

ORIGINAL RESEARCH REPORT

Pain profile of post-mastectomy pain syndrome (PMPS) in patients at a tertiary oncology center in Surabaya

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ABSTRACT

Background: Post-mastectomy pain syndrome (PMPS) is a chronic neuropathic pain condition that typically manifests around the surgical area and may persist for more than three months without an identifiable cause. However, data on PMPS in Indonesia are limited. **Objectives:** This study aims to describe the pain profile of PMPS patients at the Oncology Center of Dr. Soetomo General Hospital, Surabaya in December 2023. **Methods:** This study used a descriptive cross-sectional design and was conducted at the Oncology Center of Dr. Soetomo General Hospital, Surabaya in December 2023. The patients were selected using a consecutive sampling technique based on their medical record and examination. **Results:** A total of 180 patients were included in this study. The majority of patients were between the ages of 50 and 59 years (38.3%) and 40 and 49 years (36.1%) with a luminal A subtype (53.5%). In addition, the majority of patients were overweight (36.1%), had no educational background (72.7%), and housewives (93.3%), with a monthly income of less than five million rupiah (97.2%). The majority of PMPS patients reported radiating pain (52.7%) in the surgical area (94%), with VAS score of 4 (69%). The majority of PMPS patients reported the onset of their condition within six months post-surgery (38.8%) and between 9 and 12-months post-surgery (34.4%). Finally, the majority of PMPS patients had a Karnofsky score of 70 or less (65.6%). **Conclusion:** The pain profile of PMPS patients in Surabaya is distinctive. Oncology professionals should initiate a tailored patient- and community-oriented approaches to research, prevention, and treatment of PMPS in each of their respective community.



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qHighlights

1. The pain profile of patients with post-mastectomy pain syndrome (PMPS) in this study is distinctive.
2. This syndrome is more prevalent in the elderly, with a VAS score of 4 and the majority of pain appearing within six months post-surgery.

INTRODUCTION

Breast cancer is the most prevalent cancer among women, affecting nearly 25% of the population and becoming the fifth leading cause of cancer-related mortality (Lei et al., 2021). The International Agency for Research on Cancer (IARC) reported that there were 47.8 cases of breast cancer per 100,000 women globally in 2018. A total of 684,996 women lost their lives due to breast cancer, accounting for 15% of all patients globally (Stanislawek, 2021). According to Sung et al. (2021), breast cancer in Indonesia accounted for 65,858 cases (30.8%) with a 20.4% death rate (Sung et al., 2021). The type of medication used to treat breast cancer depends on the stage of the disease, with different treatments employed for non-invasive and invasive cancers, in order to improve the quality of life of the patients. Surgical treatment, specifically mastectomy, is recommended for patients with early invasive and locally advanced breast cancer to improve survival rates and prognosis (Adesina and Olajire, 2020; Kalvanagh and Kalvanagh, 2023).

However, this treatment is associated with a chronic post-mastectomy pain, which occurs in and around the mastectomy area for at least three months post-surgery (Calapai et al., 2021). This condition is referred to as post mastectomy pain syndrome (PMPS). PMPS is characterized by persistent neuropathic pain that occurs around the surgical area, either immediately or over time following the surgery, and can persist for longer than three months. Postoperative pain affects approximately 30% of patients who undergo surgical treatment for breast cancer. However, the exact cause of PMPS remains unknown. Some researchers suggest that it may result from damage to the nerves in the chest wall and/or axilla following a mastectomy. This condition may negatively impact the quality of life of the patients. In addition, the management of this condition may prove challenging as the existing research on PMPS is limited with no widely recognized treatment plan (Larsson et al., 2017).

A number of risk factors have been shown to increase the likelihood of an individual developing PMPS. Fabro et al. (2012) found that axillary lymph node dissection with more than 15 excised nodes was associated with a higher risk of PMPS in younger individuals (<40 years). According to Nissenbaum et al. (2010) and Schreiber et al. (2021), physical characteristics, psychological issues, and genetics can influence the development of PMPS. Nevertheless, the existing literature on PMPS in Indonesia is inadequate.

OBJECTIVES

This study aims to describe the pain profile of PMPS patients at a tertiary oncology center, namely at Dr. Soetomo General Hospital, Surabaya.

METHODS

This study used a descriptive cross-sectional design with an observational approach. Samples were taken consecutively at the Oncology Center of Dr. Soetomo General Hospital in December 2023. The inclusion criteria were as follows: (1) patients who had been diagnosed with breast cancer and provided consent to participate in this study; (2) patients who underwent a mastectomy at Dr. Soetomo Surabaya General Hospital; and (3) patients who had been diagnosed with PMPS confirmed through their medical record and examination. The International Association for the Study of Pain (IASP) defines PMPS as persistent pain that occurs immediately following a mastectomy or lumpectomy and affects the anterior thorax, axilla, and/or medial upper arm (Waltho and Rockwell, 2016). Patients with incomplete medical records were excluded from this study.

RESULTS

A total of 180 PMPS patients were included this study (Table 1). The majority of PMPS patients were between the ages of 50 and 59 years (38.3%) and 40 and 49 years (36.1%). The proportion of younger patients was low, with only two patients under the age of 30 years. The majority of patients had a body weight of 50 to 59 kg (51.8%). In addition, 34.4% of patients had a normal body mass index (BMI), while 36.1% were overweight with a BMI between 25 and 29.9. The remaining patients were underweight or obese. Furthermore, 3% of patients engaged in outdoor occupations with significant sunlight exposure, such as farming and online drivers. Meanwhile, 93% of patients were housewives.

Table 1. Demography of patients (n = 180)

| Variable | Category | Frequency (n = 180) | Percentage |
|--------------------------|--------------------------|---------------------|------------|
| Age (years) | <30 | 2 | 1.1% |
| | 30-39 | 14 | 7.7% |
| | 40-49 | 65 | 36.1% |
| | 50-59 | 69 | 38.3% |
| | ≥60 | 30 | 16.7% |
| Body Weight (kg) | <40 | 26 | 14.4% |
| | 40-49 | 31 | 17.2% |
| | 50-59 | 93 | 51.8% |
| | 60-69 | 29 | 16.1% |
| | ≥70 | 1 | 0.5% |
| Height (cm) | 140-149 | 49 | 27.2% |
| | 150-159 | 124 | 68.8% |
| | 160-169 | 6 | 3.3% |
| | ≥170 | 1 | 0.5% |
| BMI (kg/m ²) | <18,5 | 31 | 17.2% |
| | 18.5-24.9 | 62 | 34.4% |
| | 25-29.9 | 65 | 36.1% |
| | ≥30 | 22 | 12.2% |
| Occupation | Housewife | 168 | 93.3% |
| | Self-employed | 5 | 2.7% |
| | Farmer/online driver | 7 | 3.8% |
| Education | No formal education | 131 | 72.7% |
| | Elementary school | 15 | 8.3% |
| | Junior high school | 11 | 6.1% |
| | Senior high school | 22 | 12.2% |
| | College degree or higher | 1 | 0.5% |
| Monthly Income | <Rp5 million/month | 175 | 97.2% |
| | >Rp5 million/month | 5 | 2.7% |

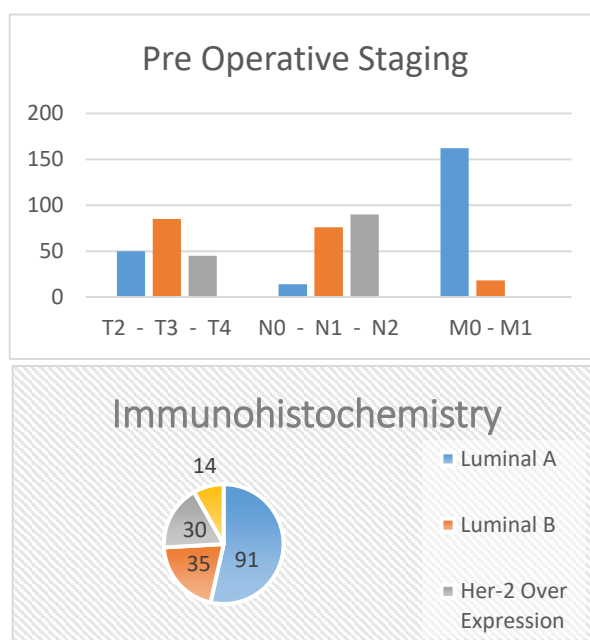


Figure 1. Staging and IHC Profile

The average household income of the patients was <Rp5 million (97.2%). The preoperative tumor, node, and metastasis (TNM) staging of the patients was categorized into T3 (47,2%), T2 (27,7%) and T4 (25%); N2 (50%), N1 (42%), and N0 (8%); as well as M0 (90%) dan M1 (10%), respectively. The medical record data revealed that only 170 patients (94%) had immunohistochemistry testing during sampling period. The most common subtypes were luminal A (53,5%), luminal B (20%), overexpression of human epidermal growth factor receptor 2 (HER2) (17%), and triple-negative breast cancer (TNBC) (8%). Of the 10 patients had no immunochemistry testing, all had been referred from other hospitals (**Figure 1**).

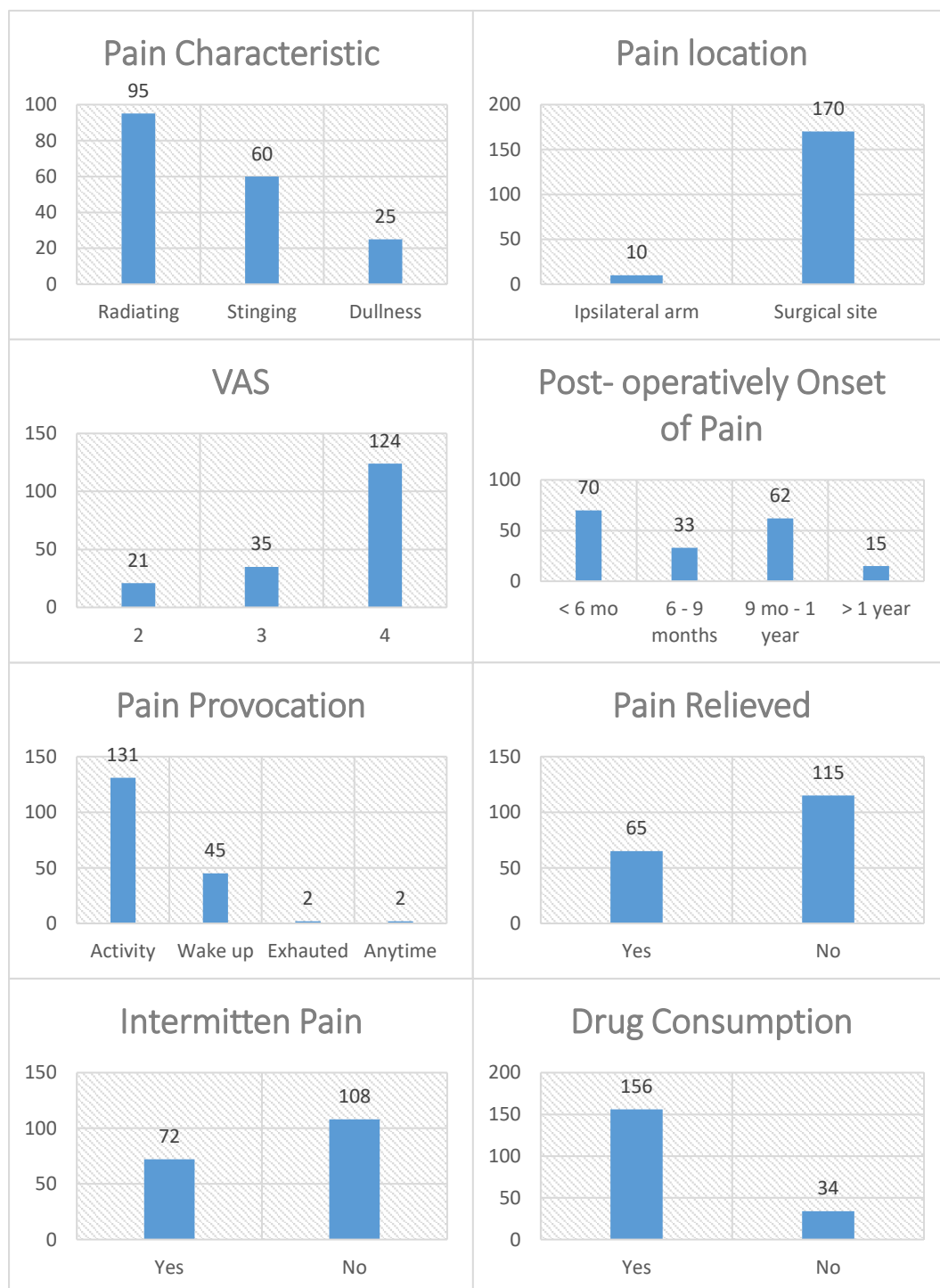


Figure 2. Pain Profile

According to Figure 2, the most common type of pain experienced by the patients was radiating pain (52.7%), followed by stinging pain (33.3%) and dull pain (14%). A total of 94% of patients reported pain in the surgical area, while the remaining 6% reported pain in the ipsilateral arm. The majority of patients had a visual analogue scale (VAS) score of 4 (69%), while the remaining had a VAS score of 3 (19%) and 2 (11.7%). Furthermore, the majority of reported pain (72.7%) occurred during the performance of activities. A comparison between the period following surgery to the onset of pain revealed that the majority of patients (68.8%) experienced pain between nine and 12 months post-surgery, while only 8.3% of patients did not experience pain until a year post-surgery. Of the 108 patients, 60% experienced persistent pain, and the majority of these individuals reported the use of painkillers to relieve their symptoms (86.7%). Only 36% of the patients experienced temporary pain.

A total of 118 patients (65.5%) had a Karnofsky score of 70 or less, while the remaining 34.4% had a score of more than 70, indicating that they could resume their regular activities. In addition, 11% of the patients had ipsilateral limb edema (Figure 3).

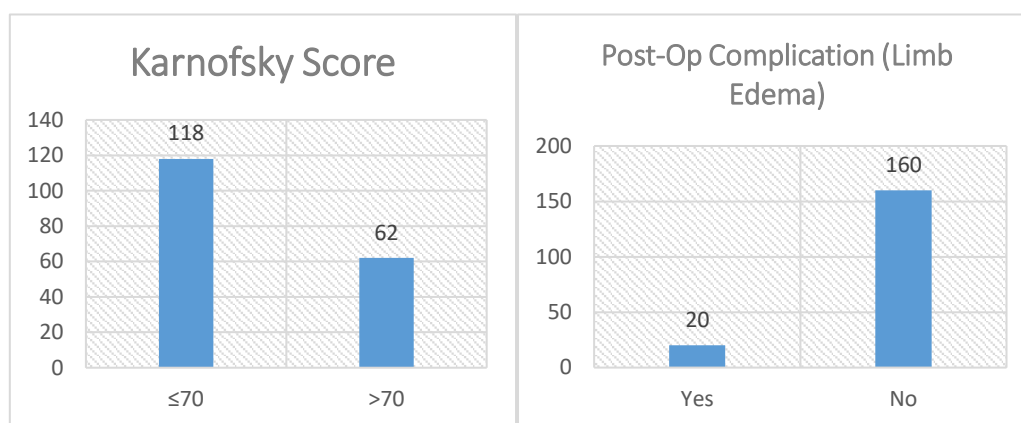


Figure 3. The Karnofsky Score and Postoperative Complication

Demography of the Patients

The results of this study indicated that the age group with the highest prevalence of PMPS was between 50 and 59 years. This is contrary to the results of a study by Fabro et al. (2012) which found that the risk of PSMP was higher in women under 40 years old (RR = 5.23; 95% CI: [1.11, 24.64]). In addition, Schreiber et al. (2021) found that an additional axillary lymph node dissection with more than 15 excised lymph nodes was associated with PSMP. The results of the univariate analysis of a study revealed that the age group of 35 years or younger was significantly associated with PMPS ($p < 0.05$), while the results of the multivariate analysis revealed that the age group of 35 years or younger was an independent risk factor for PMPS (Gong et al., 2020). However, a study found that women under the age of 50 years were 4.37 times more likely to develop PMPS (OR_¼ = 4.37; 95% CI: [2.43, 7.86]) (de Menezes Couceiro et al., 2014). The fact that younger women with breast cancer were at a higher the risk of PMPS could be attributed to a higher histopathological tumor grade, a requirement for adjuvant chemotherapy, and a higher recurrence rates, which is contrary to the findings of this study. Similarly, a study in Indonesia indicated that breast cancer was more prevalent in younger individuals with larger tumor sizes, positive axillary lymph nodes, and overexpression of HER2 (Setyawan et al., 2023). Another study found that breast cancer in individuals under the age of 50 years was associated with high-fat diets and obesity as the risk factors (Nindrea et al., 2021). Nevertheless, Shahbazi et al. (2015) found no correlation between age and PMPS. In addition, pain was found to be associated with daily activities (Ganavadiya et al., 2018).

The BMI profile indicated that the highest incidence of breast cancer was observed in the overweight group (25-29.9 kg/m²). Gong et al. (2020) reported that the incidence of PMPS was higher in individuals with a BMI of less than 30 kg/m² (96.8%) rather than those with a BMI of 30 kg/m² or more (3.2%). However, this finding is in contrast to a study by Fabro et al. (2012) which found that 30.6% of post-mastectomy patients who were obese experienced PMPS, while 33.75% of them did not experience

PMPS. As a result, the study concluded that BMI was not associated with PMPS ($p = 0.7$) (Fabro et al., 2012). Ganavadiya et al. (2018) also observed a similar phenomenon. However, Nindrea et al. (2021) found a correlation between obesity, accompanied by metabolic syndrome, hyperinsulinemia, and altered circadian rhythm, and an increased risk of cancer, including breast cancer. Therefore, it can be concluded that the incidence of breast cancer is more prevalent in individuals with a higher BMI.

In terms of educational level, PMPS was most commonly observed in individuals with senior high school education, followed by elementary school and junior high school, and least commonly observed in individuals with college degree or higher. On the other hand, prevalence of PMPS was found to be higher in lower-income individuals (< Rp5 million). A study by Lundqvist et al. (2016) reported a higher incidence of breast cancer in women with higher socioeconomic status (higher income and education level), which could be attributed to mammography screening, hormone replacement therapy, and lifestyle. However, a study by Miaskowski et al. (2012) found that patients with severe PMPS had lower educational level and income compared to those without PMPS and those with mild PMPS, which is in consistent with the results of this study. Moreover, only 170 patients had immunochemistry testing, while the remaining did not. Among 170 patients, luminal A (53.5%) was more common than luminal B (20%). A study in urkiye found no statistically significant correlation between receptor type and the incidence or symptoms of PMPS (Beyaz et al., 2016). Another potential factor is the difference in estrogen receptor status between young and old patients. Previous studies have indicated that older patients tended to exhibit reduced pain receptor sensitivity (Meijuan et al., 2013; Tait et al., 2018), which is in contrast to the findings of this study.

Pain Profile

In this study, the majority of patients reported experiencing radiating pain, followed by stinging pain and dull pain. Dull pain was the most prevalent pain characteristic in a previous study (77.3%), followed by stabbing pain (50.9%), swelling pain (32.1%), and electrical overstress pain (22.5%) (Gong et al., 2020). Similarly, Beyaz et al. (2016) observed the following characteristics: stabbing (15%), shooting (12.8%), aching (12.8%), gnawing (10.5%), nagging (10.5%), annoying (9.8%), numb (9.8%), tiring (9.8%), and tight (9%).

This study found that the majority of the patients with PMPS reported pain in the surgical area, while the remaining reported pain in the ipsilateral arm. Previous studies found that pain was most frequently experienced in the ipsilateral axilla (63.6%), followed by ipsilateral chest wall (43.4%), ipsilateral arm (28.2%), and other areas (4.1%) (Gong et al., 2020). Another study reported that pain was most frequently experienced in the arm/axilla (39%), followed by scar tissue from surgery (29.9%), chest wall (12.3%), shoulder (11%), and phantom pain. (7.8%) (Beyaz et al., 2016). Meanwhile, Stevens et al. (1995) reported that 84% of pain was experienced in the axilla, followed by medial upper arm (74%), anterior chest wall (58%), and shoulder (32%).

The pain assessment in this study obtained the highest VAS score of 4, followed by scores 3 and 2. A study by Gong et al. (2020) on 1983 patients revealed that 28 of them (5.0%) experienced severe pain (Gong et al., 2020). Another study by de Menezes Couceiro et al. (2014) reported a median VAS of 5 (4-7) in patients with PMPS. In contrast, a study by Beyaz et al. (2016) reported that the majority of patients (78.6%) experienced pain with a VAS score of 0-3, while only the remaining 21.4% experienced moderate pain with a VAS score of 4-7. The results of this study indicated that the patients experienced less severe pain compared to previous studies.

This study found that the majority of PMPS occurred within six months or between 9 and 12-months post-surgery. This finding is different from a study by Stevens et al. (1995) which found that PMPS occurs within days to weeks after breast cancer surgery. Another study suggested that the onset of PMPS occurred between two weeks to three months post-surgery (Gong et al., 2020). In addition, Stevens et al. (1995) reported that PMPS patients experienced intermittent pain (52%) and continuous pain (48%) in patients with PMPS. Furthermore, the majority of patients in this study had a history of taking painkillers to relieve the pain. Similarly, a study by Beyaz et al. (2016) reported that 89.9% of patients had tried one or more pain medications, most of which were over-the-counter medications or medications prescribed by general practitioners. Other patients tried non-pharmacological therapies or

a combination of both, such as physiotherapy, homeopathy, reflexology, acupuncture, massage, and counseling. Only 72.9% of PMPS patients reported an improvement in their pain (Beyaz et al., 2016). This finding is different from the finding of this study, in which the majority of patients reported no improvement in pain.

This study found that the majority patients with PMPS had a Karnofsky score of 70 or less. A previous study indicated that post-mastectomy patients who experienced severe pain have Karnofsky scores lower than those who did not experience pain (Miaskowski et al., 2014). Further investigation by Langford et al. (2014) supported this finding, revealing that individuals experiencing mild PMPS pain had higher Karnofsky scores than those experiencing moderate to severe PMPS pain (Becker et al., 2008).

Limb edema, which is frequently observed in post-mastectomy patients, is a complication induced by lymphedema in the upper limbs (Becker et al., 2008). In this study, PMPS patients had ipsilateral limb edema, although the grade of lymphedema was not specified. Patients with PMPS and lymphedema who underwent lymphedema surgery reported a reduction in pain, neuropathic pain, and the use of analgesic medications. Becker et al. (2008) found that lymphedema in the upper extremities post-mastectomy could be a contributing factor to PMPS in affected individuals. The majority of patients in their study reported pain, especially during the performance of activities (Becker et al., 2008). These results are consistent with those in a study by Beyaz et al. (2016) which found that pain that was exacerbated by activity (54.5%), lying down (14.3%), cold weather (10.3%), rubbing of scars on clothes (10.3%), and waking up from sleep (10.3%). Activities such as lifting, carrying, and housework were also found to exacerbate the pain. Some patients even reported pain when walking, driving, and working (Beyaz et al., 2016). Another study reported that patients with PMPS reported pain, especially they were moving or tired (Salati et al., 2023).

LIMITATION

A primary limitation of this study pertains to its research design, specifically the use of a cross-sectional design with monocentric prospective data collection. Therefore, it is essential that the findings of this study be interpreted in a descriptive and exploratory manner. Any extrapolation to another institution must be approached with caution. In addition, it should be noted that this study did not specify other potential causes or factors of PMPS. Further research is needed to address the limitations of this study.

CONCLUSION

The majority of patients with PMPS at the Tertiary Oncology Center in Surabaya were older, had a luminal A tumor, and were at a later TNM stage. Most of them experienced radiating pain in the surgical area with a VAS score of 4. PMPS typically occurred within six months post-surgery. The majority of patients with PMPS had a Karnofsky score 70 or less. These findings are different from the demography or pain profile of PMPS patients in previous studies. In other words, these findings may be specific to the Indonesian local community, as PMPS is influenced by various internal and external factors. It is recommended that all stakeholders, especially oncology professionals in breast cancer management, encourage a more tailored patient- and community-oriented approaches on research, prevention, and treatment for PMPS in their respective communities.

Conflict of Interest

The authors have no conflicts of interest to declare.

Ethical Clearance

This study received ethical approval from the Ethics Committee of dr. Soetomo General Hospital with a certificate number 1595/LOE/301.4.2/II/2024 in accordance with the Office for Human Research Protection (OHRP) under the statement of the United States Department of Health and Human Services (HHS).

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Author Contributions

RHK: conceptualization and design; data collection, analysis, and interpretation; critical revision of the article for important intellectual content, statistical expertise. **CR:** drafting of the article; critical revision of the article for important intellectual content; administrative, technical, or logistic support. **IA:** conceptualization and design; data analysis and interpretation; final approval of the article; provision of study materials or patients. **ED:** conceptualization and design; final approval of the article; statistical expertise. **FHT:** data analysis and interpretation; drafting of the article; critical revision of the article for important intellectual content.

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