins can be given orally, intramuscularly, or via an intrauterine device. The levonorgestrel-releasing IUS [LNG-IUS] is well-known for its ability to reduce menstrual bleeding and improve anaemia in fibroids patients. Progestins can efficiently regulate bleeding, but their effect on fibroid volume is unclear. According to certain research, progestins may not appreciably reduce the size of fibroids because progestins like P may promote the formation of fibroids. Danazol can help thin the endometrium before hysteroscopic surgery [19,23,24] however GnRH analogues are more effective. The United States FDA has approved the levonorgestrel-releasing IUS [LNG-IUS] to treat severe menstrual bleeding among IUS users. LNG-IUS can reduce fibroid-related uterine hemorrhage and improve anemia in women.[21,25] Inserting an IUS might be challenging for women with

submucosal fibroids, and the device may need to be removed more frequently[26,28]. However, the use of LNG-IUS may lower the rate of hysterectomy and increase patient satisfaction[27]

Selective estrogen receptor modulators[SERMS]

Selective Estrogen Receptor Modulators [SERMs] are a class of drugs that have been studied for the treatment of uterine fibroids. SERMs act on estrogen receptors in a tissue-specific way, which means they can have both agonist and antagonistic effects depending on the target tissue. They are known to have antiestrogenic properties, which can assist inhibit cell growth in fibroid tissues. Raloxifene, a widely studied SERM, has demonstrated some therapeutic benefit in fibroids in premenopausal women. Clinical investigations have shown that it can suppress cell proliferation[29,30,31,32] in fibroid tissues, however the findings have been varied, with some studies demonstrating limited effectiveness. Raloxifene may help manage fibroids-related symptoms, such as heavy monthly flow, without the endometrial agonist action[33] seen with other therapies like as tamoxifen. As a result, SERMs may be a safer option for women concerned about their endometrial health. Despite some promising results, SERMs' overall therapeutic efficacy in treating fibroids is regarded as limited. The increase in estrogen secretion that occurs after SERM treatment in premenopausal women may further affect its effectiveness.While SERMs are a promising area of research, more extensive studies are needed to fully establish their role and efficacy in the management of uterine fibroids. SERMs provide a selective approach in managing fibroid symptoms, but their overall impact on fibroid size and long-term efficacy remains unknown[34,35].

Aromatase inhibitors

Aromatase inhibitors [AIs] are used to treat uterine fibroids because of their capacity to decrease estrogen synthesis, which has been linked to fibroid growth.AIs inhibit the aromatase enzyme, which transforms androgens into estrogens, lowering estrogen levels in the blood[36].This is significant because estrogen encourages the formation of uterine fibroids.Studies have demonstrated that AIs can significantly reduce fibroid size and relieve fibroids' symptoms. In terms of efficacy for fibroids shrinkage, they are thought to be comparable to GnRH agonists[36-38].In observational studies, AIs such as letrozole and anastrozole were found to reduce fibroid volume and improve symptoms. However, there aren't many randomized controlled trials. AIs are especially appealing for usage in postmenopausal women and those with estrogen-sensitive diseases since they allow for the management of fibroids without the negative effects associated with hormonal therapy that raise estrogen levels. While encouraging, the evidence supporting the routine use of AIs for uterine fibroids is limited, and more study is needed to determine their long-term safety and efficacy[39-41].

GnRH agonists

Gonadotropin-releasing hormone [GnRH] agonists are used to treat uterine fibroids primarily because of their ability to lower estrogen levels, which can help decrease fibroids and relieve related symptoms. GnRH agonists stimulate the pituitary gland to release luteinizing hormone [LH] and follicle-stimulating hormone. This initially increases estrogen and progesterone levels, but continuous usage causes downregulation of GnRH receptors, resulting in decreased production of these hormones and, as a result, estrogen levels[42,43].The fall in estrogen levels reduces fibroid size and relieves symptoms like heavy monthly flow[44].Clinical trials have indicated that GnRH agonists can reduce fibroid volume by 50 percent or more. GnRH agonists can reduce fibroid size while also controlling bleeding and correcting anemia caused by heavy menstrual flow[45,46,47]. If additional surgical operations are required, this can make things easier. GnRH agonists have a transient effect on fibroid growth, usually lasting only as long as the medication is administered. When treatment is stopped, the volume of the fibroid often increases. GnRH agonists can also produce low estrogen-related adverse effects such hot flashes and decreased bone density. To lessen the risk of bone loss and other estrogen deficiency symptoms, add-back therapy with estrogen or progestins may be employed[48,49].

GnRH antagonists

GnRH antagonists act by directly inhibiting GnRH receptors in the pituitary gland, causing the release of luteinizing hormone [LH] and follicle-stimulating hormone [FSH] to decrease dramatically[50,51].This causes a quick drop in estrogen levels, which is critical since estrogen stimulates fibroid growth.These medicines can significantly reduce uterine and fibroid volume within a few weeks of treatment[52]. They are excellent at treating fibroids-related symptoms like heavy menstrual bleeding and pelvic pain.Unlike GnRH agonists, which first raise hormone levels before lowering them, GnRH antagonists block estrogen immediately, providing for rapid symptom relief. Clinical research has demonstrated that GnRH antagonists can significantly reduce fibroid growth and alleviate symptoms[53,54].They are very beneficial as a preoperative treatment to reduce fibroids before surgery.While GnRH antagonists have a lower risk of side effects than GnRH agonists, they can nevertheless cause low estrogen symptoms like hot flashes and vaginal dryness. They do not, however, often induce the same level of bone density loss as GnRH agonists when used for an extended period[55].

Selective progesterone receptor modulators [SPRMs]

SPRMs operate on progesterone receptors and can have agonist, antagonist, or mixed effects depending on the cellular context. They influence the effects of progesterone, which is implicated in the development and maintenance of fibroids[56].SPRMs can diminish fibroid cell proliferation and trigger apoptosis by inhibiting or modifying progesterone signaling. Clinical research have demonstrated that SPRMs such ulipristal acetate [UPA] and mifepristone can considerably reduce fibroid volume[57,58,59].According to studies, therapy with SPRMs can reduce fibroid size by 17% to 57% while simultaneously decreasing uterine volume by 9% to 53%.SPRMs are efficient at controlling heavy menstrual bleeding caused by fibroids[60,61].They can provide quick relief from bleeding symptoms, usually within a week of starting treatment ,which is faster compared to GnRH agonists. One of the primary advantages of SPRMs is their capacity to retain efficacy in lowering fibroid size and regulating symptoms for an extended length of time, even after therapy withdrawal. This makes them an excellent option for women who want to avoid surgery or protect their fertility. While SPRMs are efficacious, they can have negative effects, such as affecting the endometrium and hormonal balance[62].Long-term safety data are still being studied, and endometrial health issues may limit the usage of these drugs. SPRMs are gradually becoming acknowledged as a potential therapy option for uterine fibroids, particularly for women who want to avoid surgery or choose non-invasive management options[63].Ongoing study continues to investigate their long-term efficacy and safety in clinical practice.

Mifepristone

Mifepristone, a selective progesterone receptor modulator [SPRM], operates by inhibiting progesterone receptors in the uterus, reducing the effects of progesterone[64,65].This inhibition reduces fibroid cell proliferation and promotes extracellular matrix degradation, resulting in smaller fibroids. Mifepristone has been found in studies to considerably reduce the size of uterine fibroids while also improving symptoms including heavy monthly flow and pelvic pain. It is very useful for women with symptomatic fibroids.Mifepristone has been shown in studies to significantly reduce fibroid volume while also improving quality of life. It is frequently explored for women who desire a non-surgical option or are not suitable for surgery. Mifepristone's common adverse effects include abdominal pain, nausea, exhaustion, and changes in menstrual flow patterns[66,67].While it is generally well tolerated, it may cause endometrial alterations that require close monitoring.Mifepristone is commonly used in a cyclical fashion, with treatment durations varied depending on individual patient needs and reactions[68].Long-term use may be restricted due to the possibility of negative effects and the requirement for monitoring.

Danazol

Danazol is a synthetic steroid used to treat uterine fibroids [UF] because it inhibits sex-steroid synthesis and directly inhibits the progesterone receptor. Although it was more often used for endometriosis, some researches have looked into its usefulness for UF. A short trial of 20 women found a considerable reduction in tumor volume [about 23.6% ± 5%] and partial to total symptomatic relief, which lasted up to six months following therapy discontinuation[69].However, higher quality research is scarce, and the Cochrane Collaboration discovered no randomized controlled trials [RCTs] supporting the efficacy of danazol for UF therapy[70]. Danazol is also associated with severe side effects due to its androgenic qualities, such as hirsutism, acne and weight gain , which limits its use in clinical practice[71].

Gestrinone

Gestrinone is a steroid having antiestrogenic and antiprogestogenic characteristics that has been investigated for the treatment of uterine fibroids. It has showed potential in lowering fibroid volumes, with some trials claiming reductions of up to 60%[72].A recent open-label trial of 16 women found that gestrinone treatment led to amenorrhea [absence of menstruation] in 69% of participants after six months, as well as an average tumor volume decrease of 32% ± 10.8%. However, like danazol, there is limited convincing data to support the widespread use of gestrinone for UF therapy, and more high-quality trials are needed to confirm its efficacy and safety.

Other reliable therapeutic options

Radiofrequency ablation

Radiofrequency ablation [RFA] is a minimally invasive treatment for uterine fibroids that employs thermal energy to cause coagulative necrosis and reduce the fibroid tissue. Eleven publications showed changes in uterine or fibroid volume reduction utilizing non-commercial, off-the-shelf RFA devices, which were frequently repurposed from systems developed treating hepatic tumors.The AcessaVR System, a commercial laparoscopic RFA system [Halt Medical, Brentwood, CA], achieved a 45.1% reduction in total fibroid volume after 12 months[75].The SonataVR System, a transcervical RFA device [Gynesonics, Redwood City, CA] in commercial use in Europe and the United States, demonstrated a 66.6% reduction in total fibroid volume after 12

months.[76,77].Galen *et al.*, presented findings from pilot investigations of a commercial laparoscopic RFA device conducted across multiple centers and research[73].Yin et al. divided their patients into premenopausal and menopausal groups. However, the concept of menopausal was ambiguous, as some menopausal women looked to continue menstruation[74].The combined data from numerous research revealed that fibroid volume decreased over time. The means of the studies at each time point were combined, with the lowest and highest reported decreases included.Four articles focused on uterine volume decreases after RFA, with maximum reductions ranging from 20% to 40% and minimum reductions of 15%.

Uterine artery embolization[uae]

Uterine artery embolization [UAE] is a type of minimally-invasive procedure used to treat fibroids in the uterus[78,79].The patient is given sedatives and local anaesthesia. General anesthesia may be utilized in certain situations.To gain access to the femoral artery, a tiny incision is made in the groin.A catheter [a thin, flexible tube] is placed into the femoral artery and led to the uterine arteries using fluoroscopic [X-ray] guidance. Once the catheter is in place, small particles [typically polyvinyl alcohol or a similar substance] are injected into the uterine arteries. These particles disrupt blood supply to the fibroids, causing them to shrink . Imaging is used to monitor the treatment and ensure that the particles are properly positioned and blood supply to the fibroids is sufficiently decreased. Following the procedure, the catheter is withdrawn, and pressure is given to the incision site to prevent bleeding. Typically, the patient is examined for a few hours and may be admitted to the hospital overnight. UAE is less intrusive and has a shorter recovery period than other surgical alternatives such as hysterectomy or myomectomy.Preserves the uterus, which is critical for women who want to remain fertile.Effective in alleviating symptoms such as excessive menstrual bleeding, pelvic pain, and pressure. Post-embolization syndrome, which includes discomfort, fever, and nausea, usually goes away after a few days.There is a rare possibility injury to uterine or other organ [80,81,82].Overall, UAE is an excellent therapy choice for women who have symptomatic fibroids and want a less intrusive alternative to surgery.

Surgical methods

Hysterectomy

Hysterectomy is the most prevalent indication for uterine removal surgery, accounting for more than 30% of all such surgeries [84].In women with fibroids, hysterectomy is frequently performed for symptomatic relief, particularly when the uterus is enlarged above the size of a 12-week pregnancy or there are substantial symptoms such as heavy bleeding or pelvic pain.The treatment can be done in a variety of ways, including abdominal, vaginal, and laparoscopic techniques. The surgeon's competence, as well as the size and location of the fibroids, may influence the approach used. According to studies, a hysterectomy can significantly improve symptoms and quality of life for people suffering from fibroid concerns.[86] However, it is a permanent therapy that eliminates the potential of more pregnancies.While hysterectomy can help with symptom alleviation, it is not suggested for asymptomatic women unless there are additional concerns, such as the risk of cancer[83,84,85] Additionally, some women may develop new symptoms following a hysterectomy, such as hot flashes or weight gain.[87] Although most studies on the impact of hysterectomy on sexuality are poorly constructed, existing information suggests that it is not detrimental to sexuality[88]

Myomectomy

Myomectomy is a surgical technique that removes uterine fibroids while keeping the uterus, making it an ideal alternative for women who want to keep their fertility[89].A myomectomy is usually suggested for women who have symptomatic fibroids and want to keep their fertility intact. It is especially effective for patients who are experiencing pelvic pain, heavy menstrual bleeding or other fibroids-related issues. Several techniques can be used to accomplish the process, including: Laparotomy [an open surgical method].Laparoscopy [a minimally invasive procedure that involves small incisions and a camera]. Hysteroscopy [a procedure of removing submucosal fibroids through the cervix.]. Myomectomy can effectively treat fibroids-related problems, and many women report a considerable improvement in their quality of life after surgery. However, the recurrence rate of fibroids is predicted to be 15% to 30% after five years, depending on the number and size of the fibroids removed.While myomectomy retains the uterus and fertility, it has surgical risks similar to hysterectomy. The procedure's success can vary depending on the individual's unique circumstances, such as the size and location of the fibroids. Myomectomy is an excellent therapy choice for women with uterine fibroids who want to relieve their symptoms while maintaining their reproductive potential. It strikes a compromise between effective symptom treatment and the desire for subsequent pregnancies[90].

CONCLUSION

In conclusion, uterine fibroids are a common gynecological condition that affects a significant number of women, particularly during their reproductive years. The review has highlighted the diverse range of symptoms

associated with uterine fibroids, including heavy menstrual bleeding, pelvic pain, and infertility. The review should also cover the various diagnostic modalities used to detect and characterize uterine fibroids, including pelvic examination, imaging techniques like ultrasound and MRI. This comprehensive review has provided an in-depth analysis of the symptoms, diagnosis, and treatment options available for uterine fibroids.

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