

Risk factors and outcomes in hand-foot syndrome: A retrospective cohort study

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BACKGROUND AND STUDY AIMS

- Hand-foot syndrome (HFS) is a well-known chemotherapy-associated toxicity, impacting quality of life and treatment tolerability.¹
- HFS is characterized by pain, numbness, tingling, erythema, edema, cracking, and desquamation of the palms and soles.²
- This study investigates the influence of chemotherapy regimens and patient factors on HFS severity, timing, and treatment interruptions.

METHODS

- The primary data source for this study was the Ohio State Information Warehouse.
- *Inclusion criteria included:*
 - Age of 18 or older, diagnosed with cancer, completed chemotherapy between May 2010 and May 2023
- *Data collected:*
 - Age at the time of cancer diagnosis, sex, race, ethnicity
 - Information regarding dermatologic conditions, cancer diagnoses, chemotherapy regimens, and side effects from chemotherapy
- *Statistical analysis:*
 - Nonparametric statistical tests were used to assess associations between clinical, demographic, and treatment-related variables and HFS outcomes. Spearman’s rank correlation was used for continuous and ordinal variables, Mann-Whitney U tests for comparisons between two groups, Kruskal-Wallis tests for comparisons across multiple groups, and Chi-square tests for categorical associations. Statistical significance was set at p-value < 0.05.

RESULTS

Sample size (N)		62
Age (years) – mean (SD)		57.32 (12.208)
Sex – n (%)		
	Male	27 (43.5)
	Female	35 (56.5)
BMI – mean (SD)		27.65 (5.71)
Diabetes – n (%)		8 (12.9)
Smoking (Pack-years) – mean (SD)		5.97 (19.19)
Alcohol use (Drinks/week) – mean (SD)		1.02 (1.83)
HFS Severity – n (%)		
	Grade 1	18 (29.0)
	Grade 2	28 (45.2)
	Grade 3	10 (16.1)
HFS Distribution – n (%)		
	Hands only	12 (19.4)
	Feet only	8 (12.9)
	Both	41 (66.1)
	Missing	1 (1.6)
Functional impairment – n (%)		14 (22.6)

TABLE 1. Cohort Demographics

RESULTS

Predictor	Statistic	P-value
Age	ρ = -0.051	0.694
Sex	U = 463.0	0.893
Race	H = 3.792	0.435
BMI	ρ = -0.036	0.779
Diabetes	U = 159.5	0.235
Pack-years	ρ = -0.298	0.019*
Drinks per week	ρ = 0.087	0.544
Functional impairment	U = 247.0	0.134
HFS severity	ρ = -0.076	0.559
HFS distribution	H = 1.311	0.519
Capecitabine cumulative dose	ρ = 0.670	<0.001*
5-Fluorouracil cumulative dose	ρ = 0.944	<0.001*
Oxaliplatin cumulative dose	ρ = 0.720	<0.001*

TABLE 2. Predictors of time to HFS onset

Predictor	Statistic	P-value
Age	U = 406.5	0.348
Sex	χ ² = 0.825	0.364
Race	χ ² = 4.140	0.387
BMI	U = 446.5	0.712
Diabetes	χ ² = 7.218	0.007*
Pack-years	U = 432.5	0.512
Drinks per week	U = 278.0	0.483
Functional impairment	χ ² = 5.718	0.017*
HFS severity	χ ² = 9.536	0.023*
HFS distribution	χ ² = 1.069	0.586
HFS treatment count	U = 150.0	<0.001*
Capecitabine cumulative dose	U = 131.5	0.002*
5-Fluorouracil cumulative dose	U = 11.0	0.644
Oxaliplatin cumulative dose	U = 50.0	0.167

TABLE 3. Predictors of chemotherapy being held due to HFS

Predictor	Statistic	P-value
Age	ρ = -0.116	0.368
Sex	U = 453.5	0.774
Race	H = 4.819	0.306
BMI	ρ = 0.134	0.299
Diabetes	U = 193.0	0.606
Pack-years	ρ = -0.057	0.661
Drinks per week	ρ = -0.192	0.176
Functional impairment	U = 280.0	0.314
HFS distribution	H = 2.415	0.299
HFS onset	ρ = -0.076	0.559
HFS treatment count	ρ = 1.000	0.023*
Capecitabine cumulative dose	ρ = -0.187	0.208
5-Fluorouracil cumulative dose	ρ = 0.030	0.927
Oxaliplatin cumulative dose	ρ = 0.219	0.272

TABLE 4. Predictors of HFS severity

CONCLUSION

In this large, single-institutional analysis:

Demographic and Behavioral Factors

- Age, sex, and race were not significantly associated with time to HFS onset, severity, functional impairment, chemotherapy being held, or the number of treatments attempted.
- **BMI** was significantly associated with functional impairment (U = 215.0, p = 0.042), suggesting body composition may play a role in HFS-related limitations.
- **Pack-years** showed a weak but significant negative correlation with time to HFS onset (p = –0.298, p = 0.019), indicating earlier onset of HFS among heavier smokers.

Clinical and Treatment-Related Predictors

- **Cumulative chemotherapy exposure** was significantly associated with time to HFS onset:
 - Capecitabine: p = 0.670, p < 0.001
 - 5-FU: p = 0.944, p < 0.001
 - Oxaliplatin: p = 0.720, p < 0.001
 - These findings suggest that prolonged or higher cumulative dosing is linked to later HFS onset.
- **Cumulative capecitabine dose** was also significantly associated with:
 - Chemotherapy being held (U = 131.5, p = 0.002)
 - Functional impairment (U = 131.5, p = 0.002)

Symptom Burden and Treatment Response

- **HFS severity** was significantly associated with:
 - Chemotherapy being held (χ² = 9.536, p = 0.023)
 - Number of treatments attempted (p = 1.000, p = 0.023)
- **Chemotherapy needing to be held** was also associated with:
 - Functional impairment (χ² = 5.718, p = 0.017)
 - Diabetes (χ² = 7.218, p = 0.007)
 - Higher treatment burden (U = 150.0, p < 0.001)
- **HFS distribution** was significantly associated with functional impairment (χ² = 8.864, p = 0.012), with patients experiencing both hand and foot involvement more likely to report limitations.

REFERENCES

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