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Carpal tunnel syndrome and tenosynovitis in women with breast cancer associated with hormone therapy

A multi-institutional analysis using a clinical data warehouse

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Abstract

The study aims to evaluate the characteristics, treatments, and incidence rates of carpal tunnel syndrome (CTS) and tenosynovitis in women with breast cancer, according to the hormone therapy used. We retrospectively reviewed women with breast cancer identified from the clinical data warehouse of the six hospitals in Korea, from January 2015 to August 2020. Among them, patients with CTS or tenosynovitis were reviewed in terms of disease status and treatments. A total of 101 patients among a population of 15,504 met the study inclusion criteria, so their clinical data were analyzed. Aromatase inhibitor (AI) users frequently needed oral medication for CTS, and developed severe CTS which frequently required surgery. AI users presented with a higher incidence of CTS (1.3%) than patients without hormone therapy (0.4%), and tenosynovitis occurred at a higher rate in AI users (2.3%) compared to the tamoxifen (1.1%) and no hormone groups (0.5%). More than half of the CTS and tenosynovitis occurred within 12 months after hormone commencement. The incidence and disease characteristics of CTS and tenosynovitis differed among the groups depending on the type of hormone therapy received. Our findings will help clinicians understand clinical courses and treatments for CTS and tenosynovitis in breast cancer patients.

Abbreviations: AI = aromatase inhibitors, ATAC = Arimidex, Tamoxifen, Alone or in combination, CDW = Clinical Data Warehouse, CTS = carpal tunnel syndrome, EMG = Electromyography, EMR = Electronic medical records, IBCIS-II = International Breast Cancer Intervention Study II, IES = Intergroup Exemestane Study, OP = operation.

Keywords: aromatase inhibitors, breast cancer, carpal tunnel syndrome, tamoxifen, tenosynovitis

1. Introduction

Breast cancer is the most common cancer in females worldwide, with an estimated 2.3 million new cases annually in recent years.[1] About two-thirds of all breast cancer cases are either estrogen- or progesterone-receptor-positive. For such patients, clinicians prescribe tamoxifen or aromatase inhibitors (AIs) depending on menopausal status.[2] Among hormone therapies, AIs are the first-line therapies for advanced breast cancer in postmenopausal women, reducing recurrence by about 30% and the 10-year mortality rate by about 15% compared to tamoxifen.[3] Despite their good disease-free survival rates, AIs are associated with several musculoskeletal problems including carpal tunnel syndrome (CTS), tenosynovitis, osteoarthritis, and inflammatory arthritis.[4–7] AI recipients may complain of numbness, swelling, tingling, or stiffness.[5] Sleeping difficulties, impaired upper extremity stretching, and difficulties with daily

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activities may also be encountered; such symptoms are likely to develop within the first 6 to 8 weeks after starting an AI.[8] The prevalence of AI-induced musculoskeletal symptoms can attain 74%,[7] negatively affecting long-term compliance. Up to 68% of patients discontinue AIs because of musculoskeletal symptoms[9]; the therapeutic goal is to maximize the duration of medication tolerance. Clinicians may prescribe medications, physiotherapy, orthoses, or surgery.[10]

Several reports have described the overall incidence, time to onset, and treatment of AI- or tamoxifen-induced CTS and arthralgia.[11–15] However, few studies focused on tenosynovitis; both the overall incidence and the preferred treatments are poorly known. It is also important to understand the musculoskeletal side effects of hormone therapy, and to determine how such adverse events are currently treated. Here, we investigated the clinical features, disease status, overall incidence, and treatments for musculoskeletal adverse events (CTS and tenosynovitis) in hands or wrists associated with hormone therapies in women with breast cancer.

2. Patients and methods

2.1. Data sources

We enrolled patients from the clinical data warehouse (CDW) of the six hospitals in different cities of Korea (Seoul, Bucheon, Uijeongbu, Suwon). All clinical data were based on electronic medical records (EMRs). We retrieved the following data: date of birth; age at first diagnosis of breast cancer; body weight and height to calculate body mass index (BMI); smoking status; diabetes mellitus; date of first prescription of hormone therapy; dates of surgery, chemotherapy, and/or radiation therapy; operative records; radiological images; and electrodiagnostic findings. Additionally, each operative record includes detailed results, including the type of surgery, the procedures, and surgical findings such as lymph node metastases and mass sizes, enabling researchers to seek data specific to their research goals.

2.2. Selection and analysis of the study population

We initially identified 15,504 women with breast cancer who visited any of the six hospitals in Korea from January 1, 2015 to August 31, 2020, by searching the CDW based on disease code C50 from the 10th revision of the International Classification of Diseases (ICD-10); this code refers to breast cancer. From among these patients, we enrolled those who were first diagnosed with breast cancer between January 1, 2014 and August 31, 2018 (n = 6796), because hormones are usually prescribed within 1 year after breast cancer diagnosis. In addition, all hormone therapy was required to have been initiated between January 1, 2015 and August 31, 2018, to ensure that at least 2 years of follow-up data were available by August 2020. We chose this 2-year follow-up duration according to the Arimidex, Tamoxifen, Alone, or in Combination (ATAC) trial, in which the median time to onset of AI-induced CTS was 13.7 months.[14] Therefore, 809 patients who commenced hormone therapy before January 2015 or after August 2018 were excluded, leaving a total of 5987 patients (Fig. 1). Treatment with hormone therapy was identified by prescription codes (DC-TMF for tamoxifen, DC-EMT for exemestane, DC-ASTZ for anastrozole, and DC-LTZ for letrozole) recorded in the CDW. In total, 3149 patients (52.6%) did not receive hormone therapy at our study period, and were thus assigned to the no hormone therapy group; 2838 (47.4%) were started on either AI or tamoxifen between January 1, 2015 and August 31, 2018; 1292 were prescribed AIs (including anastrozole, letrozole, and exemestane); and 1682 were prescribed tamoxifen. Some patients received more than one type of AI. In total, 136 patients received both tamoxifen and AIs; they switched medications during the study period. Then, we collected data for women with breast cancer who experienced CTS or tenosynovitis in the designated period as outcomes, regardless of hormone therapy use. We also used ICD-10 codes when searching for CTS and tenosynovitis; the G56 code refers to CTS (median neuropathy), and the M65 and M75 codes refer to tenosynovitis, de Quervain's disease, or trigger finger. Infective tenosynovitis (ICD-10 codes A18, A54, M68) was not included in the CDW search. As a result, we identified a total of 135 women with breast cancer with ICD-10 codes for CTS or tenosynovitis; 49 had been prescribed AI, and 39 tamoxifen; 47 were not prescribed hormone therapy (Fig. 1).

For the 135 patients identified by the CDW search, the EMRs were reviewed to determine whether they were eligible for our study. We excluded patients who were previously diagnosed with CTS or tenosynovitis, and those with insufficient medical records to support the diagnoses of CTS and tenosynovitis. Patients who developed CTS or tenosynovitis before completing chemotherapy were also excluded. We restricted tenosynovitis to trigger finger and de Quervain's disease; tenosynovitis of the lower and proximal upper extremities was not included. As a result, 7 patients on AI, 7 on tamoxifen, and 20 not on hormone therapy were excluded by review of the EMRs. A total of 101 patients were therefore eligible for our study. Onset time, patient characteristics, and clinical progress (including treatments) data were reviewed for enrolled patients. We determined the onset times after the initiation of endocrine therapy, when patients first complained of musculoskeletal side effects and were diagnosed with CTS or tenosynovitis. When a specific onset date was not noted, we assumed that the date of registration of the first ICD-10 disease code (G56, M65, and M75) was the onset date. For those who switched hormone therapy during the study period, the medication evaluated was that being taken at the time of the adverse event, and thus considered to have caused that event. Treatments included oral medications, orthoses (such as splints), glucocorticoid injections, and surgeries. In addition, we classified the severity of CTS from mild to severe using the American Association of Electrodiagnostic Medicine (AAEM) electrodiagnostic guidelines.[16]

2.3. Statistical analysis

We present the group means or medians with interquartile ranges (IQRs) for continuous variables and frequencies and percentages for categorical variables. Among-group outcomes were compared using the Pearson chi-squared or Fisher's exact text. If a significant difference was apparent, between-group differences were also analyzed employing the two tests mentioned above. *P*-values $< .017$ were considered to indicate statistical significance in between-group analyses; we considered the Bonferroni correction. The Wilcoxon rank sum test was used to compare the median onset times of musculoskeletal diseases; statistical significance was based on two-tailed tests with *P*-values $< .05$. All statistical analysis was performed with the aid of SPSS software version 24.0 (SPSS Inc, Chicago, IL).

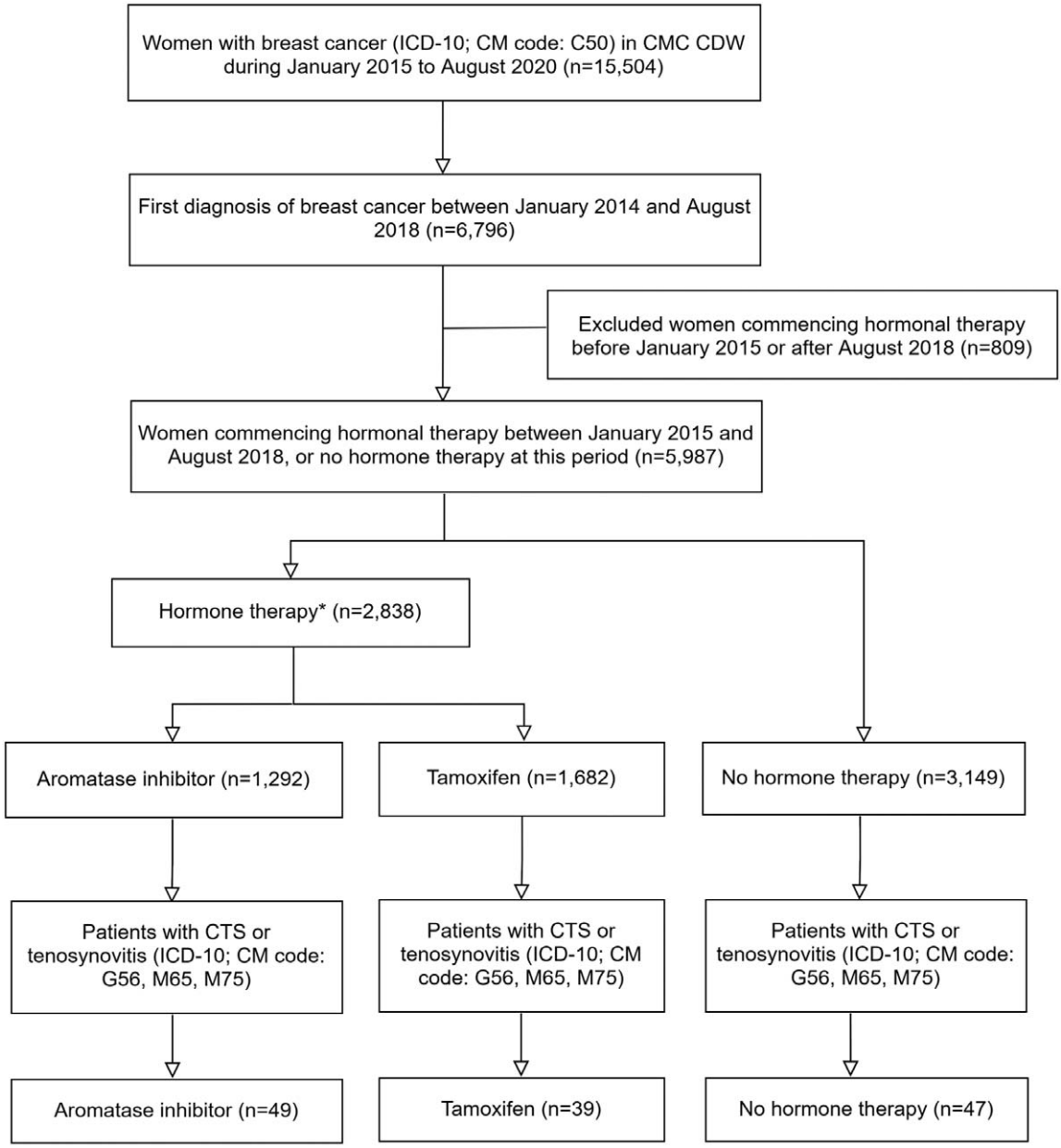

Figure 1. Flowchart of participant recruitment. Patients were identified in the clinical data warehouse (CDW) dataset. *Some patients received more than one type of hormone therapy, that is, switched therapies.

2.4. Privacy protection

This was a retrospective cohort study using EMR data from several hospitals. All data were encrypted to prevent patient identification. The original identification numbers used in the hospitals were changed to random numbers for research purposes. The data lack personal information and do not compromise patient rights. This research was approved by the Institutional Review Board of the Catholic University of Korea (approval number: XC20WIDI0182).

3. Results

Of the 101 patients with CTS or tenosynovitis, 42 were prescribed AIs, and 32 tamoxifen; 27 were not prescribed hormone therapy. The mean age at the time of initial breast cancer diagnosis was 54.0 years (IQR 47.0–59.0 years) and the mean BMI was 25.5 kg/m^2 (IQR 23.0–27.7 kg/m^2). Most of these patients were non-smokers (91.0%), and underwent chemotherapy (84.2%) and radiotherapy (79.2%). There were no significant demographic differences among the groups, except in age (Table 1).

The overall disease incidence (CTS or tenosynovitis) was 3.3% for patients on AI, 1.9% for those on tamoxifen, and 0.9% for those not on hormone therapy (Table 2). The overall disease incidence among the groups differed significantly ($P < .001$). Patients on AIs or tamoxifen were at greater risk than those not on hormone medication ($P = .019$ and $P = .004$, respectively).

Table 1

Demographics of breast cancer women with carpal tunnel syndrome and tenosynovitis, according to the treatment allocation.

	Aromatase inhibitor (n = 42)	Tamoxifen (n = 32)	No hormone therapy (n = 27)	
Risk factor	**No. (%)**	**No. (%)**	**No. (%)**	***P***
Age, years				
<60	22 (52.4%)[a,b]	28 (87.5%)	27 (100%)	
>60	20 (47.6%)[a,b]	4 (12.5%)	0 (0%)	**<.001**[*]
Total	42	32	27	
BMI, kg/m^2[c]				
<25	15 (37.5%)	18 (58.1%)	16 (61.5%)	
>25	25 (62.5%)	13 (41.9%)	10 (38.5%)	.101
Total	40	31	26	
Diabetes mellitus[c]				
Yes	11 (26.8%)	4 (12.5%)	3 (11.1%)	
No	30 (73.2%)	28 (87.5%)	24 (88.9%)	.175
Total	41	32	27	
Ever smoker[c]				
Yes	3 (7.3%)	5 (15.6%)	1 (3.7%)	
No	38 (92.7%)	27 (84.4%)	26 (96.3%)	.305
Total	41	32	27	
Chemotherapy				
Yes	32 (76.2%)	28 (87.5%)	25 (92.6%)	
No	10 (23.8%)	4 (12.5%)	2 (7.4%)	.174
Total	42	32	27	
Radiotherapy				
Yes	35 (83.3%)	23 (71.9%)	21 (77.8%)	
No	7 (16.7%)	9 (28.1%)	6 (22.2%)	0.487
Total	42	32	27	

[a] Statistically significant for no hormone therapy.
[b] Statistically significant for tamoxifen.
[c] Data for some patients were not available due to insufficient data at electrical medical records.
[*] *P* value for statistical significance (<.05).

3.1. CTS

CTS was diagnosed in 17 (1.3%) patients on AIs, 15 (0.9%) on tamoxifen, and 14 (0.4%) not on hormone therapy (Table 2). The CTS incidence differed significantly among the groups ($P = .007$). Patients on AIs had a higher incidence than patients not on hormone medication ($P < .001$). However, no significant difference was observed between patients on AIs and tamoxifen or patients on tamoxifen and no hormone medication ($P = .67$ and $P = .051$, respectively).

In total, 27 (58.7%) of patients with CTS exhibited bilateral disease. The incidence of bilateral CTS was statistically different among all groups. Patients on AIs had a higher incidence than those on tamoxifen, although the difference was not statistically significant. Most patients diagnosed with CTS underwent electrodiagnosis (89.1%). Of these, severe CTS was diagnosed in 8 patients (53.3%) on AIs, 1 (7.7%) on tamoxifen, and 4 (30.8%) not on hormone therapy. Oral medications were the most widely used treatments. AI users were prescribed drugs more frequently than patients not on hormone medications (94.1% vs 42.9%; $P = .004$). The common medications were non-steroidal anti-inflammatory drugs, acetaminophen, tramadol, antiepileptic drugs, and oral corticosteroids. Patients attempted to use one or more of these medications to relieve their symptoms. Corticosteroid injections were frequently given after oral medication. In total, 4 patients (23.5)% on AI, 4 (26.7%) on tamoxifen, and 1 (7.1%) not on hormone therapy

Table 2

Overall incidence of carpal tunnel syndrome and tenosynovitis according to the treatment allocation.

	Aromatase inhibitor (n = 1292)	Tamoxifen (n = 1682)	No hormone therapy (n = 3149)	
Clinical outcome	**No. (%)**	**No. (%)**	**No. (%)**	***P***
CTS	17 (1.3%)[a]	15 (0.9%)	14 (0.4%)	**.007**[*]
Tenosynovitis[c]	30 (2.3%)[a,b]	19 (1.1%)[a]	16 (0.5%)	**<.001**[*]
Both[d]	5 (0.4%)	2 (0.1%)	3 (0.1%)	.134
Total	42 (3.3%)[a,b]	32 (1.9%)[a]	27 (0.9%)	**<.001**[*]

CTS = carpal tunnel syndrome.
[a] Statistically significant for no hormone therapy.
[b] Statistically significant for tamoxifen.
[c] Tenosynovitis restricted to the distal upper extremities, including trigger finger and de Quervain's disease.
[d] Patients with both CTS and tenosynovitis.
[*] *P* value for statistical significance (<.05).

Table 3

Electrodiagnostic study, characteristics, and type of treatment for carpal tunnel syndrome in breast cancer women.

Clinical outcome	Aromatase inhibitor (n = 17) No. (%)	Tamoxifen (n = 15) No. (%)	No hormone therapy (n = 14) No. (%)	P
Side				
Bilateral	14 (82.4%)	6 (40.0%)	7 (50.0%)	**.039***
Unilateral	3 (17.7%)	9 (60.0%)	7 (50.0%)	
Ipsilateral to the OP site	2 (66.7%)	5 (55.6%)	5 (71.4%)	
Contralateral to the OP site	1 (33.3%)	4 (44.4%)	2 (28.6%)	
Treatment[b]				
Oral medication	16 (94.1%)[a]	11 (73.3%)	6 (42.9%)	**.007***
Triamcinolone injection	4 (24.0%)	4 (26.7%)	1 (7.1%)	.413
Surgery	7 (41.2%)	3 (20.0%)	3 (21.4%)	.364
No treatment	1 (5.9%)[a]	4 (26.7%)	7 (50.0%)	**.022***
Electrodiagnosis				
Yes	15 (88.2%)	13 (86.7%)	13 (92.9%)	
Normal	3 (20.0%)	3 (23.1%)	2 (15.4%)	.217
Mild	2 (13.3%)	5 (38.5%)	5 (38.4%)	
Moderate	2 (13.3%)	4 (30.8%)	2 (15.4%)	
Severe	8 (53.3%)	1 (7.7%)	4 (30.8%)	

OP = operation.

[a] Statistically significant for no hormone therapy.

[b] Treatments can be overlapped, since a number of patients received more than one kind of treatment.

* *P* value for statistical significance (<.05).

received triamcinolone injections into symptomatic lesions. Some patients eventually required surgical treatment. Seven cases of AI-induced CTS (41.2%) required carpal tunnel release, as did three tamoxifen users (20.0%). All surgeries but one for patients with AI-induced CTS were performed on severe CTS patients; the median time to surgery after CTS development was 110 days (IQR 26–809 days). Two AI-treated patients underwent bilateral surgeries (Table 3).

The median onset time for CTS did not differ for patients on AIs and tamoxifen (171 days [IQR 52–418 days] for AIs vs 180 days [IQR 42–460 days] for tamoxifen; $P = .976$). More than half of all CTS cases among the AI (70.6%) and tamoxifen (60.0%) users developed within 12 months of hormone therapy commencement. There was one tamoxifen user who developed CTS 36 months after drug commencement (Fig. 2).

3.2. Trigger finger and de Quervain's disease

Tenosynovitis was diagnosed in 30 (2.3%) patients on AIs, 19 (1.1%) on tamoxifen, and 16 (0.5%) not on hormone therapy (Table 2). The incidence differed significantly among the groups ($P < .001$). Patients on AIs were at higher risk than those on tamoxifen and those not on hormone medications ($P = .011$ and $P < .001$, respectively). In addition, there was a significant difference in incidence between patients on tamoxifen and those not prescribed hormone therapy ($P = .015$).

Bilateral symptoms were apparent in 9 (13.8%) women with tenosynovitis. Oral medications were more commonly prescribed for AI users (83.3%) than patients not on hormone medications (56.3%), although the difference was not statistically significant. In total, 16 patients (53.3%) on AI, 6 (31.6%) on tamoxifen, and 3 (3.75%) not on hormone therapy received triamcinolone injections into symptomatic lesions. Surgical interventions were less common than for CTS and were only used for 8 patients in total: 3 on AI, 3 on tamoxifen, and 2 not on hormone therapy (Table 4). Surgeries included A1 pulley release, tenosynovectomy, and first-extensor compartment release for those with trigger finger and de Quervain's disease.

No significant difference was observed in the median tenosynovitis onset time between patients on AIs and tamoxifen (313.5 days [IQR 170–501 days] for AI vs 250 days [IQR 73–596 days] for tamoxifen patients; $P = .134$). More than half of all tenosynovitis cases developed within 12 months after drug initiation (56.7% for AI and 52.6% for tamoxifen recipients); single cases developed after 36 months in both AI and tamoxifen users (Fig. 2).

4. Discussion

Previous large studies have reported comparative data for AIs and tamoxifen,[11,13,14] or AIs and placebo.[15] Here, we retrospectively compared the musculoskeletal side-effects of patients taking AI, tamoxifen, or no hormone therapy. The incidence of AI-induced CTS in our study was 1.3%, thus lower than that of the ATAC trial (2.6%), the Intergroup Exemestane Study (IES; 2.8%), and the International Breast Cancer Intervention Study II (IBCIS-II; 3.4%). This may reflect the different data collection method of our study, that is, registration of a relevant ICD-10 code. A recent Taiwanese study using a nationwide dataset reported an incidence (1.4%) similar to ours.[11] However, our incidence of CTS in tamoxifen users (0.9%) was similar to that of the ATAC trial (0.7%), the IES (0.7%), and the study from Taiwan (0.8%). Most CTS cases in women taking AIs developed within 12 months after drug commencement, consistent with previous studies (median time to disease onset = 0.5–1.99 years).[12–15]

CTS is caused by median nerve entrapment at the wrist; the pathogenesis includes mechanical compression, microvascular insufficiency, or ischemic injury.[17] CTS is slowly progressive and occasionally requires surgery after initial conservative management.[18] The reason why some hormone therapies trigger CTS and tenosynovitis remains unclear. The estrogen-

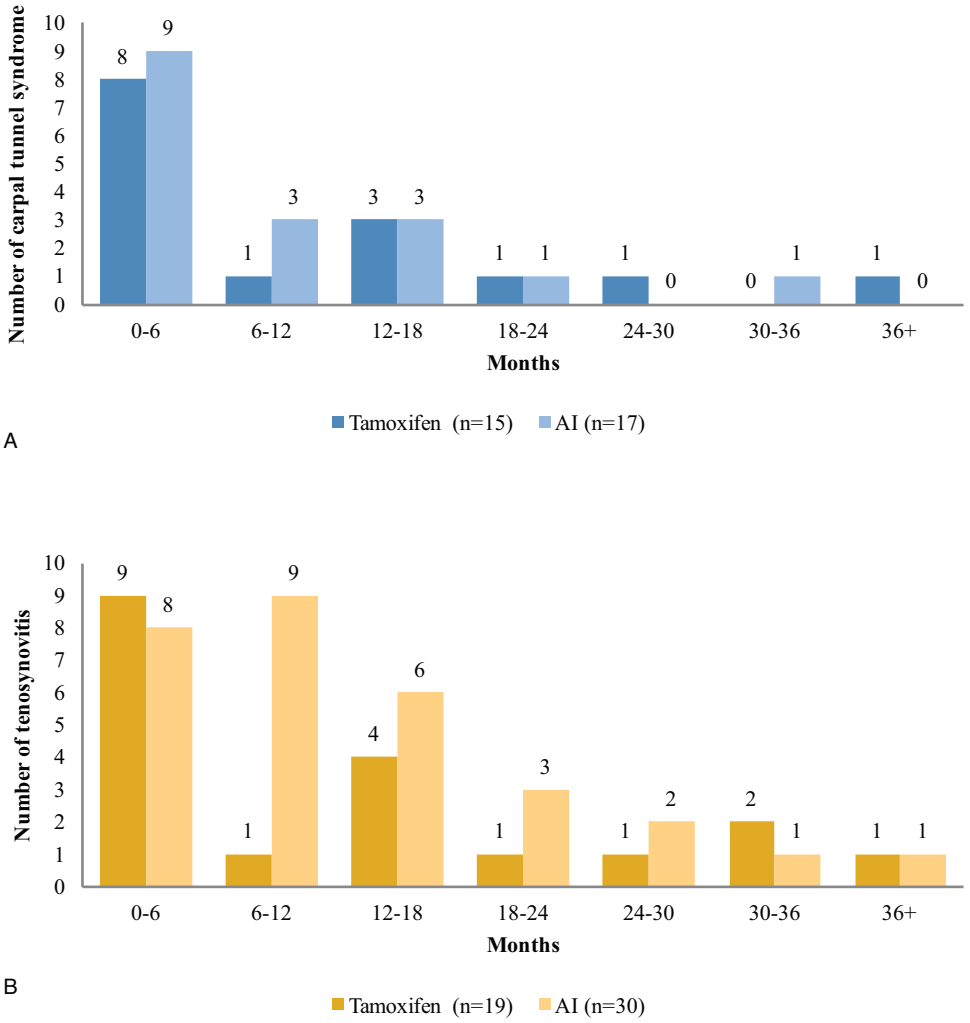

Figure 2. Histogram of newly reported (A) carpal tunnel syndrome and (B) tenosynovitis cases according to treatment allocation. AI = aromatase inhibitors.

Table 4

Characteristics and type treatment for tenosynovitis of upper extremities (trigger finger and de Quervain's disease) in breast cancer women.

	Aromatase inhibitor (n = 30)	Tamoxifen (n = 19)	No hormone therapy (n = 16)	
Clinical outcome	**No. (%)**	**No. (%)**	**No. (%)**	***P***
Side				
Bilateral	7 (23.3%)	1 (5.3%)	1 (6.3%)	.189
Unilateral	23 (76.7%)	18 (94.7%)	15 (93.8%)	
Ipsilateral to the OP site	14 (60.9%)	12 (66.7%)	10 (66.7%)	
Contralateral to the OP site	9 (39.1%)	6 (33.3%)	5 (33.3%)	
Treatment*				
Oral medication	25 (83.3%)	15 (79.0%)	9 (56.3%)	.159
Triamcinolone injection	16 (53.3%)	6 (31.6%)	6 (37.5%)	.293
Splint	2 (6.7%)	3 (15.8%)	1 (6.3%)	.544
Surgery	3 (10.0%)	3 (15.8%)	2 (12.5%)	.889
No treatment	2 (6.7%)	3 (15.8%)	2 (12.5%)	.593

OP = operation.

* Treatments can be overlapped, since a number of patients received more than one kind of treatment.

depleting effect of AI may be relevant.[6,19] This would reduce the protective antinociceptive effect of estrogens, increasing the risk of exposure to any underlying musculoskeletal pathology.[6] CTS occasionally requires surgical intervention for symptom improvement. Our surgery rate for AI-induced CTS (41.2%) was higher than that reported in prior studies: 13.8% in the ATAC trial and 27.7% in the IBCIS-II prevention trial. In contrast, the IES trial rate attained 69%, but only exemestane users were enrolled. The different results may reflect heterogeneity in study design and increased physician awareness of musculoskeletal side-effects.

We explored CTS severity as confirmed by electrodiagnosis, including both nerve conduction studies and electromyography. It is useful to objectively confirm a diagnosis even when CTS seems very probable.[20,21] Electrodiagnostic studies are recommended before invasive CTS procedures.[22] However, few studies have reported electrodiagnostic assessments of disease status, and CTS diagnoses have been based only on clinical symptoms. In the IES trial, 23 (39.7%) exemestane and tamoxifen users underwent electrodiagnosis but CTS severity was not measured.[13] Dizdar et al[23] electrodiagnosed 89 (74.2%) AI users and controls but did not measure disease severity. In our study, about 90% of all patients diagnosed with CTS underwent electrodiagnosis, with disease severity quantified according to AAEM guidelines. Our study results demonstrated that AI-induced CTS is often severe, frequently requiring surgical intervention.

We assessed upper-extremity tenosynovitis; this has not been explored in previous large studies. One prior prospective study found that AI users were >2-fold more likely to exhibit a decreased grip strength (compared to that of tamoxifen users) after 6 months, and >3.5-fold more likely to exhibit tenosynovial changes on magnetic resonance imaging (MRI).[24] Similar to CTS, AI-induced tenosynovitis is related to estrogen deprivation, which leads to attenuation of antinociceptive effects. Neither the incidence of trigger finger nor de Quervain's disease has been reported in breast cancer patients on hormone therapy, so there are no data to which we can compare ours. The incidences of trigger finger and de Quervain's disease in our study (2.3% among patients on AI and 1.1% for those on tamoxifen) were not lower than that of CTS; close attention is needed. Consequently, our results will aid future research on hormone therapy induced-tenosynovitis, including the natural history and treatment strategies.

Our study had several strengths. First, most previous studies have focused on musculoskeletal events such as arthralgia or arthritis. In contrast, we explored localized, specific disease entities (trigger finger and de Quervain's disease) that can be easily managed by clinicians. To the best of our knowledge, this is the first study to assess the incidences and treatments of trigger finger and de Quervain's disease. Second, we evaluated real-world, multiple-institutional clinical data. Use of the CDW saves time and labor compared to those required by conventional studies; large amounts of data can be collected rapidly.[25] Recently, efforts have been made to collect population-based big data quickly. Chien et al used the national health insurance research database of Taiwan to investigate real-world, population-based claims of women with breast cancer.[11] We additionally quantified disease severity, and discussed clinical progression and the treatments given, enabling clinicians to establish general treatment plans for musculoskeletal side-effects.

Our study had some limitations. The data were retrospectively retrieved from the CDW using ICD-10 codes. Thus, if a clinician did not register a disease code, we may have missed patients with CTS or tenosynovitis. This would underestimate disease incidence and reduce the clinical data available for analysis. Another limitation is that the onset dates of CTS and tenosynovitis may not be exact because they are usually the dates of medical records. Some records did not document exactly when symptoms commenced; we had to presume that the onset date was the date of first registration of the ICD-10 disease code. Thus, the times to disease onset may have been underestimated. Furthermore, because only patients with CTS or tenosynovitis were reviewed by EMRs, we could not calculate odd ratios adjusted for baselines factors, so the comparison of incidence among groups was limited and should be interpreted cautiously. Lastly, patients tend to take musculoskeletal problems to local clinics, or to ignore them, especially when symptoms are mild. If they did not return to their treating departments, we would lack information on exact onset dates, treatment options, and clinical progress. Many non-university hospitals/semi-hospitals now perform high-technology diagnoses and even surgeries, so some patients may have received surgery or electrodiagnostic evaluation in such hospitals. Some patients may also have chosen alternative medicines, acupuncture, physiotherapy, or other non-drug therapies.

5. Conclusion

In summary, the overall (CTS or tenosynovitis) disease incidence differed significantly according to the hormone treatment used. Patients with AI were more liked to develop CTS or tenosynovitis than patients without hormone therapy, and there were more cases of tenosynovitis in the AI group compared to the tamoxifen group. More than half of patients with CTS and tenosynovitis developed it within 12 months after hormone commencement. About half of CTS patients on AI developed severe CTS, which frequently required surgical intervention. Our findings will help clinicians understand the clinical courses and treatments of musculoskeletal side-effects in women with breast cancer undergoing hormone therapies.

Author contributions

Conceptualization: Dong Jae Shin, Jong In Lee.
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Validation: Jong In Lee.
Writing – original draft: Dong Jae Shin.
Writing – review & editing: Dae Heon Song, Sun Im, Sun Jae Won, Yeo Hyung Kim, Seong Hoon Lim, Jong In Lee.

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