<Original Article>

Pain and Skeletal-Related Events and Their Management Strategies by Nurses in Cancer Patients with Bone Metastases: A Scoping Review

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ABSTRACT

Background: This scoping review clarified the characteristics of pain and skeletal-related events in patients with cancer and bone metastases and examined nurse-led management strategies.
Methods: The databases searched included CINAHL, MEDLINE, and Ichushi Web. The keywords included "bone metastases," "skeletal metastases," "bone health," "skeletal-related event," "pain," "fractures, bone," "spinal cord compression," and "hypercalcemia." A scoping review was conducted, including a hand search.
Results: Ultimately, 28 studies were included. Most patients with cancer who had bone metastases experienced pain, which was more severe in those with osteolytic lesions or metastases in mobile regions of the spine. Regarding pain management, educational interventions encouraging patient self-monitoring were suggested to be effective. Pathological fractures constituted a significant proportion of bone-related events, with risk factors including advanced age, female sex, and breast cancer. Although image-based risk assessment for pathological fractures has been commonly reported, studies on specific movement support for fracture prevention are lacking.
Conclusion: Elderly women and patients with breast cancer face a high risk of pathological fractures due to bone loss, necessitating careful management of daily activities. Although careful daily life management is required, limited research exists on pain management and preventive management specific to bone metastases, suggesting the need for further research.

INTRODUCTION

Bone metastasis is a frequent occurrence in advanced cancers, particularly in prostate and breast cancers [1]. It is observed in 65–75 % and 70 % of prostate [1] and breast [2] cancer cases, respectively, together comprising 80 % of all bone metastases [3]. Among patients with bone-only metastases, the median survival is approximately 3 and 4.8 years for those with prostate [4] and breast [5] cancers, respectively, exceeding that of patients with metastases to organs, including the liver or lungs [4].

Patients with bone metastases frequently experience symptoms that substantially impair their quality of life (QoL), with pain being among the most common [6]. Pain is reported in 85 % of these patients and typically worsens with movement [7]. Persistent pain is linked to reduced mobility and physical function [8] and is strongly associated with diminished QoL [9]. Bone metastases also compromise

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bone integrity, resulting in skeletal-related events (SREs), including pathological fractures and spinal cord compression. SREs occur in approximately 50 % of affected patients [10]. Notably, pathological fractures frequently hinder independent ambulation, exacerbate pain, restrict daily activities, and further reduce QoL [8, 10, 11]. Thus, maintaining QoL in patients with bone metastases requires patient education on safe living practices, including pain management, fracture prevention, and understanding bone-related complications [12].

However, 30–40 % of oncology nurses report lacking confidence in managing patients with bone metastases and assessing fracture risk during routine practice, expressing anxiety about evaluating fracture risk and supporting lifestyle management [13]. This highlights the need to integrate research findings that provide foundational knowledge on pain, SREs, and their management in patients with bone metastases.

Therefore, this review aimed to clarify the characteristics of pain and SREs in patients with cancer and bone metastases and to examine nurse-led management strategies.

Terms and Definitions

SREs refer to a composite endpoint encompassing pathological fractures, spinal cord compression, hypercalcemia, and interventions such as radiation therapy and surgery—common complications in patients with bone metastases [14]. In this study, SREs are defined as the composite of pathological fractures, spinal cord compression, and hypercalcemia resulting from cancer-related bone metastases.

MATERIALS AND METHODS

Study design

This study employed a scoping review to enable transparent reporting and synthesize knowledge across key themes from diverse sources. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines proposed by Tricco et al. (2018) [15].

Literature specification

The databases searched included CINAHL, MEDLINE, and Ichushi Web. The English search query was as follows: (“bone metastases “OR “skeletal metastases” OR “bone health”) AND (“skeletal-related event” OR “pain” OR “fractures, bone” OR “spinal cord compression” OR “hypercalcemia”). The same search terms were applied to the Japanese literature. The search covered publications from January 2005 to June 2025, aligning with the introduction of bone-modifying agents into clinical practice for patients with cancer.

Literature screening

The inclusion criteria for the literature were studies focusing on patients with bone metastases that addressed pain, SREs, and their management. Given the limited number of nursing intervention studies, literature considered relevant to potential nursing interventions for pain relief and fracture prevention was also included. Studies that primarily evaluated the efficacy of treatments—such as bone-modifying agents, radiation therapy, surgery, radiofrequency ablation, or radioactive pharmaceuticals—for pain or pathological fractures were excluded. Additionally, two articles on pain associated with bone metastases, identified through hand searching, were included.

Literature quality assessment

Two reviewers conducted literature selection based on the predefined criteria. The quality of each report was assessed through joint review of the findings, and any discrepancies between reviewers were resolved through consensus. Quality appraisal was performed using the Joanna Briggs Institute’s Critical Appraisal Checklists [16]. The checklist for Analytical Cross-Sectional Studies, checklist for Cohort Studies, checklist for Randomized Controlled Trials, checklist for Quasi-Experimental Studies, and checklist for Qualitative Research was applied to 14 cross-sectional studies, 8 cohort studies, 3 randomized controlled trials, 2 quasi-experimental studies, and 1 qualitative descriptive study, respectively. Reports were included if they met more than half of the items on the respective checklists.

Organization of selected literature

To organize the selected literature, a matrix was created capturing key details, including author name (and country), publication year, research method, study population, objectives, and results. For pain related to bone metastases, extracted data included pain frequency and location, cancer types and sites of bone metastases associated with pain, medication use, and pain management strategies. Regarding bone-related events, information was compiled on common symptoms, risk and sites of pathological fractures, and fracture management.

RESULTS

Literature overview

After removing duplicates, the search yielded 8,850 reports (8,275 and 575 in English and Japanese, respectively). Screening based on the inclusion and exclusion criteria narrowed this number to 181 reports (174 and 7 in English and Japanese, respectively). Following a detailed review, 26 reports were selected, with an additional two identified through hand-searching, resulting in a total of 28 reports analyzed (**Figure 1**).

The 28 selected reports encompassed the following

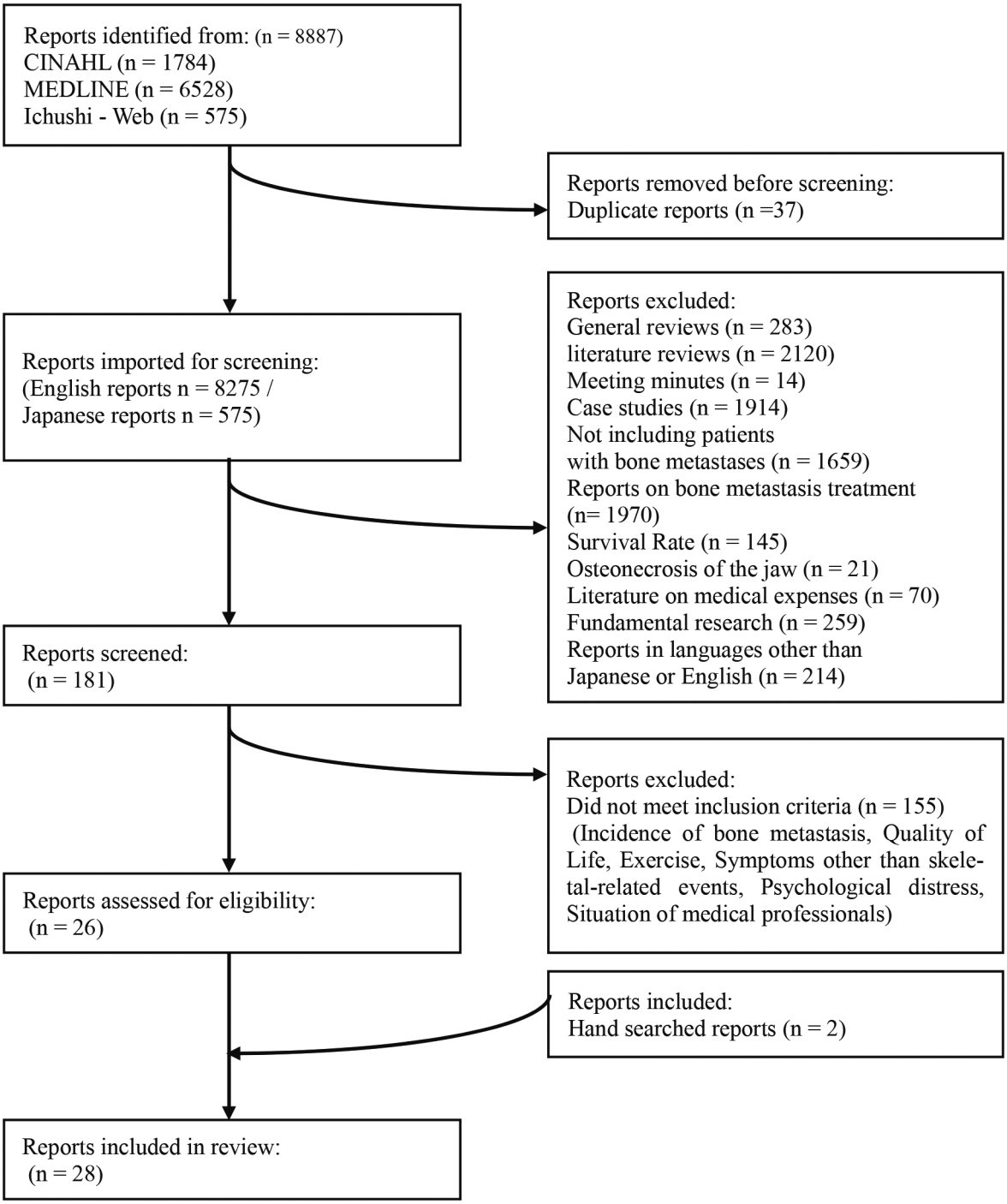

Figure 1 Literature search and sampling process

themes: 6 articles addressed pain associated with bone metastases, 5 focused on pain management, and 17 examined the incidence and management of SREs—including pathological fractures and spinal cord compression—with particular emphasis on pathological fractures.

Pain in patients with cancer and bone metastases (Table 1)

Pain was reported daily by 89 % of patients with bone metastases, regardless of cancer type [17]. Moderate to severe (numerical rating scale [NRS] ≥ 4) average pain was reported by 42.8 % of patients, with the worst pain experience reported by 67.6 % [18]. Additionally, 77.2 % of patients with prostate and breast cancer specifically reported pain [19]. Approximately 15 % of them experienced severe pain [19].

Pain was more pronounced in patients with osteolytic bone metastases, characterized by accelerated bone destruction, as observed in breast and lung cancers [20]. Patients

Table 1 Pain and its management in cancer patients with bone metastases

Author, year of publication, country	Methods	Subjects	Objectives	Results	Evaluation*
Torvik, 2008, Norway [17]	Descriptive correlation study	79 patients with bone metastases (23 %, 29 %, and 14 % with breast, prostate, and lung cancers, respectively)	To investigate differences between middle-aged and elderly patients in reported pain levels, pain management approaches, and satisfaction with pain control, as well as to assess variations in pain-related interference with patient function and quality of life between these groups.	Overall, 89 % of patients reported daily pain. Elderly patients had significantly higher scores for "worst pain" (p = 0.036) and "pain severity" (p = 0.027) than middle-aged patients; however, they were significantly less likely to use strong opioids for cancer pain (p = 0.024). Additionally, increasing age was significantly correlated with lower scores on the Cleeland Pain Management Index (p = 0.002).	8/8
Sulistio et al., 2023, Australia [18]	Descriptive correlation study	140 cancer patients with bone metastases (25.7 %, 24.3 %, and 20.0 % with breast, lung, and prostate cancers, respectively)	To describe the characteristics, pain intensity, and relationship between the Edmonton Cancer Pain Classification System (ECS-CP) and opioid consumption in cancer patients with bone metastases.	75.7 % of cancer patients with bone metastases experienced pain. Moderate to severe (NRS ≥ 4) mean pain was found in 42.8 % of patients, and 67.6 % experienced the worst pain. Three-quarters of patients were on regular opioids, with an average daily dose of 25.8 mg of oral morphine equivalent. Two - thirds of patients reported psychological distress.	7/8
Jakob et al., 2022, Switzerland [19]	Prospective observational study	486 patients with bone metastasis (64 % and 36 % with breast and prostate cancers, respectively)	To evaluate pain and health-related quality of life associated with bone metastases in patients with breast or prostate cancer undergoing treatment with bone-targeted drugs, and to investigate correlations with patient characteristics using patient-reported outcomes (PROBone).	Before initiating treatment, 77.2 % of patients with bone metastases reported experiencing pain, with approximately 15 % of them having severe pain. Breast cancer patients experienced more intense pain than prostate cancer patients. Additionally, patients who began bone-modifying agent therapy after the onset of pain reported higher pain levels and achieved less pain reduction than those who started treatment before experiencing pain.	6/8
Vassiliou et al., 2007, Greece [20]	Descriptive correlation study	80 patients with bone metastases (40 %, 25 %, and 11 % with lung, breast, and prostate cancers, respectively, and bisphosphonate-naïve patients)	To examine the relationship between clinical status—including pain, performance status, quality of life, and bone mineral density—and the type of bone metastasis (osteolytic, osteoblastic, or mixed) in patients with bone metastases.	Among the three groups, the osteolytic bone metastasis group reported the highest mean pain score (8.1 ± 2.2). This group also had the lowest physical functioning score on the EORTC QLQ - C30 (31.4 ± 14.6) and the poorest performance status (58.6 ± 9.7). Mean opioid consumption was highest in the osteolytic group, averaging 220.9 mg of oral morphine per day (range: 70.1–550 mg). Additionally, the osteolytic group exhibited the lowest mean bone mineral density, measured at 116.3 HU (CT value). Except for performance status comparisons between mixed and osteoblastic types, all examined parameters—including pain, quality of life, bone mineral density, and opioid use—showed statistically significant differences (p < 0.05).	6/8
Hindle et al., 2021, Canada [21]	Descriptive correlation study (retrospective chart review)	196 patients undergoing palliative radiation therapy for painful bone metastases (27 %, 24 %, and 23 % with lung, breast, and prostate cancers, respectively)	To determine whether vertebral segment mobility at the site of spinal metastasis affects patients' pretreatment pain or health-related quality of life (HR-QoL).	Among patients receiving palliative radiotherapy for pain, 55.6 % were using opioid analgesics. Regarding the relationship between spinal metastasis location and pain severity, patients with lesions in mobile spinal segments (C3–C6 and L2–L4) experienced significantly more severe pain than those with lesions at spinal junctions (C0–2, C7–T2, T11–L1, and L5–S1) (OR −1.37; 95 % CI −0.30 to −2.44; p = 0.012).	8/8

Zeng et al., 2011, Canada [22]	Descriptive correlation study	336 patients who received treatment for pain from bone metastases (26.8 %, 24.4 %, and 25.3 % for breast, prostate, and lung cancers, respectively)	To determine whether patients with lower body pain show higher levels of disability than patients with upper body pain among individuals with bone metastases.	Patients with bone metastases in the lower skeleton (lumbar spine, sacrum, pelvis, and femur) experiencing moderate to severe pain demonstrated greater functional impairment—including daily activities, mobility, and work capacity—than those with metastases in the upper skeleton (cervical spine, thoracic spine, and humerus).	7/8
Rustøen et al., 2012, Norway [24]	Randomized Controlled Trial	179 patients with bone metastases (36.9 % and 36.3 % with breast and prostate cancers, respectively; 87 interventions and 92 controls)	To evaluate how a pain control program (PRO - SELF) affects patients' improved knowledge of cancer pain management compared to a control group.	The pain control program is an interactive nursing support designed to provide information using academic components, build skills through ongoing nursing coaching, and teach patients how to prevent and manage disease and treatment side effects. It was delivered through repeated visits and telephone interviews with educated nurses. Patients in the PRO-SELF group showed a significant increase in knowledge scores.	11/13
Rustøen et al., 2014, Norway [25]	Randomized Controlled Trial	179 patients with bone metastases (36.9 % and 36.3 % with breast and prostate cancers, respectively; 87 interventions and 92 controls)	To evaluate the effect of the PRO-SELF intervention group on reducing pain and increasing opioid intake compared to the control group.	Both groups showed significant reductions in pain intensity scores and pain time per day during the study period. Total opioid doses increased over time in both groups; however, no significant time interaction was observed between groups in temporal changes in opioid doses (total dose, around-the-clock, and as-needed).	11/13
Ekstedt et al., 2019, Sweden [26]	Qualitative Descriptive Research	20 patients with bone metastases (35 % and 45 % with breast and prostate cancers, respectively)	To evaluate the key factors, facilitators, and inhibitors needed to improve knowledge of pain management using a pain control program (PRO - SELF)	The key elements of the intervention were the repetition of information, struggling with resistance, recording the change, and helping the patient understand the situation. Facilitators of improvement were the patient's self-awareness and bodily awareness through symptom identification, and taking an active role in their own care. The most important barriers to the success of the intervention were difficulty in processing complex information, assumptions about pain management, beliefs, attitudes, and lack of knowledge about the disease and treatment.	6/10
Geerling et al., 2023, Netherlands [27]	Randomized Controlled Trial	182 patients with painful bone metastases with NRS ≥ 5 pain before radiotherapy (92 in the intervention group and 90 in the control group), (36 %, 29 %, and 16 % with prostate, breast, and lung cancers, respectively)	To evaluate the effect of a nurse-led patient education program (PEP) with established efficacy for chronic cancer pain on pain control and quality of life in patients with painful bone metastases.	The intervention initially focused on providing information, including the mechanism of pain, the pharmacological effects of analgesics, non-pharmacological pain treatment, the impact of pain on life and coping strategies, and false beliefs. The intervention method was conducted with one face-to-face session and telephone follow-up sessions at weeks 1, 4, 8, and 12. Consequently, pain control (NRS ≤ 5) after 12 weeks improved more in the intervention group (71 %) than in the control group (52 %), and the median time to reach pain control was significantly improved in the intervention group (29 days) compared to the control group (56 days).	10/13
Andrade et al., 2010, USA [28]	Quasi-Experimental Studies	89 patients with painful bone metastases who underwent external radiotherapy	To evaluate the effect on pain by radiation therapists by writing pain worksheets centered on NRS assessment before, during, and after irradiation.	Pain improved in 50 % of patients on the fourth day of treatment and in 75 % after the end of treatment. Additionally, the frequency of patients who reported that their pain improved by ≥ 20 % increased by 75 % and 84 % on days 4 and 10, respectively, and the pain score was maintained in 83 % of patients 1 month after the end of treatment.	5/9

*Evaluation: Quality appraisal was performed using the Joanna Briggs Institute's Critical Appraisal Checklists. The score in each Critical Appraisal Checklist is indicated.

with breast cancer—who frequently present with osteolytic lesions—reported more intense pain than those with prostate cancer, who typically have osteoblastic metastases [19]. More than half of patients with painful bone metastases used opioids [21]. Among them, those with osteolytic lesions had a higher average opioid consumption (220.9 mg; oral daily morphine equivalent) than those with osteoblastic lesions (170.6 mg) [20].

Additionally, patients with osteolytic metastases demonstrated the lowest levels of physical function, based on performance status and QoL assessments, compared to those with osteoblastic or mixed lesions [20].

Patients with bone metastases located at spinal motion segments (C3–C6 and L2–L4) experienced more severe pain than those with lesions at spinal junctions (C0–2, C7–T2, T11–L1, and L5–S1) [21]. Additionally, patients experiencing moderate to severe pain from lower body metastases (lumbar spine, sacral spine, pelvis, and femur) exhibited greater functional impairment than those with metastases in the upper body (cervical spine, thoracic spine, and humerus) [22]. Patients who began bone-modifying drug treatment after experiencing pain reported more severe pain than those who started treatment before pain onset [19].

Pain management for cancer patients with bone metastases

Only five intervention studies on pain management in patients with cancer and bone metastases were identified. Rustøen et al. evaluated the effectiveness of the pain control program (PRO-SELF) developed by West et al. [23] in improving knowledge about cancer pain in patients with bone metastases [24]. The content of the program was to provide information using academic elements, build skills through ongoing nurse coaching, and provide interactive nursing support to teach patients how to prevent and manage diseases and treatment-related side effects. Educated nurses provided intervention support through regular visits and telephone calls. Consequently, significant increases were observed in knowledge scores in the intervention group. Additionally, Rustøen et al. assessed pain control using a similar pain management program in oncology outpatients with pain due to bone metastases [25]. Both groups showed significant reductions in pain intensity scores and pain time per day during the study period. Total opioid doses increased over time in both groups; however, no significant time interaction was observed between groups in temporal changes in opioid doses (total dose, around-the-clock, and as-needed). Subsequently, Ekstedt et al. used a similar pain control program to qualitatively clarify the factors necessary for patients with bone metastases to improve their knowledge of pain management, as well as identify the facilitators and inhibitors [26]. Consequently, the key elements of the intervention were the repetition of information, struggling with resistance, recording the change, and helping the patient understand the situation. Facilitators of improvement were the patient's self-awareness and bodily awareness through symptom identification, as well as taking an active role in their own care. The most important barriers to the success of the intervention were difficulty in processing complex information, assumptions about pain management, beliefs, attitudes, and lack of knowledge about the disease and treatment. Geerling et al. evaluated a nurse-led patient education program comprising one individual face-to-face session and four follow-up telephone sessions [27]. The program covered pain mechanisms, analgesic pharmacology, non-pharmacological treatments, daily life impact and coping strategies, misconception correction, pain escalation management, and self-monitoring using a pain diary. Twelve weeks post-intervention, the treatment group showed greater pain improvement and achieved pain relief 27 days earlier than the control group; however, no significant difference was observed in QoL. Andrade et al. assessed the effectiveness of daily pain monitoring by medical staff using a pain worksheet and NRS during palliative radiation therapy [28]. If pain worsened or failed to improve within 3 days, staff consulted physicians or nurses for management. Pain improved in 50 % of patients by day 4 and 75 % by treatment completion. Additionally, 75 % of patients reported at least a 20 % reduction in pain by day 4, increasing to 84 % by day 10, with 83 % maintaining this improvement 1 month after therapy ended.

SREs in cancer patients with bone metastases (Table 2)

In patients with lung cancer and bone metastases, the incidence of SREs was reported as 19.1 %, 9.0 %, and 5.7 % for pathological fractures, spinal cord compression, and hypercalcemia, respectively [29]. In patients with non-small cell lung cancer, the incidence of SREs was reported as 26.3 %, 25.3 %, and 3.2 % for pathological fractures, spinal cord compression, and hypercalcemia, respectively [30]. In patients with prostate cancer, 14 % and 15 % had pathological fractures and spinal cord compressions, respectively [31]. Among patients with castration-resistant prostate cancer, 11.9 % and 1.7 % had pathological fractures and spinal cord compressions, respectively [32]. Additionally, in patients with urological cancer, including prostate cancer, 8.2 % and 10 % reported pathological fractures and spinal cord compression, respectively [33]. In breast cancer patients, pathological fractures and spinal cord compressions were reported in 17.4 % [34] and 29.5 % [35], respectively. Furthermore, pathological fractures following radiation therapy to long bones occurred in 25.9 % of cases, with 70 % of these fractures developing within 1 month post-treatment [36]. Moreover, 28 % of patients receiving palliative care for bone metastases were reported to have pathological fractures [37]

In patients with lung cancer, pathological fractures most commonly occurred in the spine (32 %), pelvis (17.2 %),

Table 2 SREs and their management in cancer patients with bone metastases

Author, year of publication, country	Methods	Subjects	Objectives	Results	Evaluation*
Oliveira et al., 2018, Brazil [29]	Retrospective cohort study	407 lung cancer patients (including non-bone metastases)	To identify risk factors associated with pathological fracture occurrence and clarify survival rates in lung cancer patients	Among patients with bone metastases, 79 (68.7 %) experienced 122 skeletal-related events (SREs). The most common SREs were pathological fractures (19.1 %), spinal cord compression (9.0 %), and hypercalcemia (5.7 %). Pathological fractures were most frequent in patients with adenocarcinoma (23.9 %). Factors significantly associated with pathological fractures included smoking (95.5 % vs. 74.2 %, $p < 0.05$) and diagnosis of synchronous bone metastases at the time of lung cancer diagnosis (OR: 5.24, 95 % CI: 1.15–23.8; $p < 0.05$). The incidence of pathological fractures was significantly greater in the diaphysis (36.0 %) than in the epiphysis (9.5 %). The most common fracture sites were the spine (32 %), pelvis (17.2 %), femur (17.2 %), and humerus (10 %).	11/11
Silva et al., 2015, Brazil [30]	Retrospective cohort study	95 patients with non-small cell lung cancer with bone metastases	To evaluate the incidence and associated factors of SRE in patients with non-small cell lung cancer with bone metastases	Pathological fractures, spinal cord compression, and hypercalcemia occurred in 26.3 %, 25.3 %, and 3.2 % of patients, respectively. Individuals with a history of smoking, a performance status of ≥ 2, and those who had experienced multiple bone metastases were at significantly higher risk of SRE.	8/11
Nieder et al., 2010, Norway [31]	Retrospective cohort study	61 patients with prostate cancer and bone metastases who visited the Oncology Department at Nordland Hospital	To determine the risk factors, incidence, and prognostic impact of pathologic fractures and spinal cord compression in patients with prostate cancer and bone metastases	The median survival time after the diagnosis of bone metastasis was 23 months. A log-rank test revealed that hemoglobin levels ≤ 12.0 g/dL were significantly associated with shorter survival ($p = 0.03$). Performance status (ECOG) also showed a significant association with prognosis ($p = 0.01$), with survival rates of 33 % and 43 % for patients with PS2 and PS1, respectively. Additionally, age ≥ 70 years, ALP levels above the median, and LDH levels above the median were each significantly associated with reduced survival. Multivariate analysis identified PS, ALP, and LDH as independent prognostic factors. Among the patients, 15 % (9 individuals) experienced spinal cord compression, and 14 % (8 individuals) developed pathological fractures.	8/11
Kawai et al., 2015, USA [32]	Retrospective cohort study	2,234 patients with castration-resistant prostate cancer	To estimate the incidence of SRE in patients with castration-resistant prostate cancer	In patients with castration-resistant prostate cancer, SRE, pathological fractures, and spinal cord compression were observed in 40.1 %, 11.9 %, and 1.7 %, respectively.	11/11
Yokomizo et al., 2010, Japan [33]	Retrospective observational study	511 patients with urological cancer with bone metastases (69 % and 18 % with prostate and kidney cancers, respectively)	To clarify the incidence of SRE in patients with urological cancer in Japan.	In patients with urologic cancer, including prostate cancer, 8.2 %, 10 %, and 4.5 % had pathological fractures, spinal cord compression, and hypercalcemia, respectively.	8/8

Walker et al., 2013, USA [34]	Retrospective observational study: chart review	321 patients with metastatic breast cancer and bone metastases (160 treated with zoledronic acid, 147 untreated, and 14 unclassified)	To describe treatment patterns and longitudinal health-related quality of life of metastatic breast cancer patients with bone metastases across nine community oncology clinics	Among the 321 patients, 17.4 % (56 patients) experienced a fracture. The fracture rate was lower in the treatment group than in the non-treatment group (12.5 % vs. 17.7 %). Patients who sustained a fracture exhibited decreased mobility at the time of the event, experienced increased pain and anxiety, and required approximately 16 months for recovery. Fractures were significantly associated with increased pain in patients with bone metastases (p = 0.029). Furthermore, pathological fractures significantly worsened walking ability (p = 0.004), anxiety, and pain levels (p = 0.0467).	7/8
Dibekoglu et al., 2015, Türkiye [35]	Prospective observational study	139 breast cancer patients with isolated bone metastasis	To analyze the impact on fracture incidence and survival in breast cancer patients with isolated bone metastasis.	During the 41-month follow-up period, 41 (29.5 %) patients had pathological fractures. The sites of pathological fractures were 26 (63.4 %) vertebral fractures, 11 (26.8 %) femur fractures, and 4 (9.8 %) hip fractures. Fracture rates in hormone-sensitive and resistant patients were 31.2 % and 14.3 %, respectively.	7/8
Tatar et al., 2014, France [36]	Retrospective observational study	37 patients (35.1 %, 27 %, 16.3 %, and 21.6 % with lung, prostate, breast, and other cancers, respectively) receiving radiation therapy to long bones	To analyze risk factors for threatened fractures after radiotherapy for long bone metastases using CT scan-based virtual simulation	The incidence of fractures following radiotherapy was 20 % within the first month and 25.9 % by the end of the study period. Univariate analysis identified several significant predictors of fracture: presence of osteolysis (39 % vs. 10 %, p = 0.02), unclear bone margins (42 % vs. 0 %, p < 0.0005), circumferential cortical involvement ≥ 50 % (80 % vs. 5 %, p < 0.00001) or ≥ 30 % (71 % vs. 0 %, p < 0.00001), longitudinal cortical involvement ≥ 30 mm (48 % vs. 0 %, p < 0.00001) or ≥ 45 mm (67 % vs. 0 %, p < 0.00001), complete cortical thickness involvement (100 %) (40 % vs. 0 %, p = 0.0008), and a Mirels score ≥ 9 (42 % vs. 0 %, p < 0.0005). In multivariate analysis, circumferential cortical invasion of ≥ 30 % remained the only independent predictor of fracture (p = 0.00035).	8/8
Miranda et al., 2023, Brazil [37]	Retrospective cohort study	348 patients with bone metastasis (40 % were breast cancer patients)	To evaluate the incidence and factors associated with pathologic fractures and their impact on overall survival in patients with bone metastases receiving palliative care	Bone metastases were located in the axial skeleton in 72 % of cases, with 51 % exhibiting osteolytic lesions. Among the patients, 40 % had received bisphosphonate therapy, 23 % had undergone radiotherapy, and 38 % had orthopedic surgery. The overall incidence of pathological fractures was 28 %. Breast cancer patients showed a significantly higher risk of pathological fractures than those with other cancer types with bone metastases (OR 2.96; 95 % CI 1.80–4.86; p < 0.001). Additionally, patients who had not received prior radiotherapy had a greater incidence of pathological fractures than those who had (OR 5.38; 95 % CI 2.35–12.30; p < 0.001).	10/11
Rajkovic et al., 2023, Serbia [38]	Retrospective observational study	152 breast cancer patients with bone metastases	To clarify the relationship among estrogen, progesterone, HER2 receptor status, Ki67 index and the occurrence of fractures in bone metastases	The femur was the most frequent fracture site, accounting for 55 (60.4 %) cases, followed by the spine with 25 (27.5 %) cases. Breast cancer patients with bone metastases and pathological fractures exhibited a significantly higher rate of progesterone receptor positivity than those without fractures (p < 0.05).	8/8

Jairam et al., 2020, USA [39]	Descriptive correlation study	272,275 cases hospitalized for bone metastases (27.0 %, 21.4 %, and 19.0 % with lung, breast, and prostate cancers, respectively), (11,960 pathological fractures and 260,315 non-pathological fractures)	To clarify the characteristics of patients with bone metastases admitted to hospitals nationwide and identify factors associated with pathological fractures	Among an estimated 4.4 % of hospitalizations involving pathological fractures, the most common fracture sites were the spine (62.1 %), hip or femur (30.3 %), humerus (6.2 %), tibia or fibula (1.0 %), and radius (0.3 %). Patients with fractures were more likely to be older, female (OR 1.39; 95 % CI, 1.26–1.54), have received radiation therapy (OR 1.81; 95 % CI, 1.38–2.35), undergone surgery (OR 38.84; 95 % CI, 35.05–43.04), have higher comorbidity scores (OR 1.01; 95 % CI, 1.00–1.01), and be treated at hospitals located in the western region (OR 1.19; 95 % CI, 1.00–1.01). Additionally, race was associated with a reduced risk of pathological fracture (OR 0.82; 95 % CI, 0.70–0.96).	8/8
Rief et al., 2015, Germany [40]	Quasi-Experimental Studies	915 patients with bone metastases who received radiotherapy for osteolytic bone lesions in the thoracic and lumbar spine (non-small cell lung cancer 34 %, breast cancer 32 %, and kidney cancer 17 %)	To evaluate the incidence of pathological fractures after radiotherapy in patients with and without orthopedic corsets among individuals with vertebral metastases, and to evaluate the prognostic factors of pathological fractures.	The incidence of pathological fractures before radiation therapy was 7.4 % overall, with 6.8 % and 8.0 % in the corset-wearing and non-wearing groups, respectively; however, no significant difference was observed between groups (p = 0.473). Overall, the fracture rate after 6 months was 9.0 %, with 8.6 % and 9.3 % in the wearing and non-wearing groups, respectively, and no significant difference was found (p = 0.709). No prognostic factors were identified for the occurrence of pathological fractures in both groups. More fractures were recorded in the thoracic spine (62.2 %) than in the lumbar spine (37.8 %).	9/9
Sun JM et al., 2011, Korea [41]	Retrospective observational study	273 patients with non-small cell lung cancer with bone metastases	To evaluate predictors of SRE in patients with non-small cell lung cancer with bone metastases.	Survival-adjusted multiple event analysis showed that the risk of SRE was significantly higher in patients with characteristics such as smoking history, non-adenocarcinoma, PS 2–3 (Eastern Cooperative Oncology Group), and no history of epidermal growth factor receptor-tyrosine kinase inhibitors therapy. The median time to SRE after diagnosing bone metastases was 8.9 months.	8/8
Neuhaus et al., 2016, Germany [42]	Retrospective observational study	184 breast cancer patients (40 % no metastasis, 35 % soft tissue metastasis, and 25 % bone metastasis)	To clarify the relationship between the quality and quantity of bone metastases, volumetric bone mineral density measured by computed tomography, and the prevalence of vertebral fractures in breast cancer patients.	The mean bone mineral density (BMD) was 91.3 ± 34.0 cm^3, and the mean T-score was −2.5 ± 1.2, indicating that 84 % of patients had either osteopenia or osteoporosis. Vertebral fractures were observed in 23 % of patients, with 11 % and 12 % attributed to osteoporosis and bone metastases, respectively. Factors significantly associated with vertebral fractures included metastasis size (OR 2.5, $p < 0.0001$), the number of vertebrae affected (OR 1.9, $p < .001$), osteolytic lesions (OR 3.7, $p < 0.0001$), and mixed-type vertebral metastases (OR 4.1, $p < 0.0001$). In multivariate analysis, pedicle destruction remained an independent predictor of vertebral fracture ($p < 0.05$).	8/8
Shinoda et al., 2020, Japan [44]	Retrospective cohort study	154 patients with lower extremity bone metastases (23.4 %, 14.2 %, 9.7 %, and 6.5 % with lung cancer, breast cancer, renal cell carcinoma, and prostate cancer, respectively)	To re-evaluate risk factors for pathological fractures in lower extremity bone metastases based on CT images.	Surgery should be considered for medial cortical bone invasion and circumferential cortical involvement of the proximal femur (25−50 %) because of the increased risk of pathological fracture.	10/11

Eggermont et al., 2020, Netherlands [45]	Prospective cohort study	45 patients with bone metastases to the femur receiving radiation therapy for pain relief (29 %, 9 %, 31 %, and 16 % with breast cancer, prostate cancer, lung cancer, and multiple myeloma, respectively)	To compare fracture risk assessment using finite element (FE) computer models with assessments based on axial cortical invasion observed in diagnostic radiographs, as outlined in current guidelines for patients with cancer and femoral metastases.	During follow-up after palliative radiation therapy, seven femoral fractures (14 %) occurred. Comparing fracture risk assessments, the finite element (FE) computer model demonstrated higher sensitivity (100 % vs. 86 %), specificity (74 % vs. 42 %), and positive predictive value (39 % vs. 19 %) than axial cortical lesion evaluation. Negative predictive values were 100 % and 95 % for the FE model and axial cortical lesions, respectively. These results indicate that the FE computer model enhances fracture risk assessment beyond current clinical guidelines.	11/11
Sternheim, et al., 2020, Israel [46]	Retrospective cohort study	41 cancer patients with femoral metastases (31.7 %, 4.9 %, and 26.8 % with breast cancer, prostate cancer, and myeloma, respectively)	To use CT-based finite element analysis (CTFEA) to identify quantitative factors that clearly differentiate patients at imminent risk of femoral fracture from those who are not, and to accurately identify the largest site of weakness where fractures are most likely to occur.	A strain fold ratio (SFR) value of 1.48 was used as the threshold for a pathological fracture. The sensitivity of the strain magnification ratio by CTFEA was 100 %, while the Mirels score was 88 %. The specificity of the strain magnification ratio was 67 %, whereas the Mirels score was 38 %. The Area Under the Curve had an SFR of 0.905, while the Mirels score was 0.578. CTFEA was substantially more accurate in predicting fracture risk and site than the Mirels score.	9/11

*Evaluation: Quality appraisal was performed using the Joanna Briggs Institute's Critical Appraisal Checklists. The score in each Critical Appraisal Checklist is indicated.
ALP, alkaline phosphatase; LDH, lactate dehydrogenase; PS, performance status

femur (17.2 %), and humerus (10 %) [29]. In patients with breast cancer, pathological fractures most frequently occurred in the spine (63.4 %) and femur (26.8 %) [35]. Similarly, other studies have shown that the spine (27.5 %) and femur (60.4 %) have a higher frequency of pathological fractures [38]. Among patients with various cancer types, the spine (62.1 %), hip or femur (30.3 %), humerus (6.2 %), tibia or fibula (1.0 %), and radius (0.3 %) were the most frequent fracture locations [39]. Additionally, pathological fractures occurred significantly more often in the thoracic spine than in the lumbar spine [40], and the diaphysis of long bones is more prone to fracture than the epiphysis [29].

It has been shown that patients with pathological fractures subsequently experience increased pain, followed by significant aggravation of gait disturbance, anxiety, and psychological distress [34]. Recovery of gait disturbance, anxiety, and distress to pre-fracture levels typically requires approximately 16 months [34].

Risk factors for pathological fractures due to bone metastases, identified from the largest national inpatient database in the United States, include older age, female sex, receipt of radiation or surgical therapy during hospitalization, and a high burden of comorbidities [39]. Additionally, risk factors for bone-related events in lung cancer patients with bone metastases include smoking, non-adenocarcinoma, an Eastern Cooperative Oncology Group performance status of 2 to 3, and no history of epidermal growth factor receptor–tyrosine kinase inhibitor therapy [41]. In patients with lung cancer, smoking and a synchronous diagnosis of bone metastases with lung cancer have been associated with increased fracture risk [29]. Furthermore, the absence of radiation therapy for bone metastases has been linked to a higher incidence of pathological fractures [37].

Breast cancer has been strongly associated with pathological fractures [37]. Endocrine therapy in these patients negatively impacts bone density, leading to fractures related to both bone metastases and osteoporosis. Among vertebral fractures, 12 % and 11 % were attributed to bone metastases and osteoporosis, respectively [42]. Additionally, patients with breast cancer and bone metastases who experienced pathological fractures showed a significantly higher rate of progesterone receptor positivity than those without fractures [38].

Management of pathological fractures in patients with cancer and bone metastases

Only a few studies (six in total) have focused on managing pathological fractures in patients with cancer and bone metastases. Five studies identified significant risk factors for pathological fractures, varying by the site of bone metastasis. For vertebral fractures, factors significantly associated with fracture included metastatic lesion size, the number of affected vertebrae, the presence of osteolytic or mixed lesions, and pedicle destruction [42]. In long bones, univariate analysis of computed tomography (CT) imaging revealed several significant factors: osteolytic lesions, indis-

tinct bone margins, cortical bone invasion involving ≥ 30 % of the circumference, longitudinal cortical invasion ≥ 45 mm, complete cortical thickness invasion, and a Mirels score of ≥ 9 [36, 43]. Among these, cortical bone invasion of ≥ 30 % circumferentially and ≥ 45 mm longitudinally was identified as a threshold with high sensitivity and specificity [36]. Similarly, medial cortical involvement of the proximal femur and circumferential cortical involvement (25–50 %) assessed via CT imaging have also been reported as risk factors for pathological fractures [44]. Furthermore, for pathological femoral fractures, the use of patient-specific finite element modeling—incorporating bone geometry and density from quantitative CT scans—enabled the calculation of femoral fracture load and identification of high-risk patients. When compared with the commonly used clinical criterion of ≥ 30 mm longitudinal cortical invasion, the finite element model demonstrated superior sensitivity, specificity, positive predictive value, and negative predictive value [45]. Similarly, fractures have been simulated based on the strain magnification ratio using finite elements, resulting in improved sensitivity and specificity compared to the traditional Mirels score [46].

Only one study addressed the preventive management of pathological fractures. Rief et al. examined whether wearing a thoraco-lumbo-sacral orthosis could prevent pathological fractures in patients with osteolytic spinal lesions who had received radiation therapy [40]. The study found no significant difference in the incidence of pathological fractures 6 months after radiation therapy between patients who wore the orthosis and those who did not.

DISCUSSION

Pain and its management in patients with bone metastases

Pain associated with bone metastases occurs in approximately 80 % of patients, irrespective of cancer type. Severe pain is particularly common in cases of osteolytic bone metastases, which are characterized by extensive bone destruction and increased bone resorption—typically observed in breast, lung, and renal cancers. More than half of patients with bone metastases require opioid analgesics, with those having osteolytic lesions needing doses approximately 1.3 times higher than those with osteoblastic lesions. Severe pain in bone metastases is thought to be mainly caused by nerve compression and damage by tumor cells and the release of physiologically active substances—including prostaglandins, bradykinin, and tumor necrosis factor-alpha—as bone destruction progresses [47]. Furthermore, patients with osteolytic metastases exhibit the lowest performance status and physical function compared to those with osteoblastic or mixed types, likely due to pain-related limitations in movement and activity. Pain associated with bone metastases has been shown to be most severe in the movable regions of the spine. The primary cause of bone pain is believed to be mechanical distortion of the periosteum, which is densely innervated [48]. Consequently, severe pain is more likely to occur in spinal segments subjected to greater physical stress due to mobility.

Only five studies have specifically addressed pain management in patients with bone metastases, highlighting the effectiveness of providing reliable information, interactive support for patient understanding, self-monitoring using pain diaries, and monitoring utilizing pain worksheets by healthcare professionals. Particularly, body awareness through sensory perception and self-awareness of symptom and emotional changes were identified as important elements in promoting pain management. It has been suggested that patients with cancer can learn to recognize and monitor symptom changes through interactions with nurses [49]. Additionally, nurse coaching has been shown to enhance patients' awareness of their problems and adherence to treatment [50]. Pain monitoring improves patients' awareness of symptom fluctuations and promotes timely intervention, potentially contributing to pain relief. Accordingly, educating patients on self-monitoring practices may serve as an effective strategy for managing pain. Unfortunately, to date, few studies have specifically addressed self-management of pain associated with bone metastases in patients with cancer, and the evidence remains limited. In cancer pain management, effective strategies include educational programs designed to promote patient participation in pain control, nurse-targeted educational interventions [51], and interventions aimed at enhancing patients' self-management skills [52]. Pain in bone metastases involves multiple mechanisms, including nociceptive pain, neuropathic pain, and nociplastic pain, and further research on intervention and management strategies for the causes of pain will be important in the future.

Pathologic fractures with bone metastases and their management

Among SREs, pathological fractures are the most frequently reported. While incidence varies by cancer type, pathological fractures and spinal cord compression occur in approximately 10–30 % and 10–20 % of all patients with cancer, respectively. Studies from the 2000s reported pathological fractures and spinal cord compression in 52 % and 3 % of patients with breast cancer and bone metastases, respectively [53], and pathological fractures in 25 % and spinal cord compression in 8 % of patients with prostate cancer [54]. More than two decades later, the incidence of pathological fractures remains high. Thus, preventing and managing pathological fractures in patients with breast and prostate cancer—both of which commonly involve bone metastases—remain critical clinical challenges.

The spine and femur are the most common sites of pathological fractures, each accounting for approximately 30–60 % of all cases. As weight-bearing bones, they are subjected

to significant mechanical stress during daily activities, including standing, bending, and twisting. Consequently, these sites are not only more susceptible to fracture but also substantially impact patients' functional ability and daily life.

Risk factors for pathological fractures include advanced age, female sex, and the presence of osteolytic bone metastases, with patients with breast cancer being at particularly high risk. Decreased bone mineral density due to bone loss has been identified as a key contributing factor [55], and all these risk factors share the common mechanism of bone loss. In breast cancer, osteolytic metastases are frequent, and endocrine therapy in hormone receptor-positive patients further contributes to bone loss. Notably, aromatase inhibitors —commonly used in these patients—suppress estrogen biosynthesis and significantly reduce bone mineral density [56]. Consequently, fracture risk management is particularly crucial in elderly female patients with breast cancer. Moreover, when metastases are confined to the bone and do not involve other organs, patients can have a relatively long life expectancy [5]. In such cases, preventing fractures is crucial to maintaining QoL and supporting a safe, independent lifestyle. Therefore, additional empirical research is needed to advance fracture risk assessment and develop patient education focused on safe movement practices tailored to patients with breast cancer.

Only six studies have addressed the management of pathological fractures in patients with bone metastases, with five focusing on fracture risk assessment using imaging. A strong association between osteolytic bone metastases and fractures in both the vertebrae and femur has been linked to decreased bone mineral density [55]. Pedicle destruction has also been identified as a significant factor in vertebral fractures, with risk notably increasing when tumor size occupies the vertebral body in conjunction with pedicle damage [57]. For long bones, lesions exhibiting cortical bone invasion of ≥ 45 mm longitudinally and ≥ 30 % circumferentially have been associated with pathological fractures. However, clinical practice typically uses thresholds of ≥ 30 mm longitudinal and ≥ 50 % circumferential cortical invasion as indicators of imminent fracture risk [58], highlighting the need for further research to refine these criteria. Finite element models based on CT imaging simulate femoral fracture load and have demonstrated superior sensitivity and specificity in predicting fracture risk. Advances in this technology are expected to facilitate more accurate identification of high-risk patients. Currently, orthopedic surgeons primarily perform image-based bone fragility assessments; however, only 16.1 % of designated cancer medical institutions in Japan employ orthopedic specialists focused on bone metastases [59]. This limits comprehensive risk assessment and guidance on patient mobility. Implementing finite element modeling may enhance collaboration with specialists, enabling preventive fixation surgery for at-risk patients.

Research on fracture management related to daily activities remains limited. Movement restrictions vary depending on the site and extent of bone lesions, and many nurses report challenges in managing rest and fracture risk for patients with bone metastases [60], along with a lack of confidence in assessing fracture risk [13]. Additionally, only 39 % of patients express high satisfaction with the bone health information they receive [61]. To empower nurses in supporting patients with cancer and bone metastases, it is essential to integrate knowledge of bone fragility characteristics and expand empirical research focused on promoting safe daily living activities tailored to individual patient risk profiles.

CONCLUSIONS

Many patients with bone metastases experience pain, especially those with osteolytic lesions and metastases at mobile sites. Supporting patients in developing self-monitoring skills has demonstrated effectiveness in pain management. Pathological fractures are a common SRE, highlighting the importance of fracture risk management—particularly for elderly women and patients with breast cancer, who are at elevated risk. While image-based risk assessment has proven valuable for managing pathological fractures, research on daily living activities and fracture prevention strategies for patients with bone metastases remains limited. Further empirical studies in this area are needed.

AUTHOR CONTRIBUTIONS STATEMENT

Masamichi Fukuda: Conceptualization, Methodology, Formal analysis, Investigation, Writing–Original Draft, Visualization, Funding acquisition. **Kumi Suzuki**: Supervision, Project administration, Formal analysis, Investigation, Writing–review and editing.

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DECLARATION OF COMPETING INTERESTS

The authors declare no conflict of interest associated with this manuscript.

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