

Lymph and Mind: A New Perspective on Cognitive Dysfunction in Lymphedema

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Background

Lymphedema and cognitive impairment were once thought to be unrelated. However, recent discoveries of brain lymphatics and the systemic nature of primary lymphedema suggest a possible connection. Given frequent patient reports of cognitive impairment, this study investigates the relationship between primary lymphedema and cognitive dysfunction.

Methods

We assessed cognitive function in 81 patients with primary lymphedema (67 females, 14 males; mean age 45) using the Montreal Cognitive Assessment (MoCA) and Brain Fog Scale (BFS). A comparative analysis was conducted against a historical control group of 1,046 healthy individuals. A subgroup analysis compared cognitive scores of patients who underwent lymphatic reconstruction (n=12) with those who did not (n=69). Statistical differences between groups were evaluated using independent t-tests.

Results

Primary lymphedema patients had an average BFS score of 28.10±18.92 and a mean MoCA score of 27.92±2.28. Compared to controls, they showed significantly higher brain fog symptoms, including mental fatigue (10.58±5.44 vs. 8.62±4.63, p=0.0022), impaired cognitive acuity (10.57±8.44 vs. 7.81±6.18, p=0.0050), and confusion (6.95±6.56 vs. 5.18±5.71, p=0.0203). Patients with subjective cognitive complaints (n=21) had significantly higher BFS scores across all domains than those without (p<0.0001). Furthermore, patients who underwent lymphatic surgery reported lower brain fog symptoms, particularly in cognitive acuity (6.25±5.22 vs. 11.32±8.69, p=0.011) and total BFS score (19.75±11.87 vs. 29.55±19.59, p=0.027).

	Lymphedema (n=112)	Control (n=265)	Mean difference(95% CI)
BFS score	28.99 ± 18.34	21.60 ± 14.98	7.39(3.54 to 11.24)
Mental fatigue	10.89 ± 5.20	8.62 ± 4.63	2.27(1.16 to 3.38)
Impaired cognitive acuity	11.09 ± 8.30	7.81 ± 6.18	3.28(1.57 to 4.99)
Confusion	7.01 ± 6.33	5.18 ± 5.71	1.83(0.47 to 3.19)

Table 1: Comparison of BFS score between primary lymphedema patients and Polish control group

	Subjective cognitive deficit			
	Yes (n=36)	No (n=76)	Mean difference(95%CI)	P-value
Age	54.25 ± 15.14	43.53 ±18.09	10.72(4.32 to 17.12)	0.003
<45	33.25 ± 7.38	27.57 ± 9.02	5.68(-0.20 to 11.56)	0.104
≥45	60.25 ± 10.73	58.67 ± 9.27	1.58(-3.35 to 6.50)	0.521
Age (<45)	Subjective cognitive deficit			
	Yes (n=8)	No (n=37)	Mean difference(95%CI)	P-value
MoCA	27.38 ± 2.00	28.22 ± 1.60	-0.84(-2.32 to 0.64)	0.204
BFS score	41.25 ± 14.96	19.27 ± 11.35	21.98(10.99 to 32.97)	<0.001
Age (≥45)	Subjective cognitive deficit			
	Yes (n=28)	No (n=39)	Mean difference(95%CI)	P-value
MoCA	26.54 ± 2.32	28.05 ± 2.35	-1.51(-2.64 to -0.38)	0.011
BFS score	49.75 ± 15.78	20.79 ± 11.52	28.96(22.09 to 35.83)	<0.001

Table 2: Comparison of MoCA and total BFS score with primary lymphedema patients having and without having subjective cognitive deficit

Age (<45)	Lymphatic reconstruction surgery			
	Yes (n=10)	No (n=35)	Mean difference (95% CI)	P-value
MoCA	28.00 ± 1.56	28.09 ± 1.74	-0.09(-1.22 to 1.04)	0.884
BFS score	25.70 ± 12.11	22.46 ± 15.32	3.24(-5.82 to 12.30)	0.542
Age (≥45)	Lymphatic reconstruction surgery			
	Yes (n=12)	No (n=55)	Mean difference (95% CI)	P-value
MoCA	27.67 ± 1.92	27.36 ± 2.55	0.31(-0.97 to 1.59)	0.693
BFS score	23.42 ± 18.98	34.96 ± 19.32	-11.54(-23.43 to 0.35)	0.064

Table 3: Comparison of MoCA and BFS score with primary lymphedema patients having and without having lymphatic reconstruction surgery

Conclusion

: This study identifies a significant correlation between primary lymphedema and cognitive impairment. Post-surgical cognitive improvements suggest a mechanistic link between lymphatic function and cognitive performance, emphasizing the systemic nature of lymphedema and the necessity for cognitive assessments in affected patients.

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