Your Carpal Tunnel Biopsy is Positive for Amyloid. Then what?

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INTRODUCTION: Amyloidosis, an infiltrative disorder characterized by abnormal deposition of misfolded proteins, can present with carpal tunnel syndrome (CTS) as an early, and sometimes initial, clinical manifestation[1,3,7]. Studies have shown that biopsies of tenosynovial tissue obtained during carpal tunnel release are highly sensitive and specific for detecting amyloid deposition and can be performed safely with minimal added procedural time or risk[1,7]. Research indicates that between 10-20% of older patients (men over 50 and women over 60) undergoing carpal tunnel release (CTR) for idiopathic CTS have amyloid deposits identified on tenosynovial biopsy[3,7,10], and subsequent investigations often reveal previously unrecognized cardiac involvement. While current evidence supports incorporating tenosynovial biopsy into the perioperative workflow for carpal tunnel surgery, especially in patients meeting specific risk criteria or presenting with bilateral CTS[4,6,7], there is little known about what happens after patients get their positive amyloid results back. The purpose of this study is to determine how a positive tenosynovial biopsy for amyloid obtained during CTR affects the patient's future medical management.

METHODS: This study was approved by the University of Illinois College of Medicine-Rockford IRB. From July 2024 to June 2025, 355 patients underwent carpal tunnel surgery by one board-certified, fellowship-trained orthopedic surgeon. 222 of those patients (63%) met biopsy inclusion criteria determined by the risk nomogram described in Sood et al. (2021) and underwent tenosynovial biopsy during their carpal tunnel release surgery. 115 of those patients resulted in positive amyloidosis and subsequent typing (52%). Each patient was then instructed to follow up with their primary care provider (PCP), as well as having a letter sent directly to their PCP. We conducted a thorough chart review using the facility's EMR and contacted all 115 patients via phone, with 67 patients responding (52 male, 16 female), who were included in the data analysis. We collected demographics, comorbidities, pre-operative diagnostic EMG study data, post-operative QuickDash scores, and follow-up data from these patients.

RESULTS: Mean age for respondents was 74 years (range 46–90). 94% of patients were non-Hispanic White, and 6% were African American. Common comorbidities included hyperlipidemia (75%), hypertension (71.6%), smoking history (60%), osteoarthritis (52%), and diabetes (28%). Electrodiagnostic studies confirmed CTS in 91%, with 41% also showing cubital tunnel syndrome. CTS severity was 1.5% mild, 19.4% moderate, 64.2% severe, and 7.5% very severe. 69.1% of patients had bilateral symptoms. Biopsy confirmed amyloid in all cases: 64.2% were transthyretin (ATTR), 1.5% light-chain (AL), 10.4% were positive without subtyping, and 23.9% were not typed. Postoperatively, the mean QuickDASH score was 16.05 ± 18.7. Mean follow-up time from date of surgery to date of data collection was 8.71 months (SD=6.21), median was 7.0 months, and the range was 2-35 months. Peer-reviewed studies report that average post-operative QuickDASH scores after carpal tunnel release among all patients are approximately 29.8 at 3 months[12], 18.2 at 6 months[13,14,15,] and 15.9 at 12 months[15]. Following diagnosis, 83.6% patients followed up with their primary care provider, 35.7% of patients' PCPs did not initiate any workup, and 53.7% of our cohort were referred to a specialist. The most common specialist referrals following an amyloidosis diagnosis were to cardiologists (23 patients), hematologists (20 patients), neurologists (5 patients), rheumatologists (2 patients), tertiary hospitals (7 patients), and hepatologists, oncologists, geneticists, and nephrologists each had one patient referred. Six patients were noted as referred with no specific specialist listed, and 16 patients had no specialist referral recorded. Overall, 67.2% underwent additional work-up. The additional tests performed following a positive biopsy included: echocardiography in 23 patients, comprehensive metabolic panel (CMP) in 18 patients, complete blood count (CBC) in 18 patients, nuclear medicine PYP scan in 15 patients, free light chain assay in 14 patients, electrocardiogram (EKG) in 9 patients, lactate dehydrogenase in 7 patients, serum and urine protein electrophoresis (SPEP/UPEP) in 6 patients, abdominal ultrasound in 5 patients, various biopsies in 4 patients, NT-proBNP in 4 patients, troponin in 4 patients, DNA testing/ molecular diagnostics in 4 patients, cardiac MRI in 2 patients, and one patient each underwent MRI of brain, PET scan. Five patients were diagnosed with a new condition- rheumatoid arthritis, macular degeneration, cardiomyopathy, kidney and bladder cancer, with one still in workup for cancer. The patient diagnosed with cardiomyopathy was started on rosuvastatin and carvedilol as a result of the work-up after the positive amyloid biopsy. No patients were started on medications specifically for amyloid. 82% of patients expressed gratitude for the diagnosis by their orthopedic surgeon, suggesting meaningful perceived benefit and improved access to subspecialty care.

DISCUSSION: Our study emphasizes the clinical value of routine tenosynovial biopsy in at-risk patients undergoing carpal tunnel release, highlighting its role in unmasking previously unrecognized amyloidosis. Consistent with prior reports, tenosynovial amyloid deposition was detected in a considerable proportion of surgical patients meeting nomogram-based risk criteria. Importantly, our findings reveal that, despite a high incidence of specialist referrals and further diagnostic work-up among biopsy-positive patients, there remains a substantial gap in the downstream management. This shows the barriers in amyloidosis care pathways, including the need for improved communication between orthopedics, primary care, and subspecialty providers, as well as greater education regarding the clinical implications and management of incidentally discovered amyloidosis. Yet, most patients still valued the diagnosis, reflecting improved awareness and potential increased engagement with the healthcare system. Furthermore, the post-operative QuickDASH scores in our cohort were comparable to or slightly better than reported averages, suggesting that performing a biopsy did not compromise surgical outcomes. However, the absence of new amyloidosis treatment initiation, even in biopsy-positive cases, draws attention to the complexity between identification and actionable intervention. The results highlight the critical need for the development of multidisciplinary care models and standardized post-biopsy protocols to bridge the observed diagnostic–therapeutic gap. Lastly, our report has some important limitations. One such limitation of this preliminary data included, at times, short follow-up timelines after amyloid diagnosis and data collection, preventing some patients from obtaining specialist follow-up before data collection. Other variables include a difference in understanding and reporting of conditions or testing by patients, loss to follow-up, and a small sample size due to being a one-center, one-surgeon study. In general, future research should investigate the barriers to effective downstream management after tenosynovial biopsy amyloid diagnosis and explore strategies to facilitate timely evaluation, risk stratification, and disease-modifying therapy in this high-risk population.

SIGNIFICANCE/CLINICAL RELEVANCE: The percentage of hand surgeons routinely performing biopsies during CTR is not universally established in the literature, yet early detection of amyloidosis is clinically significant because it can facilitate the institution of disease-modifying therapies and specialist follow-up. By demonstrating how a patient's medical management is impacted by a positive amyloid biopsy during routine CTR, more hand surgeons could be inclined to take these critical biopsies, potentially reducing morbidity and mortality associated with amyloidosis[2,7].

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