Prevalence of Amyloid Deposition in Patients Undergoing Surgical Repair of Traumatic Distal Biceps Tendon Ruptures

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Purpose: As many as one-third of patients with heart failure secondary to systemic, wild-type transthyretin amyloidosis have an associated distal biceps tendon (DBT) rupture. Our purpose was to identify the prevalence of amyloid deposition in patients undergoing operative repair of acute traumatic DBT ruptures.

Methods: In this prospective investigation, a consecutive series of patients who underwent repair of an acute traumatic DBT rupture underwent a tendon biopsy to assess for amyloid deposition. All specimens were viewed under gross microscopy by a board-certified pathologist. For initial screening, either Congo red or Thioflavin-T immunohistochemistry analysis was conducted to determine amyloid status. If staining was positive for amyloid deposition using either technique, the tissue sample was sent to an outside facility for specific amyloid protein identification through liquid chromatography–tandem mass spectrometry. Baseline demographics were also recorded for each patient.

Results: A total of 30 patients who underwent biopsy and repair of an acute DBT rupture were included. The mean age was 48 years, and all patients were men. Seven (23%) patients had a history of carpal tunnel syndrome, and 1 (3%) patient had evidence of heart failure at the time of surgery. One (3%) patient had evidence of amyloid deposition in the DBT, which was confirmed using liquid chromatography–tandem mass spectrometry.

Conclusions: Although one-third of patients with heart failure secondary to cardiac amyloidosis have an associated DBT rupture, younger patients with acute traumatic DBT ruptures do not appear to be uniquely at risk for amyloid deposition at the time of DBT repair. Larger registry studies may be necessary to define the risk of developing cardiac amyloidosis years after sustaining an acute DBT rupture.

Type of study/level of evidence: Prognostic IV.

Systemic amyloidosis is a rare condition involving the accumulation of misfolded proteins within tissues that can result in progressive organ failure.1 The condition most predictive of a poor prognosis is cardiac deposition, which is a primary cause of morbidity and mortality because of the development of restrictive cardiomyopathy.2 There are 2 main protein precursors associated with systemic amyloidosis: transthyretin (ATTR) and immunoglobulin light chain.3,4 The 2 common subtypes of ATTR include both mutant and wild-type transthyretin (ATTRwt). Mutant ATTR is inherited, whereas ATTRwt can occur sporadically.5 The mainstay of treatment for systemic amyloidosis is the reduction of protein precursors. This can be achieved through chemotherapy, antimicrobial therapy, or biological therapies, depending on the severity and amyloid subtype.3,4,5 The most difficult ATTR amyloidosis to treat is mutant ATTR, which relies mainly on organ transplantation of the involved systems.5 Despite available therapies, prognosis for affected patients remains poor, with patients often dying within a year of diagnosis.5,6 Delayed or underdiagnosis of systemic amyloidosis may contribute to increased mortality.6

Prior investigations have reported an association between systemic amyloidosis and carpal tunnel syndrome (CTS).7–10 A recent
systematic review reported a 14% prevalence of amyloid within biopsied tenosynovium from the carpal tunnel in 1,753 CTS cases. Furthermore, Sood et al reported that a history of carpal tunnel release (CTR) or trigger digit release was independently associated with an increased risk of developing amyloidosis or heart failure. Because musculoskeletal manifestations typically occur 5–10 years before the onset of cardiovascular symptoms, the use of biopsy during common orthopedic procedures may be an appropriate screening option for systemic amyloidosis.

Within upper-extremity surgery, the association between CTS and amyloidosis is perhaps the most recognized; however, systemic amyloidosis is associated with a variety of musculoskeletal conditions. Authors in previous studies have noted that one-third of patients with ATTRwt had a distal biceps tendon (DBT) rupture, compared with just 3% of patients with other nonamyloid causes of heart failure. In nearly 40% of ATTRwt cases with DBT ruptures, the rupture was spontaneous and asymptomatic. Overall, DBT ruptures occur at a rate of 2.5 per 100,000 people annually, primarily in active, middle-aged men. In traumatic DBT ruptures, this injury is often caused by an eccentric contraction of the biceps tendon, with the elbow in flexion and the forearm in supination. Less commonly, DBT ruptures can occur with more of an attritional mechanism secondary to the progression of partial tears with repetitive microtrauma. Although it appears that spontaneous DBT ruptures occur frequently in elderly patients with heart failure secondary to cardiac amyloidosis, it remains uncertain if amyloid deposition also occurs frequently in cases of acute traumatic DBT ruptures.

The purpose of this investigation was to identify the prevalence of amyloid deposition in patients undergoing operative repair of acute traumatic DBT ruptures. Considering that 33% of patients with ATTRwt had DBT ruptures in prior investigations, we aimed to determine if younger patients with acute traumatic DBT ruptures were at a unique risk for systemic amyloidosis.

Materials and Methods

Institutional review board approval of Geisinger IRB was obtained for this investigation, which started as part of an institutional quality improvement initiative. All patients who sustained an acute traumatic DBT rupture between December 2020 and May 2022 were prospectively included if they underwent DBT repair. All tendon repairs were performed by 1 of 4 surgeons (LCG, AAA, HPO, MP) within our health care system, which includes 2 rural academic trauma centers in the Northeastern United States. A chart review was conducted to collect patient demographic information, including age, sex, race, injury characteristics, and medical comorbidities.

Distal biceps tendon repair was performed using a single incision approach and included repair with an endobutton, suture anchors, and/or interference screw, based on surgeon preference (Fig. 1). Biopsy of the DBT was performed in all cases. After identifying a complete DBT rupture and before placing a suture in the tendon, a biopsy specimen from the distal end of the biceps tendon was placed in a fixative agent (formalin) and sent to the pathology laboratory directly from the operating room. All specimens were viewed under gross microscopy by a board-certified pathologist (Fig. 2). For initial screening, either Congo red (Fig. 3) or Thioflavin-T immunohistochemistry analysis (Fig. 4) was performed to determine amyloid status. If staining was suggestive of amyloid deposition using either technique, the tissue sample was embedded in paraffin and sent to Mayo Clinic Laboratories for further analysis.

Figure 1. Single anterior incision distal biceps tendon repair with a retrieved ruptured tendon.

Figure 2. Hematoxylin and Eosin stain of distal biceps tendon tissue.

Figure 3. Polarized Congo red staining positive for the presence of amyloid.
specific amyloid protein identification through liquid chromatography–tandem mass spectrometry.26 Cases without evidence of amyloid deposition on either Congo red or Thioflavin-T immunohistochemistry analysis were considered “negative” for amyloid. Cases were considered amyloid “positive” only if they had evidence of amyloid with liquid chromatography–tandem mass spectrometry.

An a priori sample size calculation was conducted to ensure adequate precision of this prevalence study. On the basis of the prior literature, the prevalence of amyloid in DBT rupture was set at 33%, with an effect size of 0.08.27 A total of 29 patients were needed to detect a prevalence of 33% at 95% confidence.

**Results**

A total of 30 cases of acute DBT ruptures were included in this study. Demographic data are presented in the Table. The mean age of the included patients was 48 years, and 100% of the patients were men. Carpal tunnel syndrome was present in 7 (23%) of the patients, all of whom were amyloid-negative. Additional associated comorbid conditions are reported in the Table. One (3%) patient had evidence of heart failure at the time of DBT repair and did not have evidence of amyloid deposition in their DBT. No patients had a diagnosis of peripheral neuropathy, spinal stenosis, or a family history of amyloidosis.

One (3%) patient had evidence of amyloid deposition in the DBT, which was confirmed using liquid chromatography–tandem mass spectrometry. This patient was a 61-year-old man with a medical history of obstructive sleep apnea, cholelithiasis, and gastroesophageal reflux disease.

**Discussion**

The prevalence of amyloid deposition found in the DBT of patients undergoing repair after acute traumatic DBT rupture was 3% in our population with an average age of 48 years. Prior investigations have demonstrated a wide range of amyloid positivity in various musculoskeletal tissues.20,27,28 Sueyoshi et al17 noted amyloid deposition in rotator cuff tendon tissue 38% of the time in patients with a mean age of 62 years. They also noted amyloid deposition during CTR and lumbar spinal stenosis procedures at rates of 37% and 53%, respectively.17 Additionally, 10% of patients undergoing CTR were found to have a positive biopsy result for amyloid in a study by Sperry et al,10 which included men aged ≥50 years and women aged ≥60 years with bilateral symptoms. In contrast, in a group of patients undergoing trigger finger release, amyloid deposition was identified at a rate of 2%.28 The rate of amyloid deposition seen in musculoskeletal tissues remains variable and may be associated with age. However, it is clear that patients undergoing both CTR and trigger digit release are at an increased risk of developing amyloidosis and heart failure compared with the risk in controls.28 Although our current investigation noted a 3% prevalence of amyloid deposition in relatively young patients undergoing DBT repair, longer follow-up may be required to assess whether these patients are at an increased risk of later amyloid development, considering that musculoskeletal manifestations may occur 5–10 years before the onset of cardiovascular symptoms.12,13

We investigated the prevalence of amyloid deposition seen specifically in acute traumatic DBT ruptures. This contrasts with the investigation by Geller et al,13 which assessed the rate of DBT rupture in patients with heart failure. They noted that 33% of patients with amyloid cardiomyopathy had a DBT rupture (40% of whom were asymptomatic), compared with just 3% in their non-amyloid control group.1,13 The mean age of patients in their study was 75 years, compared with our population, in which the mean age was 48 years. Of note, the DBT rupture in the spontaneous, atrumatic population occurred roughly 5 years before the diagnosis of systemic amyloidosis. Considering the rate of DBT rupture noted by Geller et al13 in their population with heart failure, we designed the present investigation to determine whether younger patients with traumatic DBT ruptures are uniquely at risk for amyloid deposition.13 In the context of these prior findings and given that conventional CTS amyloid screening criteria (men aged ≥50 years and women aged ≥60 years with bilateral symptoms) identify amyloid in approximately 10% of cases, we hypothesized that our observed rate would be higher. Our 3% prevalence was lower than

**Table**

| Demographics | Bicep Tendon Rupture N = 30 |
|--------------|----------------------------|
| Age (y), mean (SD) | 48 (10) |
| Male, n (%) | 30 (100) |
| Race, White n (%) | 29 (97) |
| BMI, mean (SD) | 35 (78) |
| Tobacco use, n (%) | 5 (17) |
| Alcohol use, n (%) | 19 (63) |
| Married, n (%) | 19 (63) |
| Employed, n (%) | 25 (83) |
| Laterality, right n (%) | 16 (53) |
| ASA |  |
| 1–2 | 18 (60) |
| 3–4 | 12 (40) |
| Heart failure, n (%) | 1 (3) |
| Aortic stenosis, n (%) | 0 (0) |
| Diabetes, n (%) | 4 (27) |
| Dialysis, n (%) | 0 (0) |
| Statin use, n (%) | 7 (23) |
| Anabolic steroid use, n (%) | 1 (3) |
| Testosterone replacement, n (%) | 1 (3) |
| Carpal tunnel diagnosis, n (%) | 7 (23) |
| Carpal tunnel release, n (%) | 2 (7) |
| Trigger digit diagnosis, n (%) | 0 (0) |
| Trigger digit release, n (%) | 0 (0) |

ASA, American Society of Anesthesiologists; BMI, body mass index.

Figure 4. Thioflavin-T staining A negative and B positive for the presence of amyloid (the asterisk indicates positive area).
expected, and this is likely attributable to the relatively lower age of the patients in our series. However, given the younger mean age seen in this population, it remains uncertain whether they will develop systemic amyloidosis at a higher-than-expected rate as they age.

If patients with systemic amyloidosis are identified before the onset of cardiac manifestations, they may be successfully treated with an organ transplant or stem cell transplant, depending on the subtype.\textsuperscript{6,9,10} Hand and upper-extremity surgeons may be able to play a critical role in the identification of these patients because an early referral to cardiology services may alter the natural history of their systemic amyloidosis. However, given the low prevalence observed in our series, there may be limited clinical utility for routine tendon biopsy during DBT repair in acute traumatic cases.

This investigation has several limitations that should be considered. In addition to the relatively small sample size, one notable limitation is the potential for sampling bias because all the included patients elected to undergo repair (as opposed to nonsurgical treatment). Additionally, without longer-term follow-up, it remains uncertain whether these patients are at risk of developing systemic amyloidosis in the future. Patients in our series were younger than the typical patient population expressing symptoms of amyloidosis, and all patients were men and Caucasian. In addition, these data are from a single rural health care system with a heterogeneous patient population, and it remains uncertain if our results are generalizable to other populations.

We report a 3\% prevalence of amyloid deposition in the DBT in patients undergoing repair of an acute traumatic DBT rupture. Although one-third of patients with heart failure secondary to cardiac amyloidosis have an associated DBT rupture, younger patients with acute traumatic DBT ruptures do not appear to be uniquely at risk for amyloid deposition at the time of surgical intervention. Longer-term follow-up and larger registry studies may be necessary to define the risk of developing cardiac amyloidosis years after sustaining an acute DBT rupture.

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