

Clinical practice guideline for diagnosis and treatment of hyperplasia of the mammary glands: Chinese Society of Breast Surgery (CSBrS) practice guideline 2021

Wei Ma¹, Zi-Ning Jin¹, Xu Wang¹, Fang-Meng Fu², Wen-Hui Guo², Ying-Ying Xu¹, Bo Chen¹, Feng Jin¹, Chuan Wang², Fan Yao¹; Chinese Society of Breast Surgery

¹Department of Breast Surgery, The First Affiliated Hospital of China Medical University, Shenyang, Liaoning 110001, China;

²Department of Breast Surgery, Fujian Medical University Union Hospital, Fuzhou, Fujian 350001, China.

Hyperplasia of the mammary glands (HMG) is a non-inflammatory and non-tumorous lesion.^[1] It is a structural disorder of the mammary glands due to different degrees of hyperplasia and subinvolution of the mammary parenchyma and stroma. In the literature, HMG is also called mastopathy, fibroadenosis, fibrocystic breast disease, mastalgia, fibrocystic change, benign mammary dysplasia, or sclerosing adenosis.

Currently, there are no standardized scientifically validated diagnostic and treatment approaches for HMG. The Chinese Society of Breast Surgery (CSBrS) has reviewed the domestic literature and referred to the grading of recommendations assessment, development, and evaluation handbook to evaluate the quality of evidence on the clinical issues associated with the diagnosis and treatment of HMG, while referring to its feasibility in the actual clinical practice of Chinese breast surgeons, to formulate the CSBrS Clinical Practice Guidelines for the Diagnosis and Treatment of Hyperplasia of the Mammary Glands to provide a reference for the clinical work of Chinese breast specialists.

Level of Evidence and Recommendation Strength

Level of evidence standard^[2]

Recommendation strength standard^[2]

Recommendation strength review committee

There were 85 voting committee members for this guideline, including 71 breast surgeons (83.5%), four oncologists (4.7%), four radiologists (4.7%), two pathol-

ogists (2.4%), two radiation therapists (2.4%), and two epidemiologists (2.4%).

Target Audience

Clinicians specializing in breast diseases in China.

Recommendations

Recommendation 1: Definition.

Definition	Level of evidence	Strength of recommendation
Non-inflammatory and non-tumorous lesions of the mammary glands ^[1]	II	Strong

Recommendation 2: Clinical manifestations.

	Symptoms and signs	Level of evidence	Strength of recommendation
2.1	Cyclical/non-cyclical breast pain ^[1]	II	A
2.2	Nodular breast or diffuse distribution of thickened glands ^[1]	II	A
2.3	Nipple discharge in a few patients ^[1]	II	A

Correspondence to: Dr. Chuan Wang, Department of Breast Surgery, Fujian Medical University Union Hospital, Fuzhou, Fujian 350001, China

E-Mail: dr_chuanwang@fjmu.edu.cn

Dr. Fan Yao, Department of Breast Surgery, The First Affiliated Hospital of China Medical University, Shenyang, Liaoning 110001, China

E-Mail: yaofancmu@sina.com

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Chinese Medical Journal 2021;134(16)

Received: 20-02-2021 Edited by: Yuan-Yuan Ji

Access this article online

Quick Response Code:



Website:
www.cmj.org

DOI:
10.1097/CM9.0000000000001521

Recommendation 3: Diagnostic methods.

	Diagnostic methods	Level of evidence	Strength of recommendation
3.1	Patient history ^{[3],*}	I	A
3.2	Systematic breast exam ^{[3],†}	I	A
3.3	Ultrasonography ^{[3],‡}	I	A
3.4	Breast radiography ^{[3],§}	I	A
3.5	Breast magnetic resonance imaging ^{[3],}	I	A
3.6	Histopathological examinations ^{[3],¶}	I	A

*Patient history includes the following: breast symptoms, other concomitant symptoms, duration of symptoms, factors associated with aggravation/relief of symptoms, past history of breast or ovarian diseases, family history of breast cancer, and history of intake of reproductive hormones/oral contraceptives. In patients with breast pain, the following information is needed: type, duration, location, and severity of pain and its relationship to menstruation. History of reproductive hormones/contraceptive use. †The breast examination should consist of inspection and palpation and be performed in both the upright and supine positions. ‡Ultrasonography is much better than breast radiography for resolving nodes, cysts, and solid tumors in dense breasts. §Radiography is an important modality for detecting early carcinoma and microcarcinoma, and effective for revealing microcalcifications. ||Breast magnetic resonance imaging (MRI) is more sensitive but with a higher false positive rate than ultrasonography and breast radiography, so it should be used as a supplementary examination for high-risk patients. ¶Breast biopsy techniques include core needle biopsy (CNB), vacuum-assisted breast biopsy (VABB), and excisional biopsy.

Recommendation 4: Treatment principles.

	Treatment principles	Level of evidence	Strength of recommendation
4.1	Regular monitoring ^[3,4]	I	A
4.2	Non-medical treatments such as including psychological counseling and counseling on changes in diet and lifestyle ^[3,4]	I	A
4.3	Symptomatic treatments ^[1,5]	II	A

Discussion

HMG shows diverse, complicated, and non-specific histopathology findings, which have led to confusing definitions and terminology. After discussion, the expert panel voted to recommend the term “hyperplasia of the mammary glands (HMGs).” It defined “HMG” as a type of non-inflammatory and non-tumorous lesion of the mammary gland that is a structural disorder of the mammary glands associated with mammary parenchymal and stromal hyperplasia with subinvolution of different degrees.^[6]

The major signs/symptoms of HMG are as follows: cyclical/non-cyclical breast pain, nodular breast or nodular breast mass, with nipple discharge in some patients.^[1,6] A nodular breast includes the following: granular nodules, striped nodules, solitary mass, or locally or diffusely thickened breast. Palpation of a unilateral breast or

bilateral breasts reveals solitary or multiple firm nodules which have an unclear boundary and demonstrate cyclic changes in their nature and size over the menstrual cycle. The diagnosis of HMG is based on exclusion of other conditions, detailed history and systematic examination, clinical manifestations, auxiliary examinations, and histopathological examination of a biopsy specimen.^[6] Recommendations of Imaging and Pathological Diagnosis Methods were showed in the Supplementary file, <http://links.lww.com/CM9/A559>.

Imaging is an important step in the diagnosis of HMG, and aims to exclude other relevant diseases, especially breast cancer.

On ultrasonography, HMG manifests as thickened and enhanced echoes, internal hypoechoic nodes with irregular and unclear margins, or no attenuation or slight enhancement of posterior echoes; color Doppler ultrasonography only reveals a few punctiform or short rod-like blood-flow signals.^[7]

In more than 50% of patients with HMG and obvious masses on palpation, radiography has revealed massive high-density shadows or nodular shadows without visible borders that are sometimes accompanied by calcifications.^[8] However, dense breast tissues reduce the sensitivity of breast radiography for detecting lesions, especially malignant lesions, and the dense tissue may obscure miniature suspicious foci. Breast MRI can be used as a supplementary examination for women who are unsuitable for breast ultrasonography or radiography or at a high risk of breast cancer with negative findings on breast ultrasonography and radiography.^[9]

HMG manifests complicated and diverse histopathology findings, which leads to controversy in its classification. According to the literature, HMG is classified into the following 2 categories^[6]: (1) mastopathy, including lobular hyperplasia, fibro-adenosis, and sclerosing adenosis; (2) fibrocystic mastopathy, including cyst, ductal epithelial hyperplasia, blunt duct adenosis, and adenosis with apocrine metaplasia. The above subtypes may be present solitarily or multiply in the mammary lobules of the same patients, but the hyperplastic development of various lobules is not completely consistent.

The different histopathological manifestations of HMG show different breast risks of breast cancer.^[10] The rate of malignant transformation fibrocystic mastopathy ranges from 1% to 5%, and only fibrocystic mastopathy atypical ductal hyperplasia (ADH), as confirmed by a histopathological examination of a biopsy specimen, carries a significantly increased risk of breast cancer.^[11-15] Therefore, the treatment of HMG should focus on different clinical and histopathological manifestations.

Regular follow-up examinations and non-medical treatment are the major recommendations for patients with HMG. Patients with mild to moderately painful HMG are mainly treated by psychological counseling and lifestyle interventions^[16]; medications are considered for patients with permanent, severe breast pain.^[10] The literature indicates

that bromocriptine,^[17,18] danazol,^[19] and tamoxifen are effective against severe breast pain. However, there is little evidence to support the use of drugs to reverse the histopathological changes of HMG. Therefore, the side effects of medications should be thoroughly considered when weighing their risks and benefits. No high-level evidence is available for the clinical use of traditional Chinese medicine for treating HMG, and therefore no recommendations pertaining to traditional medicine appear in these guidelines.

Since HMG is often diffuse, local surgical resection is inappropriate. HMG is not an indication for surgical treatment, and any surgical intervention, including puncture biopsy or resection, is aimed to avoid a misdiagnosis or missed diagnosis of breast cancer.

Patients at high risk of breast cancer are those who present with ADH or whose first-degree relative(s) has/have a history of breast cancer. For these patients, physicians should implement preventive strategies, which include careful follow-up examinations, medications, and surgical interventions.

With the continuous discovery of new evidence-based information, the concept of HMG is continually being updated, with subsequent effects on clinical practice. The establishment of a standardized diagnosis of and treatments for HMG can prevent the risk of the mistaking benign disease for malignant disease, thus avoiding the improper treatment of misdiagnosed patients, waste of medical resources, and unnecessary physical and mental harm to patients.

List of compiling committee members (In alphabetical order by surname)

Zhong-Wei Cao, Bo Chen, De-Dian Chen, Lu-Yan Chen, Yuan-Jia Cheng, Xue-Ning Duan, Zhi-Min Fan, Pei-Fen Fu, Fang-Meng Fu, Bao-Liang Guo, Wen-Hui Guo, Jian Haung, Jun Jiang, Hong-Chuan Jiang, Feng Jin, Zi-Ning Jin, Hua Kang, Rui Ling, Jin-Ping Liu, Ke Liu, Qian Liu, Yin-Hua Liu, Yun-Jiang Liu, Zhen-Zhen Liu, Yong-Hui Luo, Rong Ma, Wei Ma, Da-Hua Mao, Jiang-Hua Ou, Xiang Qu, Guo-Sheng Ren, Ai-Lin Song, Er-Wei Song, Li-Li Tang, Xing-Song Tian, Chuan Wang, Fei Wang, Jian-Dong Wang, Shu Wang, Shui Wang, Xiang Wang, Xu Wang, Jiong Wu, Ke-Jin Wu, Fei Xie, Ling Xin, Ying-Ying Xu, Fan Yao, Zhi-Gang Yu, Jian-Guo Zhang, Jin Zhang, Jing-Hua Zhang, Yi Zhao, Zuo-Wei Zhao, Wei Zhu, Ang Zheng, Qiang Zou.

Conflicts of interest

The expert committee for these guidelines declares no conflict of interest. These guidelines are a reference for breast disease specialists in clinical practice. However, the guidelines are not to be used as the basis for medical evaluation, and do not play an arbitrating role in the handling of any medical disputes. The guidelines are not a reference for patients or non-breast specialists. The Chinese Society of Breast Surgery assumes no responsibility for results involving the inappropriate application of these guidelines, and reserves the right to interpret and revise the guidelines.

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How to cite this article: Ma W, Jin ZN, Wang X, Fu FM, Guo WH, Xu YY, Chen B, Jin F, Wang C, Yao F; Chinese Society of Breast Surgery. Clinical practice guideline for diagnosis and treatment of hyperplasia of the mammary glands: Chinese Society of Breast Surgery (CSBrS) practice guideline 2021. *Chin Med J* 2021;134:1891–1893. doi: 10.1097/CM9.0000000000001521