



基于乳腺癌筛查队列的超声BI-RADS分类进展影响因素分析*

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【摘要】目的 乳腺超声BI-RADS分类是评价乳腺病灶特征的重要结果,本研究目的在于探索可能导致BI-RADS分类进展的影响因素。**方法** 基于2015-2021年成都市双流区两癌筛查队列,收集超声及问卷结果,BI-RADS分类从1~2达到3类及以上,或初筛3类及以上,后续筛查类别上升者定义为进展。采用Cox比例风险回归模型探索进展可能的影响因素,运用限制性立方样条探寻变量与进展风险的非线性关联。**结果** 最终7069人纳入分析,共随访23580人年。相较于其他年龄段,40~44岁人群中检出BI-RADS 3类及以上的人数占比最高(24.83%)。Cox回归分析发现,已绝经的女性比未绝经女性BI-RADS进展风险低[风险比(hazard ratio, HR)=0.65, 95%置信区间(confidence interval, CI): 0.44~0.97];在已绝经的女性中,绝经晚(HR=1.16, 95%CI: 1.03~1.30)是BI-RADS进展的危险因素;绝经前女性肥胖(HR=0.43, 95%CI: 0.21~0.88)与进展风险负相关。**结论** 乳腺超声BI-RADS进展的危险因素与乳腺癌危险因素存在重合。可根据BI-RADS进展的高风险因素构建风险评分,优化高危人群筛查方案,提高乳腺癌筛查效率。

【关键词】 乳腺癌筛查 超声BI-RADS分类 队列研究

Factors Influencing Progression on the Ultrasound BI-RADS Categories: An Analysis Based on a Breast Cancer Screening Cohort FENG Wanting^{1,2}, TENG Yilin^{1,2}, YANG Huifang^{1,2}, XU Bin^{1,2}, LI Jiayuan^{1,2}, LUO Weidong^{2,3△}.

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【Abstract】 Objective Ultrasound categories of Breast Imaging Reporting and Data System (BI-RADS) are an important outcome used in the evaluation of the characteristics of breast lesions. In this study, we aim to explore the potential influencing factors that may cause the progression of BI-RADS categories. **Methods** Based on the cervical cancer and breast cancer screening cohort in Shuangliu District, Chengdu from 2015 to 2021, we collected ultrasound and questionnaire results. Progression was defined as changing from BI-RADS category 1 or 2 to 3 or above, or from the initial screening result of BI-RADS 3 or above to a higher category in subsequent ultrasound screenings. The Cox proportional hazards regression model was used to explore potential influencing factors for BI-RADS classification progression. A restricted cubic spline was used to explore the nonlinear association between the variables and the risk of progression. **Results** A total of 7069 participants were included in the analysis and followed up for 23580 person-years. Compared with other age groups, the proportion of participants of BI-RADS category 3 and above was highest in the 40-44 age group (24.83%). Cox regression analysis showed that postmenopausal women had a lower risk of BI-RADS progression than premenopausal women did (hazard ratio [HR]: 0.65, 95% confidence interval [CI]: 0.44-0.97). In postmenopausal women, late menopause (HR=1.16, 95% CI: 1.03-1.30) was identified as a risk factor for BI-RADS progression. Obesity in premenopausal women was negatively associated with the risk of progression (HR=0.43, 95% CI: 0.21-0.88). **Conclusion** The risk factors for progression in ultrasound BI-RADS categories overlap with the risk factors for breast cancer. A risk score based on the high-risk factors for BI-RADS progression can be constructed to optimize screening programs for high-risk populations and improve the efficiency of breast cancer screening.

【Key words】 Breast cancer screening BI-RADS ultrasound categories Cohort study

乳腺癌是我国女性最常见的恶性肿瘤,发病和死亡人数呈逐年增加趋势^[1],严重威胁女性的生命健康。2009年,我国在全国推行了农村女性“两癌”筛查项目^[2],

对适龄女性进行乳腺体检和彩超检查,结果采用乳腺影像报告和数据系统(Breast Imaging Reporting and Data System, BI-RADS)分类标准,依据超声分类结果采取进一步的措施^[3]。但目前筛查随访仅根据一次检查结果,未关注多次筛查后BI-RADS结果的变化情况,不能满足潜在高风险人群的精准健康管理需求;另外,有研究显示乳腺癌阳性发现率仅万分之五^[4],基层采用无差别的筛查方案

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难以实现筛查收益的最大化。由于乳腺影像BI-RADS分类对预测肿瘤良恶性程度具有较高的准确性^[5-6], 从低到高分类的进展可一定程度上提示病灶的变化。因此, 本研究重点关注乳腺超声影像学结果的变化, 以BI-RADS分类进展作为结局, 基于前瞻性队列收集信息, 探究BI-RADS分类进展的影响因素, 可提示筛查的重点人群, 为乳腺癌筛查分级管理、提高分流效率提供依据。

1 资料与方法

1.1 研究对象

本研究利用了2015–2021年成都市双流区妇幼保健院“两癌”筛查中乳腺癌筛查数据, 该筛查队列每年入组4 000 ~ 7 000人, 平均随访3.3年。研究纳入双流区户籍、自愿参加筛查的适龄妇女, 排除有严重精神障碍、沟通障碍、拒绝乳腺超声检查和问卷调查的妇女。纳入对象均签署知情同意书。截至2021年, 队列共纳入31 942人, 提取至少参加两年筛查的对象(7 069人), 以其第一次筛查结果为基线, 且基线未发生乳腺癌(BI-RADS 6类)构建信息库。

1.2 暴露与结局测量

超声检查使用迈瑞Mindray Resona系列超声诊断仪, 高频线阵探头L14-5WU, 频率为4.0 ~ 14.0 MHz。超声结果评估采用BI-RADS分类标准。BI-RADS分类进展定义为: 初筛未达3类、后续筛查 $\geq$ 3类者, 或初筛 $\geq$ 3类、后续筛查分类升高为进展; 且左右乳任意一侧进展则可定义为“进展”, 其他为“未进展”。由于BI-RADS 6类为病理活检证实癌, 从BI-RADS 5类到6类一般认为是穿刺确诊的过程, 故从5类升至6类不视为进展。通过问卷采集筛查对象的基本情况和乳腺癌重要或高度可疑的影响因素, 包括基本情况(年龄、文化程度、身高、体质量等)、月经史、孕产史、避孕史、哺乳史、家族史和既往乳腺检查史等。体质量指数(body mass index, BMI)根据中国标准分为肥胖($\geq 28.0 \text{ kg/m}^2$)、超重($24.0 \sim 27.9 \text{ kg/m}^2$)、体质量正常($18.5 \sim 23.9 \text{ kg/m}^2$)和体质量过低($< 18.5 \text{ kg/m}^2$)四

类。生育时期(年)=绝经年龄(未绝经者用基线年龄)—初潮年龄。乳腺癌家族史定义为一、二级亲属患有乳腺癌。

1.3 质量控制

所有检查操作均由双流妇幼保健院开展, 统一检查方法设备, 按照国家两癌筛查要求执行体检规程。BI-RADS 3类及以上保留特征影像, 由两名以上医生盲法独立评级, 判别不一致的由高年资医生复核影像确认类别。问卷录入均由统一培训后的调研员完成, 基于原始问卷使用Epidata软件, 采用双录入法录入问卷。

1.4 统计学方法

研究采用R 4.1.0软件分析, 对基线人群的基本情况 & 超声结果进行描述性分析, 计量资料用 $\bar{x} \pm s$ 描述, 采用 t 检验进行统计学分析; 计数资料采用频数和百分比描述, 使用卡方检验进行统计学分析。单因素Cox回归分析筛选 $P < 0.10$ 的变量(绝经年龄仅在绝经后女性中分析), 通过Schoenfeld残差法验证是否满足等比例风险假设, 并结合既往研究和共识确定自变量。建立多因素Cox比例风险回归模型分析各因素对超声BI-RADS分类进展的风险比(hazard ratio, HR)及其95%置信区间(confidence interval, CI)。考虑到BMI、哺乳时长和初潮年龄为连续性变量, 且单因素分析差异有统计学意义, 用限制性立方样条回归法探索上述变量与进展风险的关系, 调整年龄、BMI、文化程度、初潮年龄、月经天数、月经周期、流产次数、初产年龄、哺乳时长、活产数、宫内节育器使用和既往是否乳腺检查等潜在混杂因素, 并按是否绝经分层。设置样条回归节点数为3, 参照值为各变量的中位数。结果分析均双侧检验, $\alpha = 0.05$ 。

2 结果

2.1 基本特征

研究队列纳入31 942名基线调查对象, 平均年龄(47.94 ± 7.09)岁。其中30 571人有乳腺超声检查结果。如表1所示, 各年龄段BI-RADS 1 ~ 2类的人数占比最高,

表1 2015–2021年双流区乳腺超声筛查结果年龄分布

Table 1 Breast ultrasound screening results in Shuangliu District, Chengdu, China by age distribution between 2015 and 2021

Age/yr.	n	Category 0/case (%)	Category 1/case (%)	Category 2/case (%)	Category 3/case (%)	Category 4/case (%)	Category 5/case (%)	Category 6/case (%)
<40	3 824	10 (0.26)	1 477 (38.62)	1 539 (40.25)	674 (17.63)	106 (2.77)	16 (0.42)	2 (0.05)
40–44	6 212	5 (0.80)	1 819 (29.28)	2 846 (45.81)	1 278 (20.57)	237 (3.82)	24 (0.39)	3 (0.05)
45–49	8 137	5 (0.61)	2 544 (31.26)	3 781 (46.47)	1 470 (18.07)	282 (3.47)	47 (0.58)	8 (0.10)
50–54	6 934	11 (0.16)	2 358 (34.01)	3 452 (49.78)	904 (13.04)	183 (2.64)	18 (0.26)	8 (0.11)
55–59	3 116	5 (0.16)	1 405 (45.09)	1 329 (42.65)	322 (10.33)	37 (1.19)	9 (0.29)	9 (0.29)
60–	2 348	1 (0.43)	740 (31.52)	1 365 (58.13)	217 (9.24)	17 (0.72)	5 (0.21)	3 (0.13)
Total	30 571	37 (0.12)	10 343 (33.83)	14 315 (46.82)	4 865 (15.91)	862 (2.82)	119 (0.39)	33 (0.11)

Category 0: Additional imaging needs to be done; category 1 and 2: no malignant probability; category 3–5: benign possible with less than 2%, 2%–95%, and more than 95% malignant probability respectively; category 6: known malignancy or pathologically proven to be malignant.

40 ~ 44 岁人群 BI-RADS 在 3 类的人数占该年龄段的 20.57%, 4 类及以上的人数占比 4.26%, 比例均高于其他年

龄段。
如表 2 所示, BI-RADS 分类进展组比未进展组的平均

表 2 乳腺癌筛查队列人群基线特征

Table 2 Baseline characteristics of the breast cancer screening cohort

Variable	Total (n=31 942)	Progress group (n=670)	Non-progress group (n=6 399)	P ^a
Age/case (%)				<0.001
<40 yr.	4 151 (13.00)	112 (16.72)	719 (11.24)	
40-49 yr.	15 030 (47.05)	12 (1.79)	217 (3.39)	
50-59 yr.	10 352 (32.41)	393 (58.66)	3 417 (53.40)	
≥ 60 yr.	2 409 (7.54)	153 (22.84)	2 046 (31.97)	
Education level/case (%)				<0.001
Primary school and below	9 014 (40.51)	225 (34.04)	2 632 (41.53)	
Middle school	11 386 (51.17)	372 (56.28)	3 252 (51.31)	
High school	1 501 (6.75)	48 (7.26)	380 (5.94)	
College and above	352 (1.58)	16 (2.42)	74 (1.17)	
BMI/case (%)				0.005
<18.5 kg/m ²	830 (2.87)	17 (2.58)	129 (2.05)	
18.5-23.9 kg/m ²	16 154 (55.78)	389 (59.12)	3 381 (53.85)	
24.0-27.9 kg/m ²	9 621 (33.22)	218 (33.13)	2 239 (35.66)	
≥ 28.0 kg/m ²	2 356 (8.14)	34 (5.17)	529 (8.43)	
Age of menarche/yr., $\bar{x} \pm s$	14.06±1.77	13.96±1.53	14.19±1.68	<0.001
Menstrual cycle ^b /d, case (%)				0.572
Normal	11 796 (90.89)	589 (95.31)	5 694 (95.87)	
Abnormal	1 182 (9.11)	29 (4.69)	245 (4.13)	
Menstrual period ^b /d, case (%)				0.273
Normal	12 299 (90.21)	547 (96.99)	5 251 (95.94)	
Abnormal	1 335 (9.79)	17 (3.01)	222 (4.06)	
Menopause/case (%)				<0.001
No	17 555 (58.04)	471 (78.37)	3 738 (63.07)	
Yes	12 317 (40.72)	130 (21.63)	2 189 (36.93)	
Age at menopause ^c /yr., $\bar{x} \pm s$	48.46±3.82	48.24±3.42	48.03±3.62	0.523
Reproductive period/year, $\bar{x} \pm s$	31.59±4.87	30.52±4.62	31.32±4.53	<0.001
History of abortion/case (%)				0.943
No	6 733 (23.02)	162 (24.40)	1 537 (24.19)	
Yes	22 512 (76.98)	502 (75.60)	4 817 (75.81)	
Number of abortions ($\bar{x} \pm s$)	1.49±0.83	1.89±1.10	1.92±1.11	0.612
Age at first birth/yr., $\bar{x} \pm s$	25.13±4.77	25.13±5.06	25.01±4.69	0.607
Contraceptives/case (%)				0.409
No	4 689 (89.35)	634 (97.09)	6 093 (97.69)	
Yes	559 (10.65)	19 (2.91)	144 (2.31)	
IUD/case (%)				0.552
No	1 072 (7.45)	311 (47.63)	2 889 (46.32)	
Yes	13 325 (92.55)	342 (52.37)	3 348 (53.68)	
Duration of IUD use/year, $\bar{x} \pm s$	16.37±8.52	16.2±7.72	16.7±8.07	0.290
History of breast feeding/case (%)				0.999
No	1 710 (5.59)	26 (3.95)	245 (3.90)	
Yes	28 903 (94.41)	633 (96.05)	6 033 (96.10)	
Duration of breastfeeding/month, $\bar{x} \pm s$	12.16±5.79	10.80±5.14	11.44±5.33	0.006
Number of live births ($\bar{x} \pm s$)	1.20±0.45	1.14±0.38	1.17±0.43	0.132
Age at first birth/yr., $\bar{x} \pm s$	22.98±2.59	22.86±2.33	22.75±2.24	0.249
History of breast examination/case (%)				0.003
No	20 399 (66.10)	406 (61.42)	4 250 (67.27)	
Yes	10 463 (33.90)	255 (38.58)	2 068 (32.73)	
Family history of breast cancer/case (%)				0.093
No	12 312 (97.36)	86 (92.47)	1 337 (96.19)	
Yes	334 (2.64)	7 (7.53)	53 (3.81)	
BI-RADS categories at baseline				0.138 ^d
0	37 (0.12)	0	0	
1-2	24 658 (80.65)	460 (68.66)	4 573 (71.46)	
3-5	5 879 (19.23)	210 (31.34)	1 826 (28.54)	
6	33 (0.11)	0	0	

BMI: body mass index; IUD: intrauterine device. ^a The differences were tested between the progress group and the non-progress group. ^b According to *Guideline on Diagnosis and Treatment of Abnormal Uterine Bleeding: 2022 Revisions*, menstrual cycles lasting 21-35 days are defined as being normal and menstrual periods lasting 1-7 days are defined as being normal. ^c The analysis was performed in postmenopausal women only. ^d People of the categories of BI-RADS 0 and BI-RADS 6 were excluded from the Chi-square test.

初潮年龄更小,生育时期和哺乳时长更短($P<0.05$)。但月经情况、绝经年龄、孕产史以及家族史两组的差异均无统计学意义($P>0.05$)。

2.2 BI-RADS进展影响因素

多因素Cox回归模型分析结果显示(表3),仅已绝经和既往是否接受乳腺检查是BI-RADS分类进展的影响因素($P<0.05$)。绝经($HR=0.65$, 95%CI: 0.44 ~ 0.97)是BI-RADS进展的保护因素,而既往接受过乳腺检查与增加BI-RADS进展风险有关($HR=1.34$, 95%CI: 1.05 ~ 1.69)。

绝经前人群的BMI对BI-RADS进展有显著影响,低体

质量是BI-RADS进展的危险因素($HR=1.95$, 95%CI: 1.05 ~ 3.61),而肥胖是保护因素($HR=0.43$, 95%CI: 0.21 ~ 0.88);在绝经后人群中,绝经年龄晚和既往乳腺检查会增加BI-RADS进展的风险($P<0.05$),与上述未分层的分析结果一致。

研究进一步探索了BMI、初潮年龄、和哺乳时长(月)与BI-RADS分类进展的非线性关联,均与BI-RADS进展风险不存在非线性相关(均有非线性 $P>0.05$)。但绝经前人群的BMI与BI-RADS进展之间发现负向线性相关(整体 $P=0.0439$),见图1。

表 3 BI-RADS进展影响因素Cox回归分析
Table 3 Cox regression of the influencing factors of BI-RADS progression

Variable	HR ^a (95% CI)	<i>P</i>	Premenopausal females		Postmenopausal females	
			HR ^a (95% CI)	<i>P</i>	HR ^a (95% CI)	<i>P</i>
BMI						
<18.5 kg/m ²	1.78 (1.00-3.16)	0.051	1.95 (1.05-3.61)	0.035	0.60 (0.08-4.69)	0.627
18.5-23.9 kg/m ²	Ref		Ref		Ref	
24.0-27.9 kg/m ²	0.89 (0.69-1.15)	0.385	0.86 (0.65-1.15)	0.321	1.06 (0.58-1.95)	0.844
≥28.0 kg/m ²	0.60 (0.35-1.04)	0.071	0.43 (0.21-0.88)	0.021	1.30 (0.50-3.33)	0.591
Age of menarche	0.98 (0.90-1.07)	0.656	0.94 (0.85-1.03)	0.165	1.04 (0.88-1.22)	0.637
Menopause						
No	Ref					
Yes	0.65 (0.44-0.97)	0.034				
Age at menopause ^b					1.16 (1.03-1.30)	0.012
Duration of breastfeeding/month	0.99 (0.96-1.01)	0.237	0.98 (0.96-1.01)	0.216	0.98 (0.93-1.04)	0.553
History of breast examination						
No	Ref		Ref		Ref	
Yes	1.34 (1.05-1.69)	0.016	1.17 (0.90-1.53)	0.237	2.35 (1.32-4.19)	0.004

Ref: reference; HR: hazard ratio; CI: confidence interval. ^a Adjusted for age upon enrollment (<40, 40-49, 50-59, or ≥60 years old), educational attainment (primary school and below, middle school, high school, or college and above), menstrual cycle (normal or abnormal), menstrual period (normal or abnormal), number of abortions (continuous), IUD use (yes or no), number of live births (continuous), age at first birth (continuous), and BI-RADS categories measured at baseline (BI-RADS 1-6). ^b The analysis was performed in postmenopausal women only.

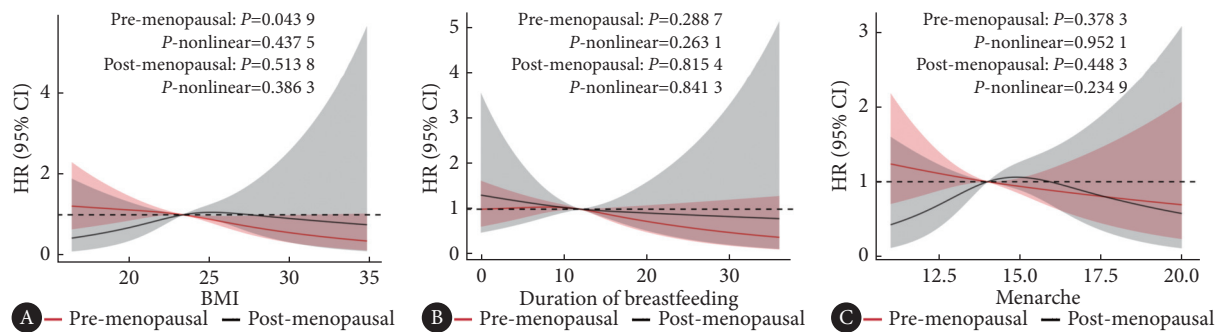


图 1 BMI、哺乳时长和初潮年龄与BI-RADS进展风险的非线性关联分析

Fig 1 Non-linear association analysis of BMI, duration of breastfeeding, and age of menarche with the risk of BI-RADS progression

The solid lines are multivariable adjusted HR, with the shadows showing 95% CI derived from restricted cubic spline regressions with three knots. The red and gray areas indicate the pre- and post-menopausal females, respectively. A, BMI, with 23.4 kg/m² as the reference value; B, duration of breastfeeding, with 12 months as the reference value; C, age at menarche, with 14 years old as the reference value. Adjusted for age at enrollment (<40, 40-49, 50-59, or ≥60 years old), educational attainment (primary school and below, middle school, high school, or college and above), menstrual cycle (normal or abnormal), menstrual period (normal or abnormal), number of abortions (continuous), IUD use (yes or no), number of live births (continuous), age at first birth (continuous), and BI-RADS categories measured at baseline.

3 讨论

本研究基于成都市大样本乳腺癌筛查队列,描述了农村女性乳腺超声筛查BI-RADS分类分布现况,并对影响乳腺影像学进展的因素进行随访研究。研究发现BI-RADS高分类多在40~50岁女性中检出,与林艳苹等^[7]的研究结果一致;BI-RADS 3类检出率(15.91%)高于广州市(5.76%)^[8]和福建省农村妇女的筛查结果(7.42%)^[9],农村地区卫生服务资源缺乏、人群文化程度低,妇女很少乳腺检查,在初筛时易出现较高的超声BI-RADS分类。

结果显示,BMI<18.5 kg/m²与绝经前女性BI-RADS进展风险正相关,而BMI≥28 kg/m²是可能的保护因素。蔡芷茵等^[10]分析健康女性BI-RADS分类影响因素,发现BMI≥28 kg/m²与BI-RADS低分类相关(比值比=0.123),与本研究结果类似。肥胖与BI-RADS分类关系的研究较少,但许多研究证实肥胖会影响乳腺癌的发生^[11-12]。对于绝经后女性,肥胖是较为确定的乳腺癌危险因素,可通过促进雌激素的合成、促进炎症因子分泌、引发胰岛素抵抗等作用机制介导乳腺癌的发生发展^[13];但肥胖在绝经前女性中的作用尚不明确。一项75万人的大型队列研究发现,绝经前体质量增加会降低患乳腺癌的风险^[14],可能是体质量增加带来的风险效应存在滞后,超出了绝经前患乳腺癌的易感窗口期^[14-15]。另一方面,体质量增加也可能通过影响激素水平降低患乳腺癌风险,有研究表明BMI高的年轻女性体内雌二醇和总睾酮的水平较低^[16],减少对乳腺细胞的刺激,从而降低绝经前乳腺癌的发生风险^[17]。本研究未发现绝经后女性BMI与BI-RADS分类的关联具有统计学意义,可能是因为本研究肥胖人群的样本量较小,且肥胖定义为BMI≥28 kg/m²,低于国外多数大样本队列研究的判定标准(BMI≥30 kg/m²),人群整体肥胖水平较低,有待未来更大样本量的研究。

长期雌激素暴露会显著增加乳腺癌发病风险,绝经年龄晚、行经年数长与患乳腺癌的风险增加有关^[18]。本研究发现绝经后女性中,绝经年龄越晚,BI-RADS进展风险越高。定期进行乳腺检查可尽早发现病变,是预防乳腺癌的有效措施^[19]。但本研究发现既往接受过乳腺检查的女性BI-RADS进展的风险更高,可能因这部分女性本身有乳腺疾病或自感乳腺不适而主动检查,本研究结果强调了两癌筛查可提早发现乳腺病变的重要意义,建议对适龄妇女定期进行乳腺检查。

乳腺癌筛查是一项长期、定期的工作,除实现“三早”预防、及时发现和干预疾病发展外,还应重视筛查后无病人群的随访管理,结合个体危险因素特征合理判断高危

人群,并应关注筛查结果的长期变化进展。乳腺超声BI-RADS分类可以提示乳腺病灶的恶性概率,BI-RADS分类进展也可一定程度上提示乳腺恶性病变的高危人群。本研究所发现的BI-RADS进展的危险因素如未绝经、绝经年龄晚、绝经前低体质量,与乳腺癌发病存在共同的风险因素^[15,18-21],对此类高风险人群,应当在筛查后及时分流,重点关注乳腺影像学结果,以及乳腺结节等良性病变的进展变化,可以尽早发现和预防乳腺病灶的进展,同时对这部分高危人群的分级管理也可提高筛查效率。本研究优势在于创新性地选取了乳腺超声BI-RADS进展为研究结局,实现了预防关口的提前;研究样本量较大,问卷收集信息丰富,乳腺检查和人体测量均由双流妇幼保健院医师进行,降低测量偏倚。研究也存在一定局限性,本研究为单中心,对结果的解读和外推仍谨慎,未来还需更多来自其他区域的研究证据;信息收集存在缺失,导致部分变量无法纳入分析;研究没有实现对队列中的个体连续随访。另外,在项目实施过程中,存在部分女性未按要求参与筛查、未及时复查等,导致两次筛查间隔时间过短或过长,这也提示卫生部门应充分宣传筛查政策和动员,基层工作人员应及时跟进随访登记进一步探索可能影响乳腺超声结果进展的原因,为优化乳腺筛查分级管理方案,指导乳腺癌筛查工作提供理论依据,促进乳腺癌防治关口前移。

* * *

作者贡献声明 冯琬婷负责论文构思、正式分析、调查研究、研究方法、可视化和初稿写作,滕屹霖和杨会芳负责调查研究、研究方法、可视化和初稿写作,许彬负责论文构思、正式分析、调查研究和研究项目管理,李佳圆负责论文构思、研究项目管理、提供资源、监督指导和审读与编辑写作,罗伟东负责论文构思、调查研究、研究项目管理、提供资源、监督指导和审读与编辑写作。所有作者已经同意将文章提交给本刊,且对将要发表版本进行最终定稿,并同意对工作的所有方面负责。

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