

# 176P The effectiveness of long-term physical activity after exercise and educational programs on breast cancer-related lymphoedema: secondary analyses from a randomized controlled trial: The Setouchi Breast Project 10.

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## Background

Breast cancer–related lymphedema (BCRL) is a complication in patients who received breast cancer surgeries<sup>1</sup>). A meta-analysis showed that the incidence of BCRL ranged between 8.4–21.4%<sup>2</sup>). Regular physical activity (PA) have various beneficial effects on breast cancer patients<sup>3</sup>). Several studies indicated that exercise might reduce the incidence of lymphedema<sup>4,5</sup>). However, it is unclear the association between higher PA and preventive effect on BCRL. The aim of this study was to investigate the effectiveness of long-term PA after exercise and educational programs on BCRL.

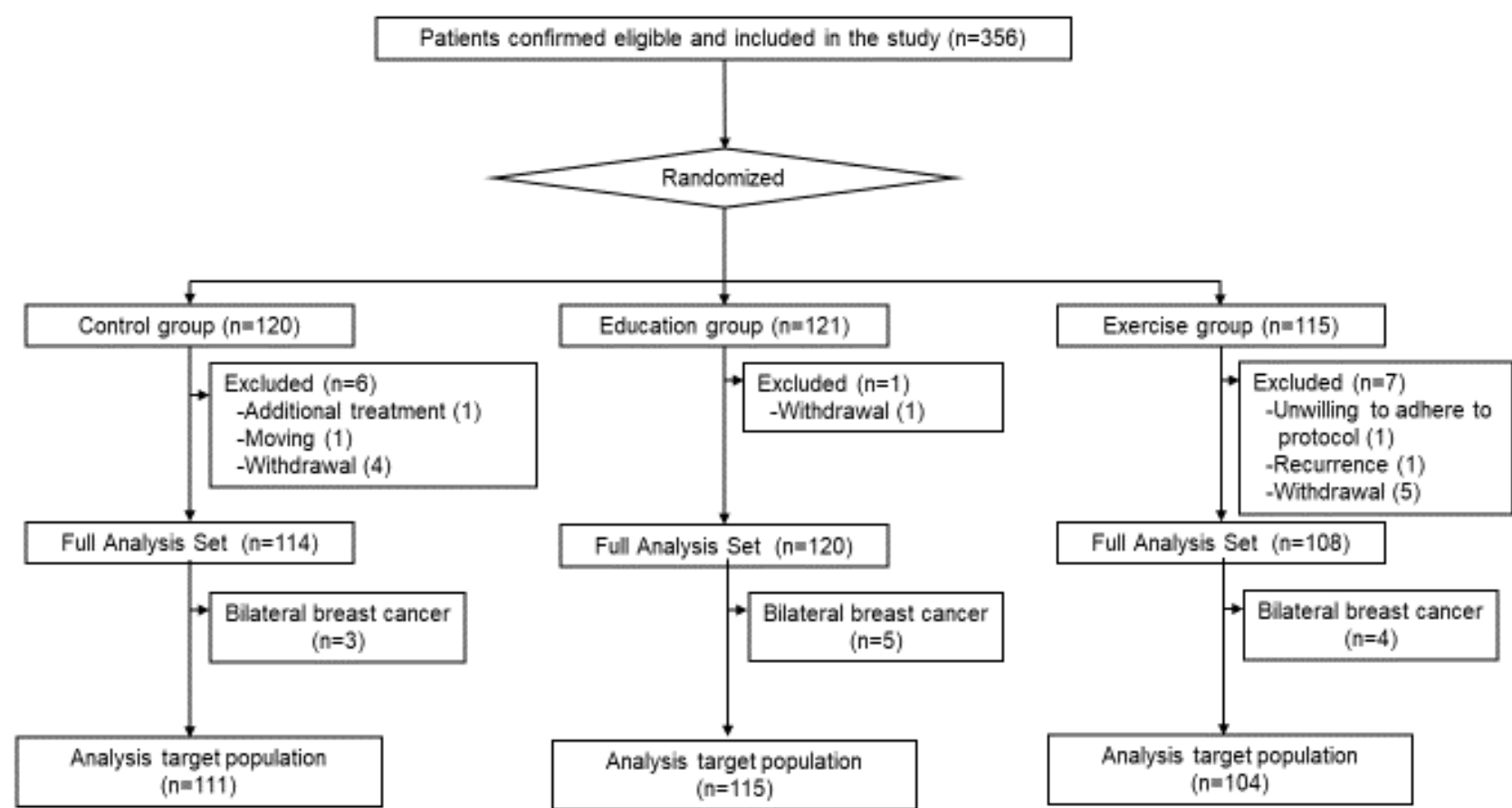
## Methods

This study was secondary analyses from a prospective randomized controlled trial evaluating the efficacy of exercise and educational programs on long-term PA compared with usual care. Participants with stage 0–III breast cancer were randomly assigned in this study. The secondary endpoint was to assess the incidence of and preventive effect on BCRL at 1year after intervention.

BCRL was measured the ways with arm-circumference measurements. Arm-circumference measurements were taken on both arms at 4 points: the circumference of the thumb base or the metacarpophalangeal joints, the wrist joints, 5 cm distal to the midpoint of the lateral epicondyle, and 10 cm proximal to the midpoint of the lateral epicondyle. BCRL was defined as a difference of greater than 2.0 cm between the affected and non-affected arm circumferences at any of measurement points.

Participants in the control group were provided with an educational brochure on lifestyle after breast cancer treatment without any additional direct instruction by medical staff. In the education group, participants had to attend at least one instructional class on lifestyle (exercise and diet) for breast cancer survivors by breast medical doctors within 3 months of registration using an educational brochure. In the exercise program group, participants received a 30-min exercise program consisting of three parts, including aerobic exercise, workout, and stretching, three times a week for 4 months (16 weeks).

Figure.1 Participants’ flowchart



We enrolled breast cancer patients from March 2016 to March 2020 and randomly assigned them to the control (n = 111), education (n = 115), or exercise (n = 104) group.

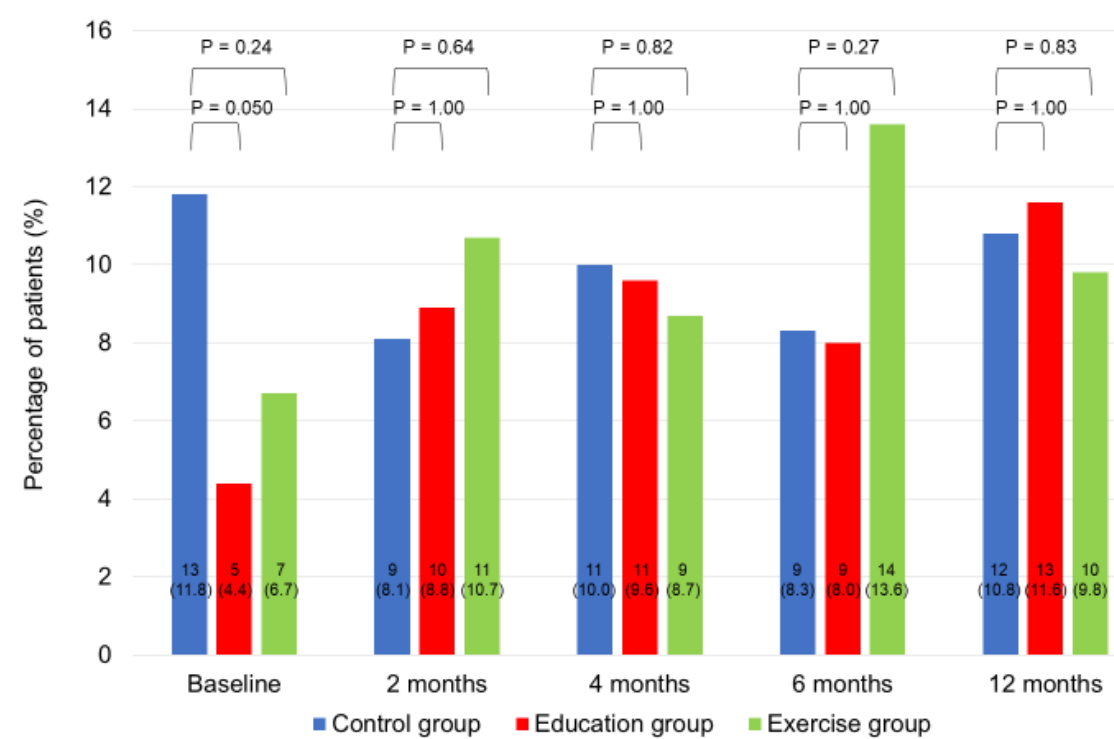
SD, standard deviation; BMI, body mass index; HER2, human epidermal growth factor receptor type2. \*: P values were calculated by Kruskal-Wallis test.

## Results

Table1. Patient characteristics at baseline

Characteristic	Control group N = 111 (%)	Education group N = 115 (%)	Exercise group N = 104 (%)	P value
Age (years)				
mean (SD)	55.2 (11.3)	54.4 (10.8)	55.4 (10.4)	0.75*
BMI (kg/m2)				
mean (SD)	23.3 (3.8)	23.0 (3.1)	23.3 (3.4)	0.77*
Obesity rate				
Non-obesity	73 (65.8)	86 (75.4)	74 (71.2)	0.28
Obesity	38 (34.2)	28 (24.6)	30 (28.8)	
Stage				
0	11 (9.9)	11 (9.6)	14 (13.5)	0.74
I	56 (50.5)	50 (43.5)	47 (45.2)	
II	33 (29.7)	43 (37.4)	31 (29.8)	
III	11 (9.9)	10 (8.7)	12 (11.5)	
missing	-	1 (0.9)	-	
Breast surgery				
mastectomy	65 (58.6)	68 (59.1)	60 (57.7)	0.98
breast conserving surgery	46 (41.4)	47 (40.9)	44 (42.3)	
Surgical side				
right	62 (55.9)	53 (46.1)	46 (44.2)	0.18
left	49 (44.1)	62 (53.9)	58 (55.8)	
Surgery for axilla				
axillary dissection	33 (29.7)	38 (33.0)	34 (32.7)	0.59
sentinel node biopsy	76 (68.5)	76 (66.1)	66 (63.5)	
no axillary surgery	2 (1.8)	1 (0.9)	4 (3.8)	
Number of axillary lymph node metastases				
0	80 (72.1)	83 (72.2)	76 (73.1)	0.80
1–3	20 (18.0)	21 (18.3)	20 (19.2)	
4–10	4 (3.6)	7 (6.1)	4 (3.8)	
Over 10	3 (2.7)	2 (1.7)	-	
missing	4 (3.6)	2 (1.7)	4 (3.8)	
Estrogen receptor status				
positive	89 (80.2)	92 (80.0)	81 (77.9)	0.70
negative	22 (19.8)	22 (19.1)	23 (22.1)	
unknown	-	1 (0.9)	-	
Progesterone receptor status				
positive	82 (73.9)	80 (69.6)	77 (74.0)	0.66
negative	29 (26.1)	34 (29.6)	27 (26.0)	
Unknown	-	1 (0.9)	-	
HER2 status				
positive	32 (28.8)	18 (15.7)	23 (22.1)	0.027
negative	75 (67.6)	93 (80.9)	71 (68.3)	
Unknown	4 (3.6)	4 (3.5)	10 (9.6)	
(Neo) adjuvant chemotherapy				
yes	58 (52.3)	60 (52.2)	52 (50.0)	0.93
no	53 (47.7)	55 (47.8)	52 (50.0)	
Docetaxel for (neo) adjuvant chemotherapy				
yes	26 (23.4)	23 (20.0)	18 (17.3)	0.54
no	85 (76.6)	92 (80.0)	86 (82.7)	
Endocrine therapy				
yes	82 (73.9)	89 (77.4)	71 (68.3)	0.71
no	29 (26.1)	26 (22.6)	33 (31.7)	
Radiotherapy				
yes	59 (53.2)	72 (62.6)	55 (52.9)	0.25
no	52 (46.8)	43 (37.4)	49 (47.1)	

Figure 2. Percentage of patients with breast cancer-related lymphoedema at each measurement points



There were no significant differences in the incidence of BCRL at 1 year between the exercise and control groups (9.8% and 10.8%, P = 0.83) and between the education and control groups (11.6% and 10.8%, P = 1.00).

Table2. Univariate and multivariate analyses for the lymphedema at baseline

	Univariate Analysis			Multivariate Analysis		
	HR	95%CI	p	HR	95%CI	p
Age	1.01	0.99–1.03	0.25			
Breast surgery (Mastectomy vs. Breast conserving)	1.51	0.96–2.35	0.072	1.21	0.75–1.95	0.45
Obesity rate (Obesity vs. Non-Obesity)	1.74	1.13–2.69	0.013	1.65	1.07–2.56	0.024
Surgery for axilla (Axillary dissection vs. SNB or no surgery)	2.45	1.60–3.77	<0.001	2.11	1.34–3.31	0.001
(Neo) adjuvant chemotherapy (yes vs. no)	1.07	0.70–1.65	0.75			
Docetaxel for (neo) adjuvant chemotherapy (yes vs. no)	0.85	0.49–1.46	0.55			
Endocrine therapy (yes vs. no)	0.78	0.49–1.22	0.27			
Radiotherapy (yes vs. no)	1.44	0.92–2.24	0.11			
Physical activity (>5 vs. ≤5METs/week)	0.87	0.55–1.36	0.53			
Intervention						
Exercise vs. Control	1.26	0.73–2.15	0.41			
Education vs. Control	1.32	0.78–2.21	0.30	1.21	0.75–1.95	0.45

CI, confidence interval; HR, hazard ratio; METs, metabolic equivalents; SNB, sentinel node biopsy

## Conclusion

Although the effectiveness of long-term PA after intervention on BCRL was not observed, among patients with axillary dissection, the high PA at baseline compared to the low PA may have a lower BCRL. Future studies to investigate appropriate interventions and subgroups to prevent on BCRL should be needed.

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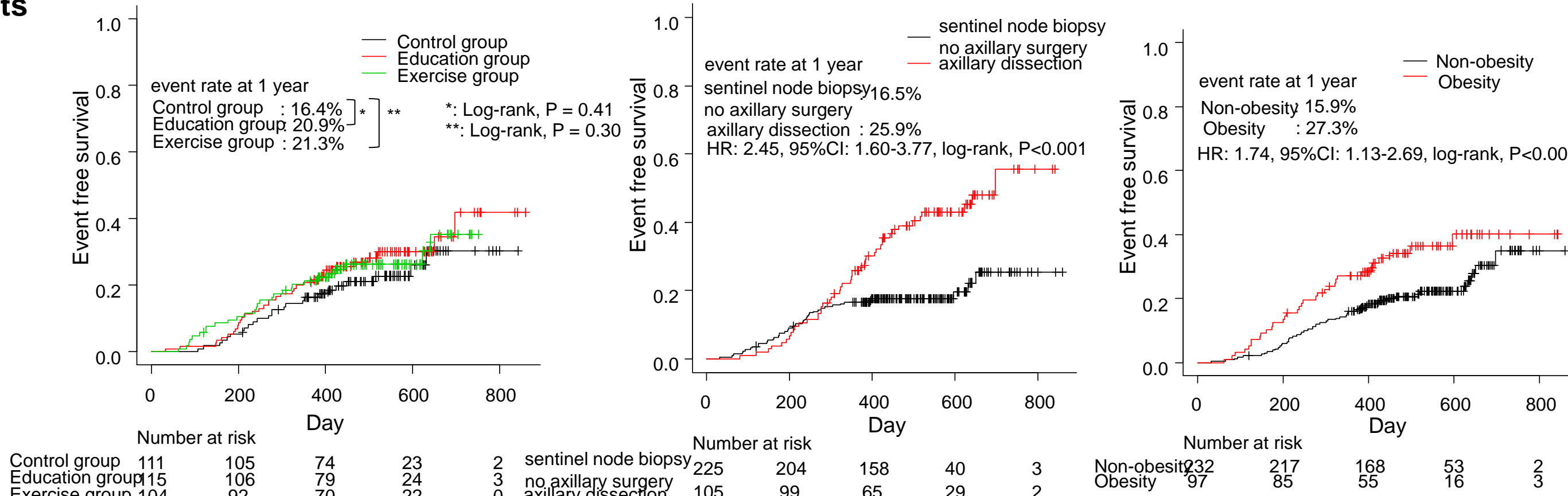
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## Acknowledgements

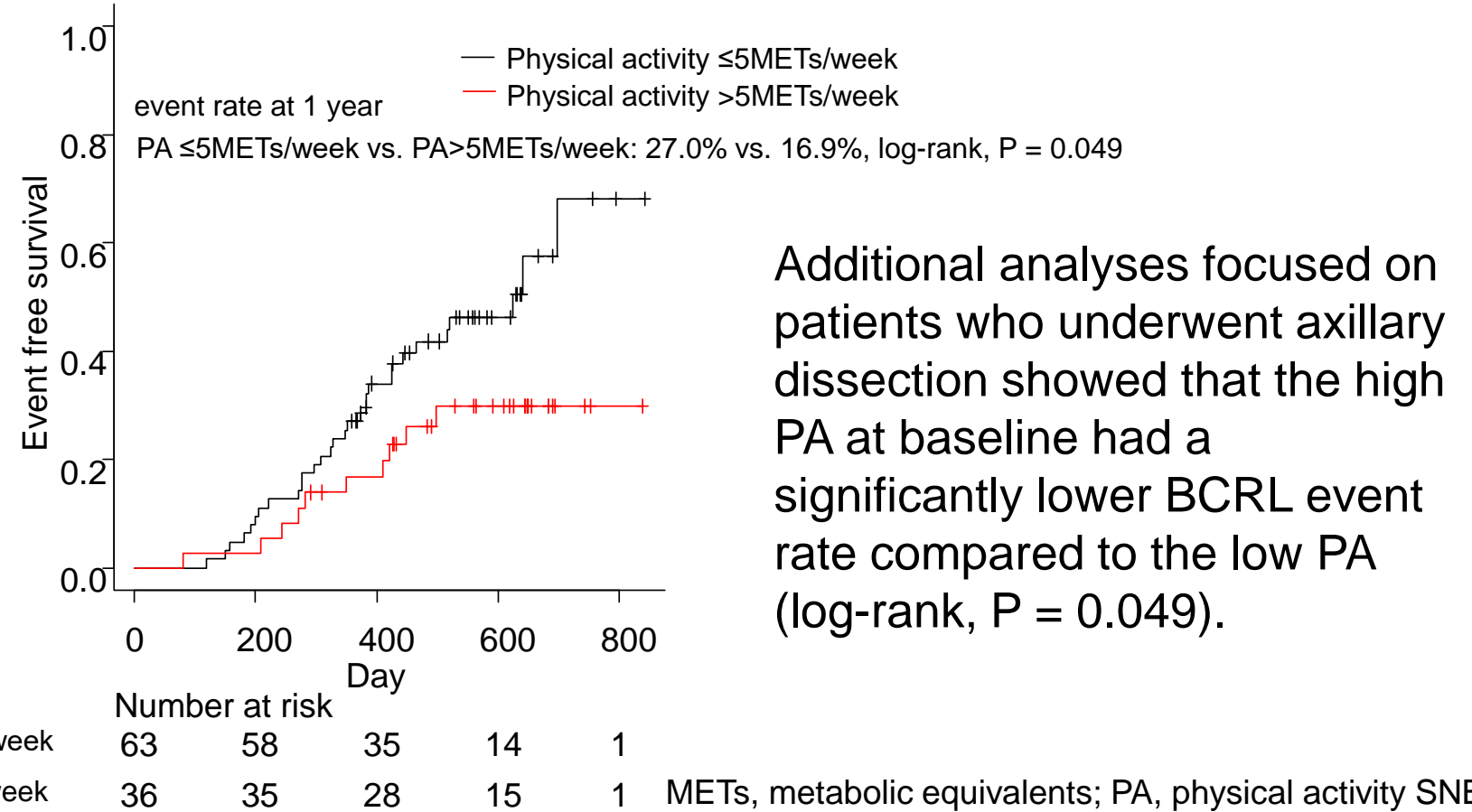
The results of this research were presented in Japanese at the 2021 Chugoku-Shikoku Breast Cancer Society Regional Meeting. This study was conducted as a research support project for the Setouchi Breast Project Comprehensive Support Organization and was supported by JSPS KAKENHI Grant Number 15K01714 and 19K10622.

Figure 3. Time to onset of lymphedema by interventions (A), surgery for axilla (B), obesity rate (C)



There were no significant differences in time to onset of BCRL from surgery between the exercise and control groups (event rate at 1 year: 21.3% and 16.4%, log-rank, P = 0.41) and between the education and control groups (event rate at 1 year: 20.9% and 16.4%, log-rank, P = 0.30). The incidence of BCRL in patients with axillary dissection and obesity was significantly higher compared with that in patients with sentinel node biopsy or no surgery (25.9% and 16.5%, log-rank P < 0.001) and non-obesity (27.3% and 15.9%, log-rank P = 0.012), respectively.

Figure 4. Time to onset of lymphedema in patients who received axillary dissection by physical activity at baseline



Additional analyses focused on patients who underwent axillary dissection showed that the high PA at baseline had a significantly lower BCRL event rate compared to the low PA (log-rank, P = 0.049).