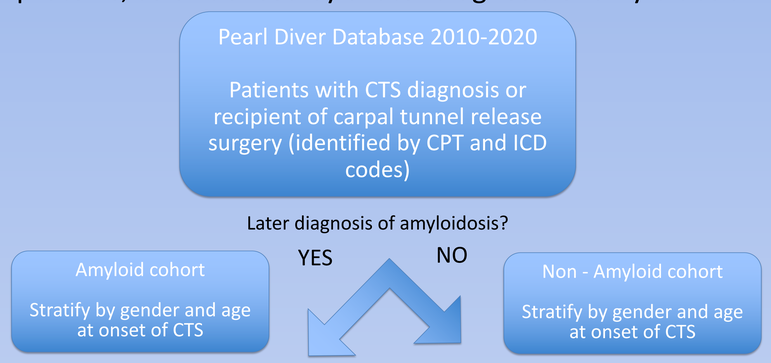
THE GEORGE WASHINGTON UNIVERSITY
WASHINGTON, DC

Amyloidosis and Carpal Tunnel Syndrome: A Database Study of Associated Risk Factors and Comorbidities

Sasha Narain, Amy Zhao, Peter Howard, Rachel Ranson, Alex Gu, Thakkar, O'Malley

Background & Methods

- Immunoglobulin light chain and transthyretin systemic amyloidoses are diseases of improper protein folding that can result in the accumulation of proteins in the soft tissues
- Accumulation of these proteins in the carpal tunnel can result in carpal tunnel syndrome (CTS), a compressive neuropathy of the median nerve
- The aim of this study was to investigate which patient specific factors in those diagnosed with CTS suggest that the compression may be due to accumulation of amyloid proteins, as evidenced by a later diagnosis of amyloidosis.



Pearson chi-squared analysis of comorbidities in Amyloid vs Non amyloid groups

Table 1: Incidence of amyloidosis in patients with CTS by age and gender

	Total	Male		Female	
		n	%	n	%
Total	1071	595		476	
Gender					
Male	595	595		0	
Female	476	0		476	
Age*					
40 to 44	21	7	33.33%	14	66.67%
45 to 49	54	22	40.74%	32	59.26%
50 to 54	102	36	35.29%	66	64.71%
55 to 59	172	80	46.51%	92	53.49%
60 to 64	213	122	57.28%	91	42.72%
65 to 69	248	152	61.29%	96	38.71%
70 to 74	357	214	59.94%	143	40.06%
75 to 79	357	208	58.26%	149	41.74%
80 to 84	206	125	60.68%	81	39.32%

*Age groupings represent patient age at the time of CTS diagnosis.

Results

Table 2: Comorbidities of patients with CTS with or without later diagnosis of amyloidosis.

	Control Cohort		Amyloidosis Cohort		
	n	%	n	%	P-value†
Comorbidity*	689975		1071		
Congestive Heart Failure	3519	0.51%	18	1.68%	<0.001
Arrhythmias	7879	1.14%	23	2.15%	0.018
Valvular Disease	4760	0.69%	12	1.12%	0.309
Pulmonary Circulation Disorders	1725	0.25%	7	0.65%	<0.001
Peripheral Vascular Disease	5188	0.75%	16	1.49%	0.041
Hypertension	14558	2.11%	39	3.64%	<0.001
Paralysis	568	0.08%	3	0.28%	1.000
Other neurological disorders	1832	0.27%	4	0.37%	0.725
Chronic Pulmonary Disease	7927	1.15%	19	1.77%	0.097
Hypothyroidism	5834	0.85%	14	1.31%	0.394
Chronic Kidney Disease	3926	0.57%	20	1.87%	<0.001
Liver Disease	2886	0.42%	10	0.93%	0.003
Peptic Ulcer Disease	529	0.08%	0	0.00%	<0.001
Lymphoma	7947	1.15%	57	5.32%	<0.001
Cancer Met	21189	3.07%	83	7.75%	<0.001
Cancer No Met	97934	14.19%	274	25.58%	<0.001
Rheumatoid Arthritis and Collagen Vascular Disease	4704	0.68%	15	1.40%	0.053
Coagulopathy	67823	9.83%	254	23.72%	<0.001
Fluid and electrolyte disorders	6806	0.99%	25	2.33%	<0.001
Blood loss anemia	1102	0.16%	2	0.19%	1.000
Deficiency anemia	3944	0.57%	16	1.49%	0.003
Alcohol abuse	9939	1.44%	12	1.12%	0.476
Drug abuse	86778	12.58%	104	9.71%	0.036
Psychoses	27454	3.98%	41	3.83%	0.231
Depression	315458	45.72%	457	42.67%	0.010
Obesity	2452	0.36%	5	0.47%	0.613
Smoking	2565	0.37%	3	0.28%	0.860
Osteoporosis	57533	8.34%	111	10.36%	0.069
Diabetes	5957	0.86%	17	1.59%	0.018
Vitamin D Deficiency	139820	20.26%	221	20.63%	0.580
Dementia	5555	0.81%	13	1.21%	0.319

*Comorbidities are analyzed at time of carpal tunnel syndrome diagnosis.
†All p values are for comparisons between the group of interest and the control group; bolding indicates significance of $p < 0.05$.

Results

- Of 689,975 patients with CTS identified, 5,454 (0.76%) were later diagnosed with amyloidosis.
- Most men were aged 60 years or older at the onset of CTS, and most women were between the ages of 40-59 at the onset of CTS
- Comorbidity analysis demonstrated that, compared to the control cohort, the amyloidosis cohort had a five-fold higher incidence of lymphoma, a two-fold higher incidence of cancer, a two-fold higher incidence of pulmonary circulation diseases, a three-fold higher incidence of coagulopathy, and higher incidences of cardiac comorbidities, among others.

Conclusion

This study demonstrates that amongst all patients presenting with CTS, those who are men aged 60 or older, women aged 45-59, or who present with additional comorbidities including lymphoma, pulmonary circulation diseases, coagulopathy, and cardiac comorbidities are more likely to later be diagnosed with amyloidosis.

Presence of these patient demographics may suggest that the CTS symptoms are caused by amyloid protein deposits in the carpal tunnel. This may lead physicians to consider obtaining a biopsy in this population to potentially diagnose a patient's amyloidosis prior to the development of end organ symptoms. Implementation of this strategy offers the opportunity for early diagnosis and intervention of systemic amyloidoses, improving patient health and safety, and reducing economic burden on the healthcare system.

Acknowledgements
This research is the result of collaboration across George Washington University, Johns Hopkins University, and Virginia Commonwealth University through the Orthopedic Research Collaborative