The interrelation between cancer-related fatigue and diabetes: An analysis of 440 patients with breast cancer undergoing chemotherapy and controls

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Cancer-related fatigue is prevalent and debilitating

- Cancer-related fatigue is persistent fatigue after a cancer diagnosis that is not proportional to recent activity and is not relieved by sleep or rest.
- It affects 30-90% of patients during and after their cancer experience.
- ~1/3 of cancer survivors experience fatigue up to 6 years after treatment.
- Its severity can impair the ability to perform activities of daily living, greatly reduce quality of life, and increase mortality.
- The etiology and pathophysiology of cancer-related fatigue are largely not understood, precluding the design of effective, evidence-based treatments.
- Metabolic dysfunction is an increasingly recognized mechanism underlying the pathology of cancer-related fatigue.

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Diabetes and cancer often coexist

- The prevalence of diabetes mellitus in the United States is approximately 10.5%.
- Diabetes is a well-established risk factor for breast cancer.
- Diabetes accelerates the progression of cancer and increases its aggressiveness.
- In regard to supportive care, diabetes is sometimes associated with increased prevalence and severity of specific symptoms and side effects including fatigue, pain, cognitive impairment, anxiety, depression, and chemotherapy-induced peripheral neuropathy, some of which develop during cancer treatment.

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Is diabetes associated with worse cancer-related fatigue?

- With a shared symptom burden and possibly shared pathophysiology, it is important to evaluate whether the coexistence of diabetes and cancer is associated with worse fatigue than cancer alone during chemotherapy treatment for breast cancer and into early survivorship.
- These data could help clinicians identify patients who are at greater risk for fatigue, as well as shed light on biological mechanisms underlying cancer-related fatigue that could be leveraged in future prophylactic agents or treatments.

Methods

- This was a secondary analysis of a multisite observational cohort that followed patients from before chemotherapy to after chemotherapy and 6 months post-chemotherapy (PI: Janelsins).
- Patients were recruited from 22 community oncology practice sites across the United States.
- Eligibility for patients: female, stage I-IIIC breast cancer, be scheduled for chemotherapy, be chemotherapy naïve, >20 y old, no central nervous system or neurodegenerative diseases, no recent major psychological illness, no plans for radiation concurrent with their chemotherapy.
- Eligibility for controls: same as patients except the cancer diagnosis, within 5 years of age of the paired case participant.
- Patient-reported fatigue was assessed using the Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF)
- Diabetes status was obtained from the medical record at baseline.
- Repeated measures mixed models were used to model CRF over time controlling for relevant co-variates.

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Demographics

	Total participants	Cancer with diabetes	Cancer without diabetes	Control with diabetes	Control without diabetes
n	674	51	388	16	219
Age	52.8±10.5	58.6±8.6	52.5±10.7	53.3±9.8	52.0±10.2
BMI: overweight or obese	469 (69.6%)	46 (90.2%)	266 (68.6%)	13 (81.3%)	144 (65.8%)
Regular exercise	334 (49.6%)	20 (39.2%)	180 (46.4%)	5 (31.3%)	129 (59.7%)
Smoking (never)	403 (59.8%)	34 (66.7%)	219 (56.4%)	9 (56.3%)	141 (65.3%)
Menopausal status					
Pre-menopausal	209 (31.0%)	4 (7.8%)	136 (35.1%)	4 (25.0%)	65 (30.1%)
Post-menopausal	346 (51.3%)	34 (66.7%)	200 (51.5%)	7 (43.8%)	105 (48.6%)
Peri-menopausal	67 (9.9%)	6 (11.8%)	27 (7.0%)	3 (18.8%)	31 (14.4%)
Medically induced	52 (7.7%)	7 (13.7%)	25 (6.4%)	2 (12.5%)	18 (8.3%)
White race	610 (90.5%)	37 (72.5%)	354 (91.2%)	15 (93.8%)	204 (94.4%)
Education: at least some college	552 (81.9%)	36 (70.6%)	304 (78.4%)	13 (81.3%)	199 (92.1%)
Married/long-term relationship	494 (73.3%)	33 (64.7%)	289 (74.5%)	8 (50.0%)	164 (75.9%)
Baseline anxiety*	33.4±12.0	36.9±13.3	36.0±12.3	26.8±5.7	28.4±9.8
Baseline depression†	0.58±0.87	0.73±0.92	0.67±0.91	0.75±1.13	0.37±0.72

*Anxiety was measured using the Spielberger Trait Anxiety Inventory
†Depression was assessed using item 21 on the Multidimensional Fatigue Symptom Inventory-Short Form

Diabetes was significantly associated with fatigue

	All participants			Patients only			Controls only		
	Est.	SE	p	Diff.	SE	p	Diff.	SE	p
Total MFSI	4.46	1.72	0.010	4.11	1.98	0.039	5.43	3.27	0.098
General fatigue	1.55	1.12	0.169	1.78	0.69	0.010	1.55	1.12	0.169
Physical fatigue	1.18	0.46	0.010	0.83	0.53	0.119	2.17	0.88	0.014
Mental fatigue	0.94	0.46	0.042	1.14	0.53	0.032	0.36	0.88	0.683
Emotional fatigue	0.17	0.33	0.614	0.21	0.38	0.588	0.06	0.61	0.927
Vigor	-0.77	0.46	0.091	-0.56	0.53	0.286	-1.34	0.87	0.123

Models adjusted for cancer status (y/n), time, age, BMI, exercise habits, smoking habits, marital status, menopausal status, baseline anxiety, and baseline depression

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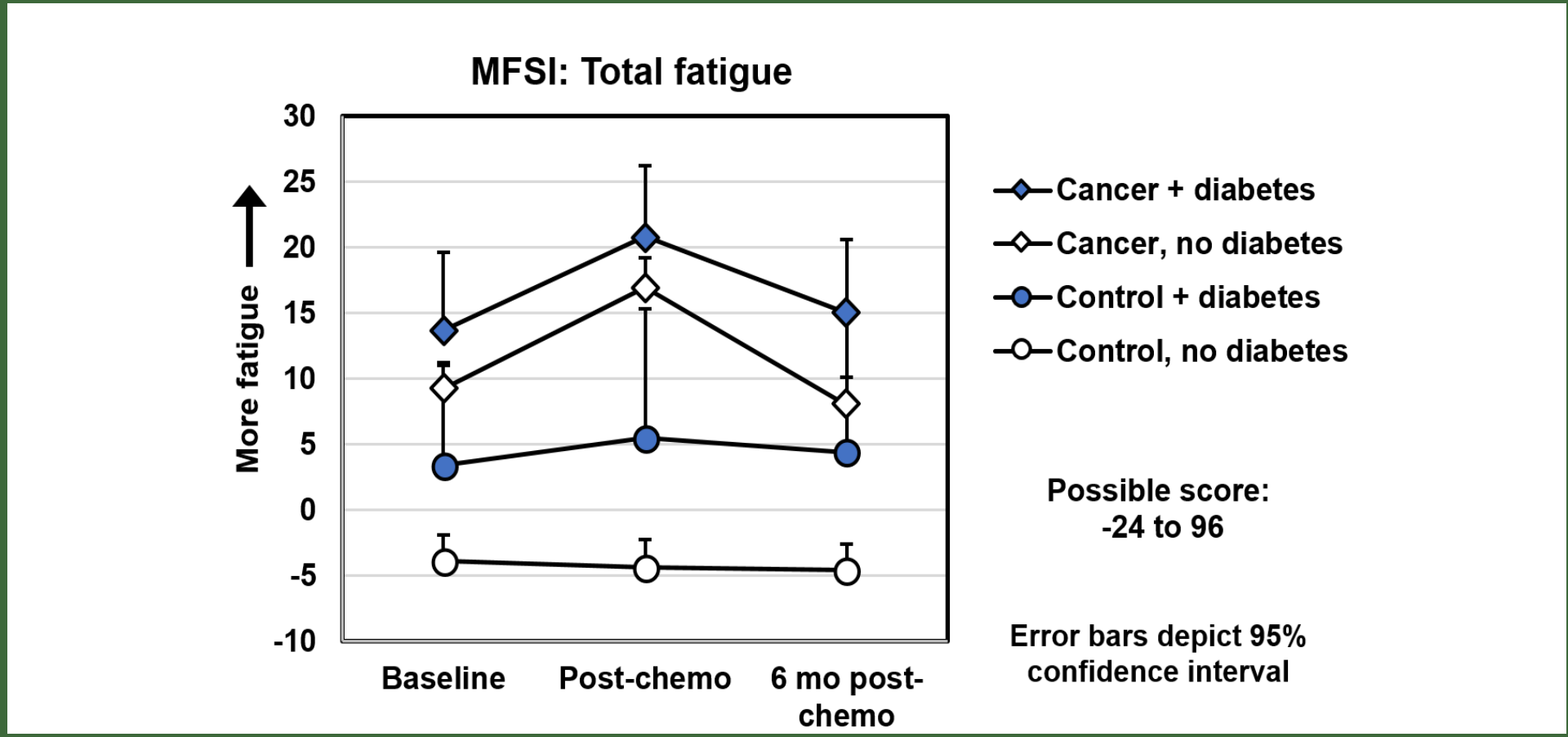
Fatigue trajectories before, immediately post-chemotherapy, and 6-months post-chemotherapy



Unadjusted values

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Conclusions

- Diabetes contributes to cancer-related fatigue to a clinically meaningful degree before, during, and after chemotherapy treatment for female breast cancer after controlling for demographics, clinical characteristics, and lifestyle factors.
- These results suggest that glycemic control during the cancer experience can reduce the burden of acute and long-term side effects of cancer and its treatments in addition to promoting the efficacy of anti-neoplastic therapy and improving survival.
- It is important for clinicians to encourage metabolic health, perhaps via healthy lifestyle practices (e.g., diet, exercise, sleep, not smoking) during the cancer experience in order to reduce the burden of diabetes on fatigue.

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