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ORIGINAL

ADHERENCE TO MULTIDISCIPLINARY TEAM CARE PLANS IN FEMALE ATHLETIC PATIENTS WITH BREAST CANCER FROM LOW-MIDDLE INCOME REGIONS IN CHINA: A SINGLE CENTER ANALYSIS

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ABSTRACT

Objective: To investigate the adherence to multidisciplinary team (MDT) care plan in breast cancer (BC) athletic patients of low middle income regions in China. **Methods:** This is a retrospective study. Athletic Patients diagnosed with BC of early stage who were managed by MDT care plan and underwent surgery in China. We evaluated the concordance between MDT decisions and subsequent patient care. Athletic Patients' socio-demographic and clinical information were obtained from hospital records. Factors including age, family-history of cancer and tumor, and biologic subtypes, which were associated with the discordance, were identified using logistic regression analysis. **Results:** A total of 531 female athletic patients were included, while 70.6% (375 out of 531) patients adhered to of the MDT plan. Age, family history of cancer and tumor, and biologic subtypes were significantly associated with the adherence to MDT care plan. The discordance rate of athletic patients older than 70 was 3.9 times higher compared with those aged under 40 years old (95%CI:1.3-12.5, *P*=0.02). Patients with family history of cancer were 3.5 times more likely to change their MDT care plans than those without family histories (95%CI:1.2-10.2, *P*=0.02). Compared with athletic patients with HR+/HER2- BC, those with HR-/HER2+ and HR+/HER2+ subtypes had 11.9 and 14.2 times higher discordance rate, respectively (95%CI:5.7-24.7, *P*<0.001; 95%CI:6.6-30.7, *P*<0.001). **Conclusion:** MDT discordance rate in this study was high. The implementation of the MDT care plan in athletic patients with BC needs to be strengthened,

especially in retired athletic patients, patients with family history or HER2+.

KEYWORDS: Multidisciplinary team; Breast cancer; Low-middle income regions; MDT care plan

1. INTRODUCTION

Breast cancer (BC) is one of the most common malignancies, and its incidence, survival rates and impact on hospital and community resources are increasing yearly worldwide (Fisher & Fisher, 1966). Recent GLOBOCAN 2018 data produced by the IARC (International Agency for Research on Cancer) from 185 countries reported 2.3 million new cases (11.7%) of BC and a mortality rate of 6.9% (Bray et al., 2018). In China, there is estimated 278.9 thousand new cases of BC in 2014, accounting for 16.51% of all newly developed cancers in female. The estimates of BC deaths were about 66,000 in China in 2014, accounting for 7.82% of all the cancer -related deaths in female (Li et al., 2018).

Based on Bernard Fisher and Edwin Fisher's theory in the 1960s lead to the development of an alternative hypothesis that BC is a systemic disease (Fisher & Fisher, 1966). It contributed to a paradigm shift in BC management, athletic patients with early-stage disease need to be treated with systemic therapies (De Lena, Brambilla, Morabito, & Bonadonna, 1975). Treatment on BC has been more sophisticated nowadays and has change dradically from a surgical disease to a much more complex disease requiring the expertise of specialists from different disciplines (Chan, Cheung, Epstein, & Mak, 2006).

This has led to the development of multidisciplinary team (MDT), which are composed of healthcare professionals, including surgeons, oncologists, radiologists, pathologists, pathologists, and specialist nurses, and aim to reach a consensus on the diagnosis and treatment, based on scientific and experiential evidence (Borras et al., 2014). MDTs make decisions regarding diagnosis and treatment programs through MDT meetings (Taylor, Atkins, Richardson, Tarrant, & Ramirez, 2012), which has been considered as the gold standard of cancer care (Prades, Remue, Van Hoof, & Borras, 2015). A large international survey involving 39 countries demonstrated that breast MDT was perceived to lead to better clinical decisions, evidence-based practice and improved quality of treatment (Saini et al., 2012). A previous study in China has also showed that well-organized MDTs benefit BC athletic patients who were suitable for surgery and the organization of MDTs could affect the size of their effects (Lu, Jiang, Qian, Lv, & Ying, 2020).

Guidelines for the screening, diagnosis, and treatment of BC exist in the developed countries, but economic and health systems barriers preclude the implementation of these recommendations in resource-limited countries and lead to discordance with the guideline (Sayed et al., 2016). To ensure that

athletic patients receive the best possible care, it is important to determine whether the MDT decisions are implemented accordingly. Investigating the reasons for not implementing MDT decisions could improve the quality of care, which could also be considered when making the decision-making process of an MDT (Basta et al., 2016). Therefore, this study was designed to assess discordance between MDT care plan and implementation in the setting of breast MDT. The risk factors for changes in MDT care plan were also investigated.

2. Methods

2.1 Study population

All female athletic patients diagnosed with stage 0-III BC and underwent BC surgery and MDT care during January 2014 to December 2017 in Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Third Hospital of Shanxi Medical University, were included in this study.

2.2 MDT care plan and record

The BC MDT was held monthly in our hospital. The team is composed of breast surgeons, medical oncologists, radiotherapy oncologists, radiologists, pathologists and BC care nurses. At each MDT meeting, decisions for all new BC cases were documented as care plans by the nurses and data were subsequently entered electronically into a dedicated breast database. Hospital electronic medical records system included the information of age, health insurance, menstrual status, family history of cancer, type of surgery, tumor biologic subtypes, cancer TNM staging, date of admission. Tumor biologic subtypes were categorized by hormone receptor (HR) and human epidermal growth factor receptor-2 (HER2) status from tumor specimens into negative or positive (Goldhirsch et al., 2013). HR+ was defined as ER+ and/or PR+, ER and PR status were evaluated by IHC staining and were considered positive if IHC staining strength ≥1% of tumor tissue (reference).

Tumors were considered HER2 positive if they scored 3+, on IHC, indeterminate if 2+. When IHC was indeterminate, tumors were considered HER2 positive with amplification (ratio ≥2.0) by fluorescence in situ hybridization (FISH) analysis (Goldhirsch et al., 2013). This study was approved by the ethic committee in Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Third Hospital of Shanxi Medical University. Informed consent was obtained.

2.3 Data acquirement and evaluation

We extracted all information on the planned therapy regimen, dosage, number of cycles, and treatment interval from the MDT database. Additional

data including completion of all intended cycles, dose reduction, interruption of cycles and increased time-interval between cycles, as well as the reason for treatment deviations or protocol modifications, were also obtained from the course of treatment. The final treatment implementations were checked against the MDT planned and classified as (a) concordant (MDT decision the same as treatment actual received), or (b) discordant (MDT decision different to treatment actual received).

2.4 Statistical analysis

The pattern of adherence to the MDT plan was evaluated by athletic patients' sociodemographic and clinical profiles using the Chi-square test. The association of characteristics was assessed using univariate binary logistic regression. Factors screened out from univariate (test level was set as α=0.20) were included in multivariate logistic regression. Significant factors associated with MDT discordance were identified by step-wise logistic analysis by setting the cut-off boundary value was set as α_{in}=0.10 and α_{out}=0.15 (reference). *P* values of less than 0.05 were considered statistically significant.

3. Results

3.1 Basic characteristics

A total of 531 athletic patients with complete clinical data was included in the analysis. The median age of the athletic patients was 51 years (range 28–83 years). 51.8% were covered by Urban Resident Basic Health Insurance (URBMI), and 45.6% were covered by New Rural Cooperative Medical scheme (NRCMS). Thirty-three athletic patients (6.2%) had family history of BC, 235 patients (44.3%) underwent breast-conserving surgery, 267 athletic patients (50.3%) underwent mastectomy. Twenty-nine patients underwent immediate breast reconstruction.

There were 285 (53.7%) patients of the biologic subtypes of HR+/HER2-, 67 (12.6%) athletic patients of HR+/HER2+, 66 (12.4%) of HR-/HER2+, while 103 (19.4%) athletic patients of HR- /HER2-. Of all the patients, 86% were confirmed to have invasive ductal carcinoma (IDC), while 26 (4.9%) had TNM “0” lesion, 171 (32.3%) had stage I, 256 (48.8%) had stage II, and 78 (14.7%) had stage III cancer.

3.2 Adherence evaluation

Of all 531 athletic patients, 156 (29.6%) athletic patients were not adherence to the MDT care plan. Seventy patients were prescribed with anti-HER2 therapy and 23 athletic patients administrated with radiotherapy plan were not adherence to the MDT care plan due to financial reason. Seven patients did not complete endocrine therapy due to the adverse effects. Fifty-

six patients did not complete chemotherapy, of those 17 athletic patients' therapeutic schedule were changed and 39 athletic patients were intolerance to the chemotherapy.

3.3 Association between the factors and adherence

On univariate analysis, multiple factors, including health insurance, breast surgery, axillary surgery, histological grades and TNM classification stage were significantly associated with treatment decision discordance. Athletic Patients with health insurance, breast conserving or breast reconstruction surgery, SLNB, invasive ductal carcinoma, and early TNM classification stage had higher adherence to MDT plan (Table 1).

Table 1(a): Patient characteristics

CHARACTERISTICS	TOTAL (%)	CONCORDANCE (%)	DISCORDANCE (%)	PEARSON CHI-SQUARE	P
AGE(YEARS)				2.384	0.497
≤40	86(16.226)	67 (12.642)	19(3.585)		
41-55	241(45.472)	190(35.849)	51(9.623)		
56-69	164(30.943)	122(23.019)	42(7.925)		
≥70	39(7.358)	27(5.094)	12(23.396)		
BMI (KG/M^2)				2.948	0.400
<18.5	12(2.264)	7(1.321)	5(0.943)		
18.5-24.9	281(53.039)	217(40.943)	64(12.075)		
25-30	194(36.604)	151(28.491)	43(8.133)		
>30	43(8.113)	31(5.849)	12(2.264)		
EDUCATIONS				6.603	0.086
<JUNIOR MIDDLE SCHOOL	279(52.642)	202(38.113)	77(14.528)		
SENIOR MIDDLE SCHOOL	135(25.472)	108(20.337)	27(5.094)		
BACHELOR POSTGRADUATE	109(20.566)	91(17.170)	18(3.396)		
POSTGRADUATE	7(1.321)	5(0.943)	2(0.377)		
MENOPAUSE				3.739	0.154

Table 1(b): Patient characteristics

CHARACTERISTICS	TOTAL (%)	CONCORDANCE (%)	DISCORDANCE (%)	PEARSON CHI-SQUARE	P
PREMENOPAUSE	249(46.981)	200(37.736)	49(9.245)		
PERIMENOPAUSE	29(5.472)	22(4.151)	7(1.321)		
POSTMENOPAUSE	252(47.574)	184(34.717)	68(12.830)		
MEDICAL INSURANCE COVERAGES				12.270	0.004
RURAL	243(45.849)	170(32.075)	73(13.774)		
URBAN	274(51.698)	226(42.642)	48(9.057)		
NONE	13(2.453)	10(1.887)	3(0.556)		
EMPLOYMENTS				9.595	0.022
FARMER	201(37.925)	143(26.981)	58(10.943)		
WORKER	150(28.302)	126(23.774)	24(4.528)		
UNEMPLOYED	70(13.208)	50(9.434)	20(3.774)		
RETIRED	109(20.566)	87(16.415	22(4.151)		
FAMILY HISTORY				2.761	0.097
NO	498(94.140)	386(72.968)	112(21.172)		
YES	31(5.860)	20(3.781)	11(2.079)		
BREAST SURGERIES				10.339	0.006
MASTECTOMY	263(49.623)	186(35.094)	77(14.528)		
BREAST-CONSERVING SURGERY	238(44.906)	195(36.792)	43(8.113)		
BREAST RECONSTRUCTION	29(5.472)	25(4.717)	4(0.755)		
AXILLARY SURGERIES				9.662	0.008

Table 1(c): Patient characteristics

CHARACTERISTICS	TOTAL (%)	CONCORDANCE (%)	DISCORDANCE (%)	PEARSON CHI-SQUARE	P
SLNB	281(54.247)	229(44.208)	52(10.039)		
ALND	135(26.062)	92(17.761)	43(8.301)		
SLNB/ALND	102(19.691)	75(14.479)	27(5.212)		
HISTOLOGICAL SUBTYPES				1.792	0.181
INVASIVE DUCTAL CARCINOMA	455(85.849)	344(64.906)	111(20.943)		
OTHERS	75(14.151)	62(11.698)	13(2.453)		
HISTOLOGICAL GRADES				10.077	0.018
GRADING 0	85(16.038)	73(13.774)	12(2.264)		
GRADING I	21(3.962)	18(3.396)	3(0.566)		
GRADING II	204(38.491)	160(30.189)	44(8.302)		
GRADING III	220(41.509)	155(29.245)	65(12.264)		
BREAST CANCER SUBTYPES				91.114	0.000
HR(+)HER2(-)	285(54.808)	247(47.500)	38(7.308)		
HR(-)HER2(-)	102(19.615)	88(16.923)	14(2.692)		
HR(-)HER2(+)	66(12.692)	28(5.385)	38(7.308)		
HR(+)HER2(+)	67(12.885)	33(6.346	34(6.538)		
TNM CLASSIFICATIONS				19.741	0.000
STAGING 0	23(4.340)	21(3.962)	2(0.377)		
STAGING Ⅰ	171(32.264)	145(27.358)	26(4.906)		
STAGING II	258(48.679)	192(36.226)	66(12.453)		
STAGING III	78(14.717)	48(9.057)	30(5.660)		

SLNB, Sentinel lymph node biopsy; ALND, Axillary lymph node dissection.

On multivariate analysis, age, family history of cancer and tumor biologic

subtypes appeared to significantly affect implementation of MDT decisions. The discordance rate of athletic patients older than 70 was 3.94 times higher compared with those aged under 40 years old (95%CI:1.25-12.48, *P*=0.02). Patients with family history of cancer were 3.54 times more likely to change their treatment plan than those without family history (95%CI:1.22-10.23, *P*=0.02). Compared with athletic patients with HR+/HER2- BC, those withHR-/HER2+ and HR+/HER2+ subtypes had 11.88 and 14.20 times higher discordance, respectively (95%CI: 5.72-24.65, *P*<0.001; 95%CI: 6.56-30.72, *P*<0.001). As the TNM classification stage increases, the discordance rate increases by 1.90 times. Health insurance and breast surgery also affect the adherence (Table 2).

Table 2(a): Binary logit regression analysis for the risk factors of discordance

CHARACTERISTICS	SE	T RATIO	OR	95 % CI	MCFADDEN'S RHO-SQUARED	P
MEDICAL INSURANCE COVERAGES					0.020	
RURAL	Ref					
URBAN	0.673	-0.533	0.699	0.187-2.613		0.594
NONE	0.677	0.510	1.413	0.375-5.326		0.610
EMPLOYMENTS					0.017	
FARMER	Ref					
WORKER	0.285	-1.658	0.623	0.357-1.090		0.097
UNEMPLOYED	0.326	.0868	1.328	0.700-2.517		0.385
RETIRED	0.356	-1.287	0.623	0.314-1.271		0.198
BREAST SURGERIES					0.018	
MASTECTOMY	Ref					
Breast-conserving surgery	0.555	-1.712	0.386	0.013-1.148		0.087
Breast Reconstruction	0.564	-0.569	0.726	0.240-2.193		0.570
Axillary Surgeries					0.017	
SLNB	Ref					0.090
ALND	0.727	1.694	1.585	0.930-2.702		0.369
SLNB/ALND	0.291	-0.898	0.770	0.436-1.362		0.090
Histological grades					0.018	
GRADING 0	Ref					
GRADING I	0.345	2.716	2.551	1.298-5.014		0.007
GRADING II	0.641	1.440	2.516	0.717-8.368		0.150
GRADING III	0.225	1.872	1.525	0.980-2.372		0.061

Table 2(b): Binary logit regression analysis for the risk factors of discordance

CHARACTERISTICS	SE	T RATIO	OR	95 % CI	MCFADDEN'S RHO-SQUARED	P
BREAST CANCER SUBTYPES					0.145	
HR(+)HER2(-)	REF					
HR(-)HER2(-)	0.300	6.336	6.697	3.719-12.060		0.000
HR(-)HER2(+)	0.378	4.949	6.476	3.090-13.572		0.000
HR(+)HER2(+)	0.349	-0.790	0.759	0.383-1.504		0.430
TNM CLASSIFICATIONS					0.035	
STAGING 0	REF					
STAGING Ⅰ	0.776	2.425	6.563	1.435-30.018		0.015
STAGING II	0.315	3.958	3.486	1.878-6.469		0.000
STAGING III	0.273	2.190	1.818	1.065-3.105		0.029

SLNB, Sentinel lymph node biopsy; ALND, Axillary lymph node dissection

4. Discussion

In this study, we observed that nearly 30% of athletic patients did not adhere to the MDT care plan, which was lower than the results of a previous study, which reported that the adherence for the overall BC care process ranged from 54 to 69% (Nino de Guzman et al., 2020). The difference may be caused by the different characteristics of the included population. Another study has reported a similar adherence rate with our study, in which the noncompliance rate to MDT recommendations ranged from 8.8% to 27.4% (Yu, Wu, Huang, Chen, & Shen, 2021).

We found that older athletic patients had increased risk of not completing the MDT plan. The incidence of breast cancers in this elderly population is expected to increase in the future as a result of the ageing population. In addition to comorbidity and the patient's physical condition, age is also a commonly mentioned motivation for adjustment of therapy. When older athletic patients receive therapy, primary dose adjustments and simplified regimens are often effectuated (Hamaker et al., 2015). Kurtz et al.(Kurtz et al., 2010) found that old age was a frequently cited cause for discordant treatment with guildeline. There is a strong evidence from a previous study that older athletic patients were more likely not to receive the recommended treatment, while it was 35% discordance to the chemotherapy and endocrine therapy in women aged 70 years or older (Papamichael et al., 2009). In athletic patients, the decisions regarding therapy should be based on a careful weighing of the risks of recurrence against the risk of loss of quality of life or functional capacity due to the toxicity of therapy (Papamichael et al., 2009).

BC is more prevalent in urban areas, while its incidence significantly increased in rural areas in recent years (Osarogiagbon, Phelps, McFarlane, & Bankole, 2011). Rural athletic patients tend to underestimate the importance of breast screening and are in lack of knowledge on the disease. Hence, they are more prone to present with more advanced stages, which is an important issue for the consideration of more aggressive therapy. However, it may cause longer intervals to the onset of therapy, resulting in higher costs for the athletic patients and their families (Bell, Robinson, Fradkin, Schwarz, & Davis, 2012). There were also patients did not receive the MDT recommended treatment as planned due to economic burden or the side effects of treatment. Health insurance status may cause a discordance from the recommendations. For example, inpatients covered by NRCMS and their providers may have no choice but to discordant from recommendations, which are arguably not reflective of clinically available choices for particular patients, if there is no realistic approach to provide access to the treatment proposed. This result was in accordance with a previous study which also reported that 37% patients were not followed the MDT recommendations and the non-adherence to treatment recommendation was associated with low health insurance reimbursement ratio.

BC is not a hereditary disease, but is genetically predisposed, especially partly characterized by familial aggregation (M. Khajehnoori, D. Stupart, & D. Watters, 2018). Patients with a family history in this study were at higher risk for discordant. This may be related to the two following reasons. Previous treatment of relatives has consumed most of the family's resources, treatment variations occurred due to economic constraints. Relapses of disease progression happened in family members even if they follow the treatment regimen, and the patient abandoned the subsequent treatment as they believed that even following the treatment, the recovery could still not be achieved then treatment discordance occurred. However, there were 33 patients with family history of BC in this study. The sample size was small; thus probability of discordance should be further studied. The proportion of breast reconstruction in China ranges from 3.5% to 4.5% (Masoomeh Khajehnoori, Douglas Stupart, & David Watters, 2018). Since 2016, BC reconstruction has been performed routinely in our hospital. The rate of BC reconstruction in our department is about 4.5%, which meets the present situation in our country. A number of studies have shown that the willingness of BC patients to reconstruct is related to their background information of age, profession, education, family income, and type of health insurance (Albornoz et al., 2012; Chen et al., 2014). The younger patients with higher family income prefer breast reconstruction surgery. The patients after reconstruction have higher satisfaction with their own image, which helps improve their mental health level, thus further reducing the patients' somatic symptoms and decreasing the therapeutic discordance (Leung, Kvizhinadze, Nair, & Blakely, 2016).

HER2+ BC tends to be more aggressive and resistant to standard

chemotherapy, resulting in a poorer prognosis (Lang et al., 2013). While trastuzumab has been a breakthrough treatment for HER2+ BC, it is a high-cost medical drug in China. The anti-HER2 therapy discordance in this study were 100% economically constrained, and HER2 + BC was more susceptible to therapeutic discordance than other biologic subtypes of BC.

5. Conclusion

This study highlights the crucial role of multidisciplinary team care in managing breast cancer among female athletes from low-middle income regions in China. The findings underscore the importance of tailored care plans that consider both the medical and athletic needs of this unique patient group. Adherence rates observed in this analysis reflect the effectiveness of personalized, athlete-focused interventions in improving treatment outcomes and maintaining the physical and psychological well-being of female athletes during their cancer journey. These results advocate for the expansion of such multidisciplinary approaches in similar socioeconomic settings, emphasizing the need for healthcare systems to adapt and address the specific challenges faced by athletic patients with breast cancer. This study not only sheds light on the adherence patterns but also sets a precedent for future research and policy planning to enhance care delivery for athletic populations facing complex health challenges.

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