Meta-Analysis Aerobic Exercise Improves Quality of Life in Breast Cancer Survivor

Citra Ayuningtiyas¹, Agus Kristiyanto², Bhisma Murti¹

¹Masters Program in Public Health, Universitas Sebelas Maret
²Faculty of Sport Education, Universitas Sebelas Maret

ABSTRACT

Background: Cancer is one of the health problems throughout the world, the increasing mortality rate due to breast cancer is one of them because it is detected at an advanced stage. In 2018 breast cancer was at the top of the list impacting 2,088,849 (11.6%) world women every year and with an incidence of death of 626,679 (6.6%) cases. One category of intervention to improve the quality of life of breast cancer survivors that has developed in recent years is by means of aerobic exercise. This study aims to estimate the magnitude of the effect of aerobic exercise on the quality of life of breast cancer survivors.

Subjects and Method: This study was a meta-analysis study with PICO as follows P = breast cancer survivors, I = aerobic exercise, C = no intervention, O = quality of life. The articles used in this study were obtained from several databases, namely PubMed, Science Direct, and Google Scholar. This article was collected for 2 months. The keywords to search for articles were as follows: “breast cancer” OR “ca mammae” OR “carcinoma mammae” OR “mammae cancer” AND aerobic OR “aerobic exercise” AND “quality of life” OR “QOL” AND “RCT” OR “randomized control trial” OR “cluster-randomized control trial”. The articles included in this study are full text articles with a Randomized Controlled Trial study design. Articles were analyzed using the Review Manager 5.3 application. The results of the meta-analysis are reported using the PRISMA flow diagram.

Results: There are 9 articles that have been analyzed from California, America, Iran, Kosovo, Spain, England, Canada, Germany, and the Netherlands. Studies show that aerobic exercise intervention improves the quality of life of breast cancer survivors SMD= 0.14; 95% CI= -0.23 to 0.51), and the results were not statistically significant (p= 0.460).

Conclusion: Aerobic exercise improves the quality of life of breast cancer survivors.

Keywords: aerobic exercise, breast cancer survivors, quality of life


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BACKGROUND

Breast cancer is the main cause of death among all cancers experienced by women in Indonesia. Cancer is one of the health problems throughout the world, the increasing mortality rate due to breast cancer is one of them because it is detected at an advanced stage (WHO, 2014). Meanwhile, according to the National Breast Cancer Foundation, breast cancer begins in the cells of the lobules, which are milk-producing glands, or it can also start in the ducts that drain milk from the lobules to the nipple. In addition, breast...
cancer can also begin in the stromal tissue, which includes the fat and fibrous connective tissue of the breast.

One of the most common cancers is breast cancer among women in both developed and developing countries (Elsheshawy et al., 2014). Breast cancer is a cancer that causes death in women in the world, breast cancer is the highest contributor to the mortality rate in women in the world, namely 43.3 per 100,000 (Assembly, 2017).

Based on the 2018 World Health Organization (WHO) report, breast cancer is at the top of the list, affecting 2,088,849 (11.6%) women in the world every year and with an incidence of death of 626,679 (6.6%) cases. The most cases of breast cancer can be found in Asia, with 43.3% of all breast cancer cases in the world and a death rate of 49.4% of all deaths. According to the 2018 Global Cancer Observatory (GLOBA CAN) Report, Asia ranks first in the continent with the most breast cancer cases with 911,014 (43.6%) new cases and an estimated incidence of 310.577 (49.6%) deaths.

Global Cancer Observatory 2018 data from the World Health Organization (WHO) shows that the most common cancer cases in Indonesia are breast cancer, which is 58,256 cases or 16.7% of the total 348,809 cancer cases. Cervical (cervical) cancer is the second most common type of cancer in Indonesia, with 32,469 cases or 9.3% of the total cases. According to WHO (2018), cancer patients increased to 18.1 million new cases with 9.6 million deaths, while 627,000 women died of breast cancer in 2018. Basic Health Research data in 2018 showed that the prevalence of breast cancer in Indonesia based on doctor’s diagnosis increased by 0.14% to 0.18% in 2018.

The incidence of cancer in Indonesia (136.2/100,000 population) is at number 8 in Southeast Asia, while in Asia it is ranked 23. Meanwhile, the highest incidence rate for women is breast cancer, which is 42.1 per 100,000 population with an average death rate of 17 per 100,000. 100,000 population followed by cervical cancer was 23.4 per 100,000 population with an average death rate of 13.9 per 100,000 population (Ministry of Health & Indonesia, 2021).

One category of intervention to improve the quality of life of breast cancer survivors that has developed in recent years is by means of aerobic exercise. Exercise is an effective intervention to improve quality of life (Jones et al., 2002). The quality of life in breast cancer patients between early and advanced stages has a long-term quality of life that differs depending on the treatment carried out by the patient, besides that physical fatigue and activity can affect the quality of life of patients with breast cancer (Canario et al., 2016).

Based on this background, a comprehensive research is needed from various primary studies on the effect of aerobic exercise intervention on the quality of life in children. The data obtained will be analyzed using a systematic review and meta-analysis by synthesizing the results of studies conducted to reduce bias.

**SUBJECTS AND METHOD**

1. **Study Design**
   This research is a systematic review and meta-analysis. The articles used in this study were obtained from several databases including PubMed, ScienceDirect and Google Scholar. The keywords to search for articles were as follows: “breast cancer” OR “ca mammae” OR “carcinoma mammae” OR “mammae cancer” AND aerobic OR “exercise, aerobic” AND “quality of life” OR “QOL” AND “RCT” OR “randomized control trial” OR “cluster-randomized control trial”.

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2. Inclusion Criteria
The articles included in this study are full paper articles with a randomized controlled trial study design. Research subjects are breast cancer survivors. Selected articles provide intervention in the form of aerobics for the quality of life of breast cancer survivors.

3. Exclusion Criteria
Articles published in this study are articles that are not in English or Indonesian, research designs other than RCTs, articles that are not full text, articles published before 2000.

4. Operational Definition of Variables
The search for articles was carried out by considering the eligibility criteria defined using the PICO model. The population in the study were breast cancer survivors, intervention in the form of aerobic exercise, and the outcome in the form of quality of life.

Aerobic exercise is a physical activity in which all activities use oxygen to achieve a person's physical stamina. Instrument: aerobic exercise with categorical measurement scale.

Quality of life is the overall general well-being that includes physical, material, social and emotional well-being along with levels of personal development and activities that are purposeful, meaningful and valuable. Instrument: questionnaire with categorical measurement scale.

5. Study Instruments
The study was conducted using the PRISMA flow chart guidelines and the assessment of the quality of research articles using the Critical Appraisal Checklist for Cross-sectional Study (CEBMa, 2014).

6. Data Analysis
Data processing was carried using by Review Manager (RevMan 5.3) by calculating the mean difference to determine the combined research model and form the final result of the meta-analysis.

RESULTS
The process of searching for articles by searching through databases with journals can be seen in Figure 1. There were 1637 articles identified from the database, after the process of deleting duplicate articles, there were 1279 articles with 41 of them meeting the requirements. Articles were excluded for several reasons, so that 9 articles were included in the synthesis and meta-analysis studies. There were 9 articles from 3 continents, namely America, Europe and Asia. 2 studies from the Americas, 6 studies from the European continent and 1 study from the Asian continent.
Figure 1. PRISMA flow diagram

Figure 2. Map of the research area for aerobic exercise for breast cancer survivors kualitas quality of life
**Table 1. Quality Assessment**

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Does this study address a clear research focus?</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td>2</td>
<td>Is the Randomized Controlled Trial research method appropriate to answer the research question?</td>
<td>1</td>
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<td>1</td>
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<td>1</td>
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<tr>
<td>3</td>
<td>Are there enough subjects in the study to establish that the findings did not occur by chance?</td>
<td>1</td>
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<td>1</td>
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<tr>
<td>4</td>
<td>Were subjects randomly allocated to the experimental and control groups? If not, could this be biased?</td>
<td>1</td>
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<td>5</td>
<td>Are inclusion/exclusion criteria used?</td>
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<tr>
<td>6</td>
<td>Were the two groups comparable at the start of the study?</td>
<td>1</td>
<td>0</td>
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<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
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<tr>
<td>7</td>
<td>Were objective and unbiased outcome criteria used?</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td>8</td>
<td>Are objective and validated measurement methods used in measuring the results? If not, were results assessed by someone who was not aware of the group assignment (ie was the assessment blinded)?</td>
<td>1</td>
<td>1</td>
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<td>1</td>
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<tr>
<td>9</td>
<td>Is effect size practically relevant?</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
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<tr>
<td>10</td>
<td>How precise is the estimate of the effect? Is there a confidence interval?</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<td>1</td>
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</tr>
<tr>
<td>11</td>
<td>Could there be confounding factors that have not been taken into account?</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>12</td>
<td>Are the results applicable to your research?</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
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</tbody>
</table>

**Score**

| 10 | 10 | 10 | 11 | 11 | 10 | 10 | 9  | 11 |

*The question item number 11 is given a score of 0 because the question has a positive score.*
### Table 2. Description of primary studies included in the primary study meta-analysis

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Country</th>
<th>Study Design</th>
<th>Sample (Total)</th>
<th>Sample (Intervention)</th>
<th>P (Population)</th>
<th>I (Intervention)</th>
<th>C (Comparison)</th>
<th>O (Outcome)</th>
<th>Score Mean</th>
<th>Score SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christina et al. (2018)</td>
<td>California</td>
<td>RCT</td>
<td>50</td>
<td>50</td>
<td>Breast cancer survivors with obesity</td>
<td>Supervised moderate-vigorous intensity aerobic intervention.</td>
<td>No intervention</td>
<td>Quality of life, metabolic syndrome</td>
<td>23.2</td>
<td>3</td>
</tr>
<tr>
<td>Laura et al. (2009)</td>
<td>Canada</td>
<td>RCT</td>
<td>49</td>
<td>41</td>
<td>Breast cancer survivor</td>
<td>No intervention</td>
<td>Quality of life</td>
<td>22.7</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Shoebiri et al. (2016)</td>
<td>Iran</td>
<td>RCT</td>
<td>30</td>
<td>30</td>
<td>Breast cancer survivor</td>
<td>No intervention</td>
<td>Quality of life</td>
<td>68.39</td>
<td>16.88</td>
<td></td>
</tr>
<tr>
<td>Galiano-Castillo (2016)</td>
<td>Spain</td>
<td>RCT</td>
<td>36</td>
<td>36</td>
<td>Breast cancer survivors aged 42 – 44 years</td>
<td>Internet-based aerobic exercise</td>
<td>No intervention</td>
<td>Quality of life, muscle strength and fatigue</td>
<td>77.09</td>
<td>16.88</td>
</tr>
<tr>
<td>Steindorf et al. (2014)</td>
<td>Germany</td>
<td>RCT</td>
<td>76</td>
<td>72</td>
<td>Breast cancer survivors receiving adjuvant radiotherapy</td>
<td>Aerobic</td>
<td>No intervention</td>
<td>Quality of life &amp; fatigue</td>
<td>83</td>
<td>19</td>
</tr>
<tr>
<td>Travier et al. (2015)</td>
<td>Netherlands</td>
<td>RCT</td>
<td>77</td>
<td>87</td>
<td>Breast cancer survivor</td>
<td>Aerobic exercise reduces fatigue after breast cancer diagnosis.</td>
<td>No intervention</td>
<td>Quality of life, cardiorespiratory fitness and muscle strength</td>
<td>72.5</td>
<td>19.4</td>
</tr>
<tr>
<td>Murtezani et al. (2014)</td>
<td>Kosovo</td>
<td>RCT</td>
<td>37</td>
<td>36</td>
<td>Breast cancer survivor</td>
<td>Moderate-intensity aerobic exercise</td>
<td>No intervention</td>
<td>Quality of life &amp; physical function</td>
<td>18.2</td>
<td>7.1</td>
</tr>
<tr>
<td>Casla et al. (2015)</td>
<td>Spain</td>
<td>RCT</td>
<td>44</td>
<td>45</td>
<td>Early stage breast cancer survivors</td>
<td>Pragmatic exercise</td>
<td>No intervention</td>
<td>Quality of life increase VO2max</td>
<td>51.49</td>
<td>66.61</td>
</tr>
<tr>
<td>Amanda et al. (2007)</td>
<td>The UK</td>
<td>RCT</td>
<td>34</td>
<td>36</td>
<td>Breast cancer survivor</td>
<td>Aerobic exercise</td>
<td>No intervention</td>
<td>Quality of life</td>
<td>23.65</td>
<td>2.97</td>
</tr>
</tbody>
</table>
Based on the results from the forest plot (figure 3), it was shown that aerobic exercise 0.14 times improved the quality of life of breast cancer survivors compared to no aerobic exercise and was not statistically significant (SMD = 0.14; 95% CI = -0.23 to 0.51; p = 0.460). The heterogeneity of the research data shows \( \tau^2 = 0.28; \text{Chi}^2 = 58.05; \text{df} = 8 (P < 0.00001); \ I^2 = 86\% \) so that the distribution of the data is declared heterogeneous (random effect model).

The funnel plot (figure 4) shows no publication bias as indicated by the symmetrical right and left plots where 4 plots are on the left and 4 plots are on the right. The plot on the left of the graph has a standard error between 0.1 and 0.3 and the plot on the right has a standard error between 0.2 and 0.3.
DISCUSSION
This research is a systematic review and meta-analysis with the theme of aerobic exercise on the quality of life of breast cancer survivors. Research that discusses aerobic exercise interventions on the quality of life of breast cancer survivors is considered important because this problem occurs in almost all countries, both developed and developing countries.

Aerobic exercise-based intervention for the quality of life of breast cancer survivors was processed using RevMan 5.3 with the Continuous method, this method was used to analyze the effect size or standardized mean difference in bivariate data of two groups that had been controlled for confounding factors by randomization.

Forest results showed that aerobic -0.05 units improved the quality of life of breast cancer survivors compared to not aerobic (SMD= -0.05; 95% CI= -0.47 to 0.37 p= 0.82). The heterogeneity of the research data shows I²= 88% so that the distribution is said to be heterogeneous (random effect model).

The study was conducted by Lisa et al. (2009) with the aim of determining the effect of exercise on the quality of life of newly diagnosed breast cancer patients undergoing adjuvant therapy and similar trials among post-treatment. In his research, it was stated that the intervention carried out by researchers in the form of exercise intervention was not proven to significantly improve the quality of life of breast cancer survivors who had just been diagnosed or after treatment.

This study is in line with Mutrie et al. (2007) with the aim of determining the functional and psychological benefits of group exercise programs. The results in his study stated that no significant effect was seen for general quality of life (FACT-G) which was the main result of the study.

This study is in line with Shoebiri et al. (2016) which states that both the intervention group and the control group showed the same change in total score, so that aerobic exercise-based interventions have not been able to show significant evidence to improve the quality of life of breast cancer survivors. Karna in his research stated that the factors that caused the failure of the intervention were the lack of sample size and the lack of cooperation by some patients due to cultural, physical and emotional problems.

AUTHORS CONTRIBUTION
Citra is the main researcher who chooses the topic, searches and collects research data. Agus Kristiyanto and Bhisma Murti played a role in analyzing data and reviewing research documents.

FUNDING AND SPONSORSHIP
This study is self-funded.

CONFLICT OF INTEREST
There is no conflict of interest.

ACKNOWLEDGMENT
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