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Fibroadenoma treatment strategies

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Abstract

Background. Fibroadenoma is a very common benign tumor in young women. Surgery is the standard treatment for fibroadenomas. However, cosmetic changes after breast surgery cause psychological problems that impair patients' quality of life. For these reasons, nowadays it is very important to individualize the treatment of fibroadenomas using nonsurgical treatment methods.

Aim: to review feasible treatment methods for fibroadenoma and indications, with a focus on recent advancements.

Methods. A literature review was conducted in the PubMed database, using the keywords. "fibroadenoma", "fibroadenoma treatment", "fibroadenoma advancements", and "fibroadenoma treatment management". The date was from 2014 to 2024, and the study was limited to English-language publications (n = 47).

Results. Fibroadenomas, often managed with traditional surgical excision (500,000 surgeries/year worldwide), can also be observed due to their low malignancy risk (0.002 - 0.0125 %). Observation is suitable for non-growing, asymptomatic lumps, especially in patients under 35. Minimally invasive methods offer aesthetic and recovery advantages over surgery, but surgical excision remains common for larger or symptomatic fibroadenomas. Pharmacological treatments like Metformin show potential, but others, like Ormeloxifene, are less effective and have significant side effects.

Conclusions. The treatment of fibroadenomas depends on the size, symptoms, and patient preference. Small, nongrowing fibroadenomas usually require regular checkups, while larger, symptomatic, or growing tumors may need surgical resection or minimally invasive procedures. Minimally invasive approaches offer advantages in recovery, cosmetic outcome, and safety, and can save time, help avoid scars, and reduce surgical costs.

Keywords: fibroadenoma, fibroadenoma treatment, fibroadenoma advancements, fibroadenoma treatment management.

1. Introduction

Fibroadenomas are benign breast tumors that are common among women aged 14-35 years. About 10 % of women worldwide will have fibroadenomas in their lifetime (1). As mentioned above, fibroadenomas are most common in women and very rare in men (2). Iatrogenic male fibroadenomas occur due to prostate carcinoma treatment and in male-to-male transgender people as a result of estrogen therapy (3). Of all breast biopsies fibroadenoma accounts for 30 to 75 % (4). The pathogenesis of fibroadenoma is not well-known. It is believed that fibroadenoma develops due to changes in hormone levels, obesity and family history (5). The connective tissues of the stroma and epithelium of fibroadenoma contain estrogen and progesterone receptors that can cause excessive growth of breast tissue. MED12 (the mediator complex subunit 12) gene also promotes the formation of fibroadenomas (1). Fibroadenoma in the family history can be an important risk factor for the development of fibroadenoma (6). It is usually unilateral, non-cancerous, and a painless breast tumor that resolves itself in approximately 60 % of all fibroadenoma cases and therefore is less common in post-menopausal women (7). For this reason, fibroadenomas are usually observed. Although the likelihood of malignancy is low (0.002 to 0.0125 %) (8), surgery is the standard treatment for fibroadenoma. However, cosmetic changes after breast surgery or permanent thoughts about the malignancy in observation often lead to psychological problems, which impair patients' quality of life (9). This article aims to review feasible treatment methods for fibroadenoma and indications, with a focus on recent advancements.

2. Methods

A literature review was conducted in the Medline (PubMed) database. The included data varied from 2014 to 2024. A detailed search, including the

keywords "fibroadenoma", "fibroadenoma treatment", "fibroadenoma advancements", "fibroadenoma treatment management" has revealed a total of 276 articles. Records titles and abstracts limited to English language (n = 148). Full-text articles assessed for eligibility (n = 47).

3. Results

3.1. Treatment Strategies

Even though nowadays there is a diversity of fibroadenoma treatment options, the most common ones are traditional methods, for example, surgical excision (500,000 surgeries/year worldwide) and observation (8). The other treatment options for fibroadenoma are presented in **Error! Reference source not found.** (8,10,11). The goals of nonsurgical treatment of breast fibroadenoma are to stop lesion growth and reduce palpable mass while maintaining acceptable cosmetic results (12).

3.1.1. Observation

Removing the lump solves the problem, but surgery is not always needed and may have bad cosmetic outcomes as well as be a burden on the healthcare system, especially when some of these lumps disappear on their own (13). Fibroadenomas with no symptoms that are not growing rapidly and cause no cosmetic issues can be observed yearly by performing an ultrasound. However, if the patient is worried about observation and experiences anxiety about malignancy despite the low risk (less than 1%), removal of asymptomatic fibroadenomas may be considered. Indications for observation also include patients younger than 35 years old, sonographically typical fibroadenoma (14). It is recommended to perform clinical palpation and ultrasonography every 6 months. In patients whose disease is stable should be observed for 2 years, the observation interval may be extended to every 12 months (10).

Table 1. *Nonsurgical treatment and indications*

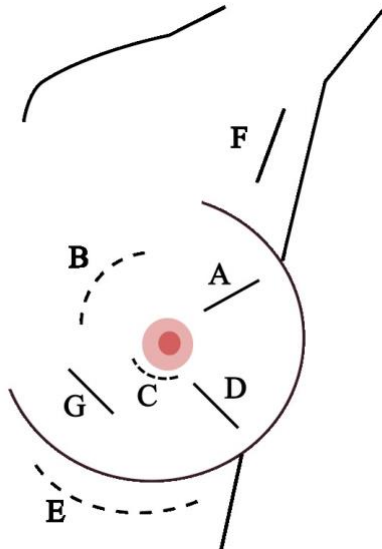
Treatment methods	Indications
Percutaneous ultrasound-guided cryoablation.	Visible on ultrasound. Confirmed histologically with core biopsy. Size less than 4 cm. Lesion near the skin.
Vacuum-assisted breast biopsy.	Smaller than 2-3 cm.
Laser ablation.	Size less than 20 mm.
Percutaneous microwave treatment.	Fibroadenomas > 2 cm. Adjacent to the areola.
Radiofrequency-assisted excision.	Multiple fibroadenoma.
High-intensity focused ultrasound.	Distance from the skin of ≤ 23 mm to the posterior, ≥ 5 mm from the anterior border of the fibroadenoma, and ≥ 11 mm from the focal point of the ultrasound treatment. The chest wall must be >1 cm from the posterior margin of the tumor.
Pharmacological methods.	Multiple fibroadenomas.

3.1.2. Surgical excision

Fibroadenoma size varies from 2 to 3 cm. Although, masses can range from < 1 cm to greater than 10 cm. The ones that are greater than 5 cm require surgical excision. Usually, they are found in the upper-outer quadrant of the breast (15). Surgical excision indications are shown in Table 2 (16–18). Fibroadenomas can be removed using either local or general anesthesia (19). Surgical resections for various benign breast tumors leave a significant scar. The optimal incisions to minimize visible scarring are inframammary and circumareolar. The size and location of a fibroadenoma influence the choice of incision site (Figure 1) (15). Radial and directly extended incisions (Figure A, D) should not be used in conservative breast surgery (20). Areolar or periareolar incision (Figure B, C) is used for fibroadenomas near the areola, offering good access and cosmetic outcomes. Superior circumareolar incision (Figure B) is used if the lump is further away. Periareolar incision (Figure C) is suitable for patients with an areolar diameter > 3.5-5 cm, mass-to-areola distance < 5 cm, fibroadenoma < 3 cm, and

age < 35. Contraindications include small areola, tumor > 5 cm, mass-to-areola distance > 6 cm, suspected malignancy, and age > 35 (21). With the periareolar technique, postoperative complications occurred faster (22). An inframammary incision (Figure E) is used if the lump is deep in the breast. This incision provides optimal tissue visualization and hides scars in the lower breast crease. It poses a low risk of breastfeeding issues and is suitable for fibroadenomas in the lower inner to lower outer breast quadrant (23). Axillary incision (Figure F) is used if the fibroadenoma is near the armpit. The surgeon may use an axillary incision to access it, resulting in less visible scarring on the breast but leaving a scar in the armpit (24). The choice of incision type depends on various factors, such as fibroadenoma location, size, the patient's preferences, or the surgeon's expertise. Nowadays, the requirements for a beautiful post-operative breast appearance are higher (25). It's essential to discuss these options with the surgeon to determine the most suitable approach for a specific case.

Figure 1. Incisions for removing lumps from the breast. A - superolateral radial incision, B - superior circumareolar incision, C - periareolar incision, D - inferolateral radial incision. E - inframammary fold incision, F - axillary incision, G - other incision.



3.1.3. Percutaneous ultrasound-guided cryoablation

Cryoablation uses the cytotoxic effects of cold to create tumor necrosis (26). Cryoablation is a safe and effective nonsurgical treatment for breast fibroadenomas, with optimal response in tumors smaller than 2 cm. Ultrasound follow-up is recommended every 6 months for 2 years (27). Cryoablation causes little discomfort after the procedure and does not result in deformity. The results show that 75 % of lesions are no longer palpable after treatment at 1-year follow-up (16).

3.1.4. Vacuum-assisted percutaneous therapeutic excisional biopsy

Vacuum-assisted breast biopsy (VAB) is effective at excising smaller fibroadenomas (less than 15 mm), but it is less successful with larger lesions (28). Complete excision effectiveness has been reported to be in a range from 70 to 100 % (29). Clinicians and patients favor VAB for its efficacy in lesion

removal, improved cosmetic outcomes, and suitability as a day-care procedure (30).

3.1.5. Percutaneous interstitial laser ablation

Percutaneous interstitial laser ablation (ILA) uses a portable diode laser to generate heat in tissues. The photothermal effect can be followed by magnetic resonance thermometry or by internal and accessory temperature monitors placed into the tissue (31). ILA relies on imaging for guidance, prioritizing demarcated lesions no larger than 20 mm (32). Major side effects include skin burns, and the most serious complication is pneumothorax (33). The treatment is done under local anesthesia with minimal pain and discomfort. It is aesthetically superior to lumpectomy (32).

3.1.6. Percutaneous microwave treatment

Percutaneous microwave treatment (MWA) is a promising thermal ablation technique (34). MWA offers better cosmetic results, less pain, and fewer complications, but surgery is still better because the recurrence rate is lower (35). Some studies showed that MWA is a very efficient treatment for fibroadenomas > 2 cm, without damage to normal tissue (36). The results of a study of 122 patients showed that cosmetic results after treatment with MWA were excellent (90.2 %) (34).

3.1.7. Radiofrequency-assisted excision

Radiofrequency-assisted excision (RFA) uses low-frequency radio waves and causes localized coagulative tissue necrosis (26). RFA works by heating water molecules and causing coagulation. The treatment goal for RFA is to ablate the whole lesion plus a 1 cm tissue rim to between 50–100° C for 9 minutes (31). The procedure is well tolerated by patients and is associated with minimal complications (37). RFA has advantages in the treatment of multiple fibroadenomas. Conducted

studies show that RFA can become the most suitable method for treating fibroadenomas due to such advantages as a high rate of complete ablation, little damage to the surrounding tissues, quick recovery after the procedure, and a cosmetic result that satisfies patients (8,38).

3.1.8. High-intensity focused ultrasound

High-intensity focused ultrasound (HIFU) is an ablation technique that uses an ultrasound beam to pass through the tissue as a high-frequency pressure wave that passes through the tissue causing protein denaturation and necrosis. Surrounding tissues are preserved (39). HIFU surgery is an effective and safe noninvasive alternative technique for the treatment of breast fibroadenoma (40). According to the studies, although the HIFU method is safe, but in some cases, coagulation necrosis of cells was found after this treatment (41). The efficacy and safety of HIFU therapy for breast fibroadenomas larger than 3 cm are unclear (42). Recurrence occurs in approximately 4 % of cases treated this way and is more likely in patients with multiple lesions, larger lesions, and hematoma at surgery. HIFU has shown promising results (16).

3.1.9. Pharmacological methods

Although fibroadenomas are relatively benign, they can cause significant psychological distress. Patients often worry about misdiagnosis, potential malignancy, and fear when touching the lump, which are common concerns with conservative treatment (43). Metformin, an anti-hyperglycemic agent, is being studied for various medical conditions. Metformin exhibits effects on breast cancer cells. Given fibroadenoma's estrogen-dependent and proliferative nature, along with Metformin's low incidence of side effects, metformin might have therapeutic potential for treating fibroadenoma (44). Ormeloxifene is a new

nonsteroidal drug that produces estrogen agonist and strong antagonist activity and is used to treat fibroadenoma. However multiple studies have reported that Ormeloxifene was not effective in fibroadenoma treatment and had side effects, such as hot flashes, irregular menstruation, headaches, depression, thromboembolic events, eye disease, leg cramps, endometrial hyperplasia, and more (45).

3.2. Evaluation of treatment methods for fibroadenoma

Recent systematic reviews indicate that minimally invasive methods for breast treatment offer significant advantages over traditional surgery in terms of patient recovery, aesthetic outcomes, and overall safety. Ardila C. M. et al. found that these techniques result in better aesthetic results, less postoperative morbidity, and improved clinical outcomes compared to conventional surgery (46). According to Zhang W. et al. study, the MWA technique is found to be an effective, safe, and promising alternative to traditional surgical methods (47). In most cases, fibroadenomas require no intervention as they naturally diminish with time (1). However, for some reasons explained in Table 2, surgery might be advisable. Despite this, many women opt against surgery due to the benign nature of these lesions, which pose no enduring risk of malignancy. Usually, women do not feel comfortable being observed for psychological reasons. Surgical procedures can rarely result in complications, such as wound infections, scar formation, and breast deformity. According to Peek et al., minimally invasive, time-consuming ablative techniques are MWA, cryoablation and HIFU. Minimally invasive and time-efficient are LA and RFA (39). Minimally invasive methods of treating fibroadenomas vary greatly depending on the equipment available at the hospital. It is difficult to evaluate the effectiveness of each of them.

Comparative studies are needed to compare ablation methods and determine which one is most promising. However, ongoing research into the causes of fibroadenomas may reveal new therapeutic targets that could be used in drug development. And finally, the most important part - patient involvement in treatment. Applying the analyzed treatment methods in practice can offer the patient more treatment alternatives.

Table 2. *Surgical excision indications*

Surgical excision indications
Mass greater than 5 cm.
Rapid grow.
Nonmobile, hard, enlarging, tender (can be smaller than 5 cm).
Fixed to the overlying skin or nipple areolar complex.
Associated with axillary or supraclavicular lymphadenopathy.
The patient is experiencing anxiety because of the mass.
Breast asymmetry.

4. Conclusion

According to this review of the literature, the treatment of fibroadenomas depends on the indications, psychological patient status and preferences of the patient. For small, stable fibroadenomas, regular surveillance is usually sufficient, but if the tumor is large or symptoms are severe, surgical resection or minimally invasive procedures such as ultrasound biopsy or laser ablation may be necessary. Compared to traditional surgical methods, minimally invasive fibroadenoma resection methods are better due to faster recovery of patients, smaller postoperative scars and complications, and better psychological well-being

of patients. It is necessary to pay attention to medical treatment, because of the possibility to save time, avoid postoperative scars, and reduce the costs of surgical operations.

Conflict of Interest

The authors have declared that no competing interests exist.

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