

Carpal Tunnel Syndrome: (and Other Orthopaedic Conditions)

A "RED FLAG" for Amyloid Cardiomyopathy

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Patients with Amyloid Cardiomyopathy

- >50% Have CTS
- Spinal Stenosis
- Peripheral Neuropathy
- Distal Biceps Rupture
- Trigger Finger
- Rotator Cuff Tear
- Family History (A-Fib, CHF, Amyloid)

Historic Bibliography...

TABLE 1. Selected Pathology Studies That Identified Amyloid in Carpal Tunnel Biopsy Specimens

Year Published	Type of Study	Patients (n)	Amyloid-Positive Patients (n)	Amyloid-Positive* (%)	Source of Study Samples (Time Period)	Reference
1965	Retrospective (CTS)	177	12	6.8	Mayo Clinic, U.S. (1930–1960)	Yamaguchi et al ³⁴
1974	Retrospective (CTS)	87	2	2.3	Duke University, U.S. (1960–1969)	Bastian ¹⁷
1987	Retrospective (CTS)	45	2	4.4	North Staffordshire Medical Centre, U.K.	Neal et al ³⁵
1987	Retrospective (CTS)	108	23 (severe in 5)	21.3 (severe in 4.6)	University of Mainz, Germany (1975–1986)	Stein et al ¹⁶
1989	Retrospective (CTS) with follow-up	1500	152	10.1	Mayo Clinic, U.S. (1968–1977)	Kyle et al ³⁶
1996	Retrospective (CTS) with follow-up	108	10 (severe in 2)	9.3 (severe in 1.9)	Toranomon Hospital, Japan	Nakamichi and Tachibana ³⁷
2001	Retrospective (trigger finger)	47	11	23.4	Nuffield Orthopaedic Centre, U.K.	Cordiner-Lawrie et al ²⁵
2011	Prospective (CTS)	100	34 (severe in 15)	34 (severe in 15)	Nagano Prefecture, Japan (2008–2010)	Sekijima et al ³⁸
2017	Prospective (CTS)	147	29	19.7	Hospital Universitario de León, Spain (2006–2007)	Fernandez Fuertes et al ³⁹
2018	Retrospective (CTS)	4990	582	11.7	Amyloid Registry Kiel, Germany (2010–2018)	Hahn et al ³³
2018	Prospective (CTS) with follow-up	98	10	10.2 [†]	Cleveland Clinic, U.S. (2016–2017)	Sperry et al ²

*Note that the proportion of patients with CTS found to have amyloid deposits in these studies varies widely, from 2.3% to 34%. It is important to note the many differences among these studies, including the patient populations studied and whether or how the extent of amyloid deposition was graded. In studies that further categorized infiltration in amyloid-positive biopsies as severe, the proportion of patients with substantial amounts of amyloid decreased to 1.9% to 15%.

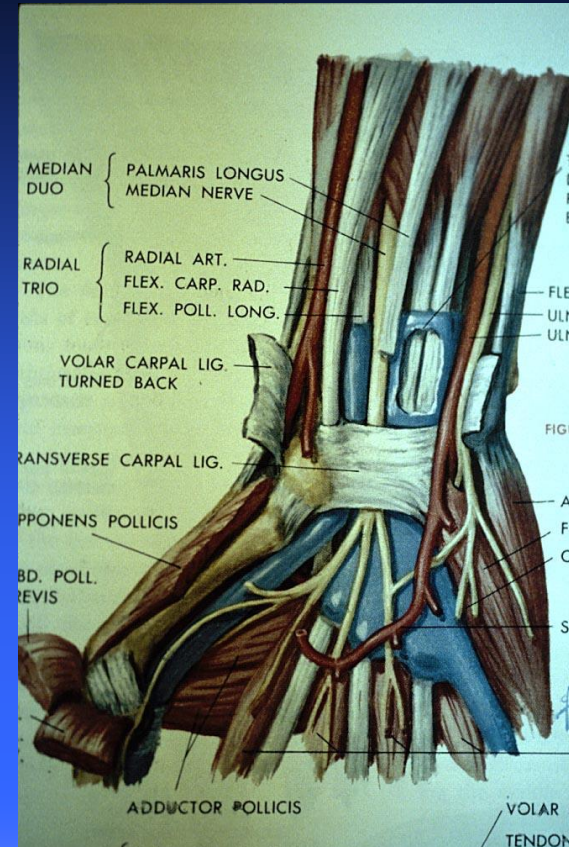
†Twelve percent of patients with bilateral carpal tunnel symptoms or previous contralateral release surgery.

Phone Call...

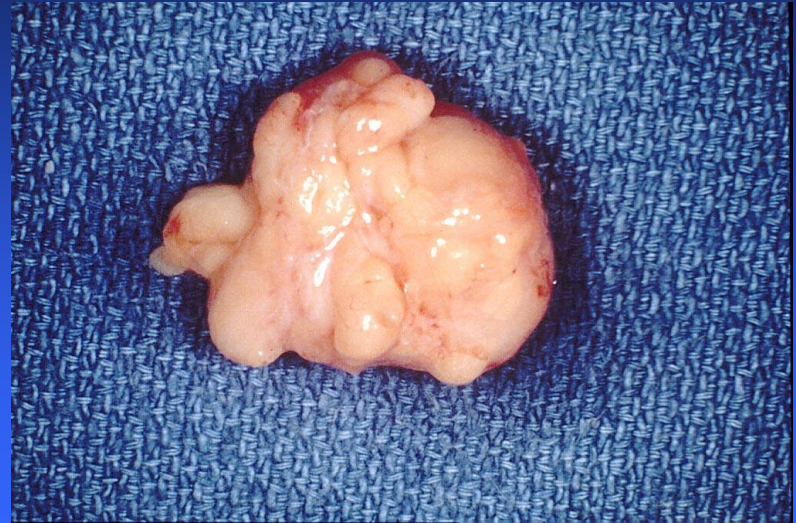
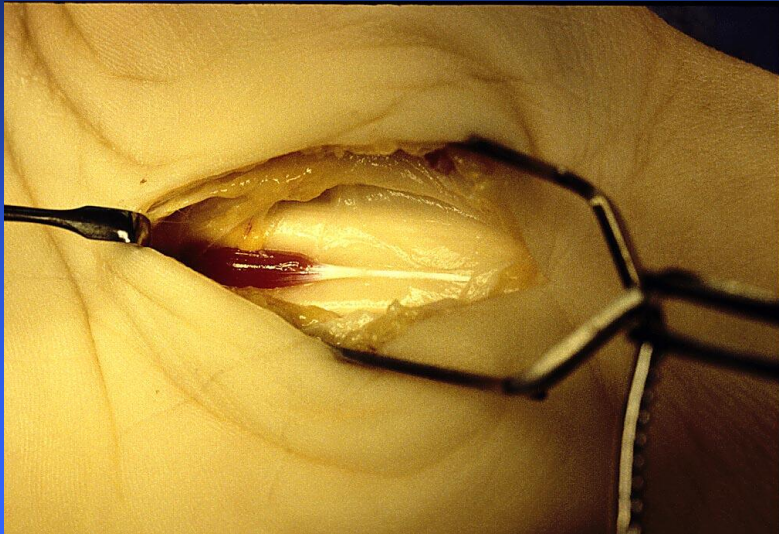
- “Can We Collaborate...”
- Set Up a **TEAM**...
- Set Up a Protocol / IRB Approval
- Open Lines of Communication
- Meet Regularly (F-2-F / Conf. Call)
- **Hand Surgeons**
- **Cardiologists**
- **Pathologists**
- **PAs, RNs, OR Staff**

Advantages of Open Surgery vs. Endoscopic

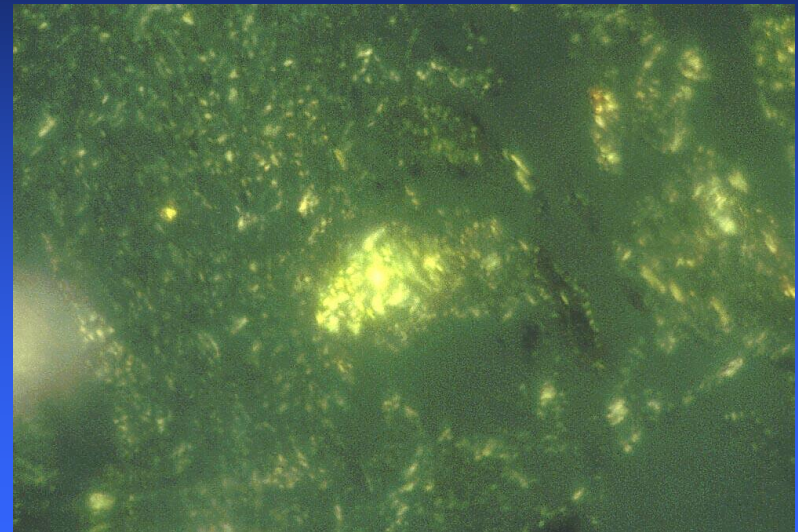
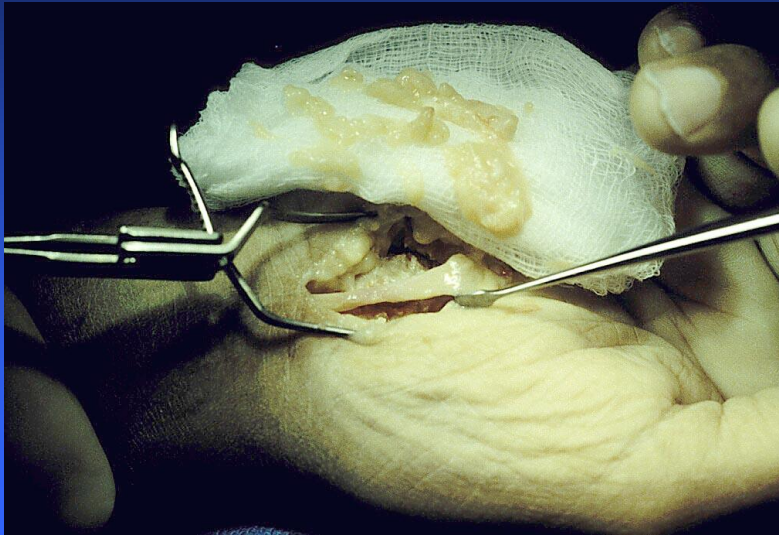
- Visualization of median nerve and its branches
- Ability to release neural adhesions
- Visualization of **all** canal contents and pathology



Hidden Pathology....

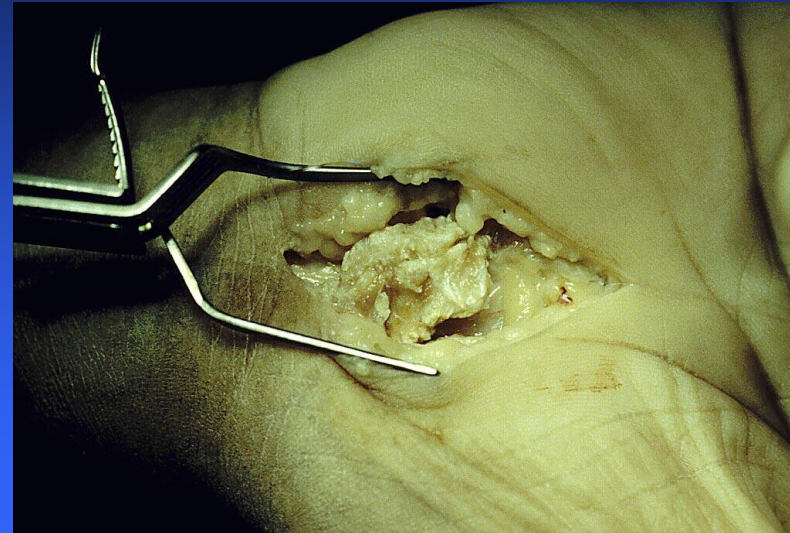


Gout / Sarcoid / Amyloid TenoSynovium



Z-Plasty Repair of Transverse Carpal Ligament

- Reestablishes retinacular function
- Restores grip strength
- Protects nerve
- Early Recovery
- Similar to Endoscopic



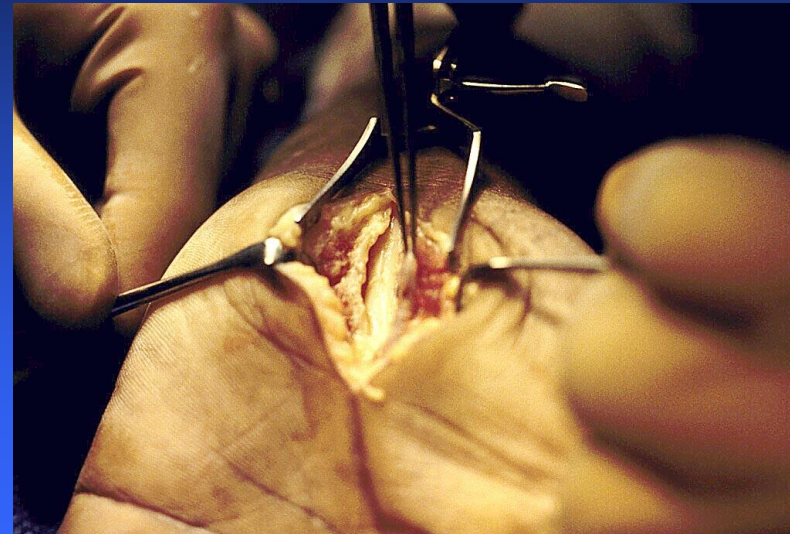
DATA...

Primary Prospective Study

120 Patients:

Open Release 64

Z-Plasty 56

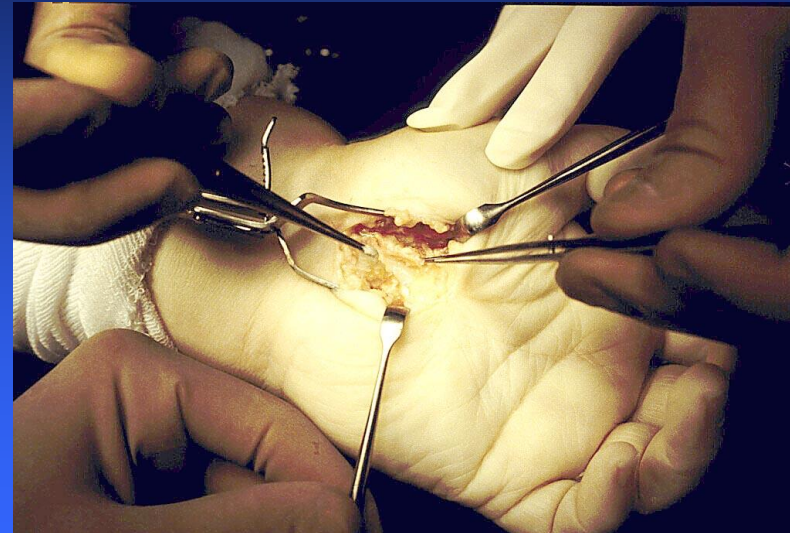


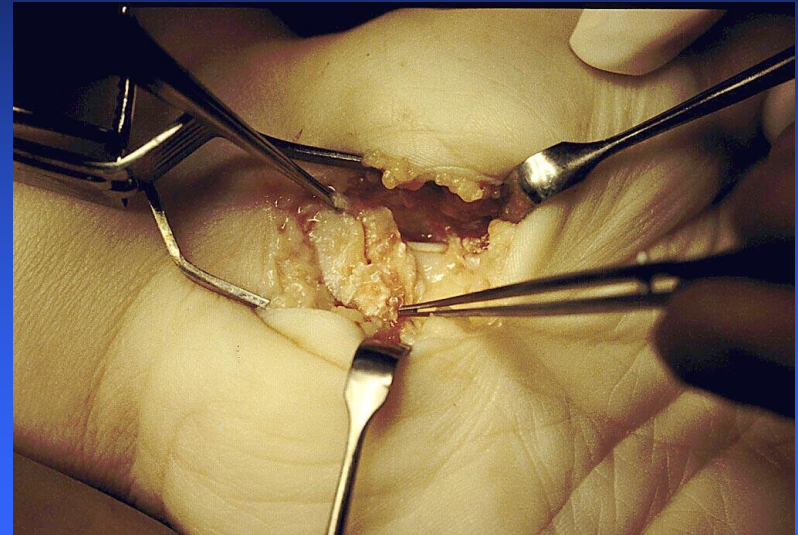
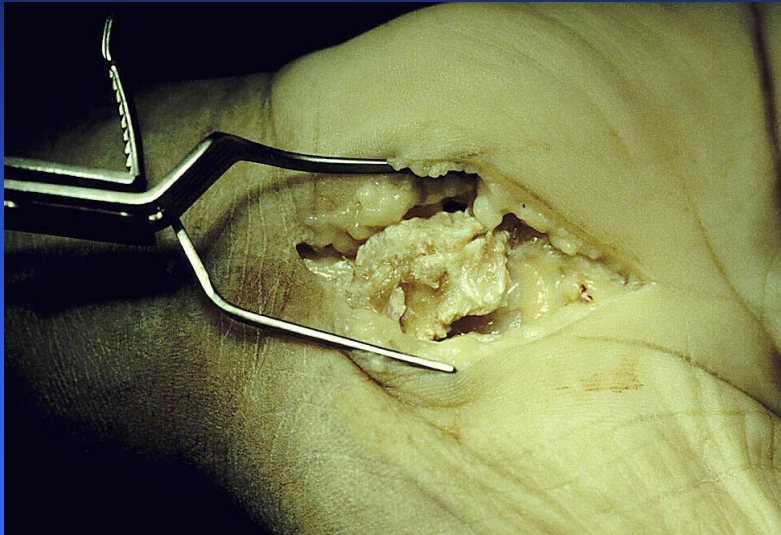
Surgical Technique - Z-Plasty

**Rotation & Secure
Approximation of
Flaps**

**Ensure Relaxed/but
Complete Coverage
of Nerve
in Palm**

Skin Closure





Return to Work/Function

	BWC	Non BWC
Z-plasty	24 days (7-62)	9 days (1-28)
Open Release	36 days (7-96)	16 days (1-37)

Results

	<u>1</u> <u>wk</u>	<u>3</u> <u>wks</u>	<u>6</u> <u>wks</u>	<u>12</u> <u>wks</u>	<u>6</u> <u>mnths</u>	<u>12</u> <u>mnths</u>
<u>Pre-op Symptoms</u>						
Open Release	81%	91%	94%	94%	94%	94%
Z-Plasty	79%	91%	93%	93%	93%	93%
<u>“Pillar Pain” (0-10)</u>						
Open Release	5	4	2	1	0	0
Z-Plasty	3	1	1	0	0	0
<u>Grip Strength (% Contra.)</u>						
Open Release	-	48%	58%	63%	84%	86%
Z-Plasty	-	64%	72%	81%	88%	88%

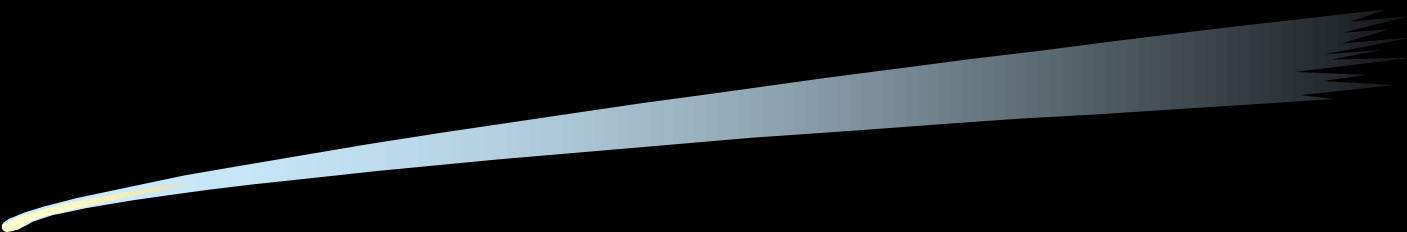
Note: No change at > 2 Year follow-up

18 years...>1500 Surgeries

- Nerve Injury..... 0
- Vascular Injury..... 0
- Tendon Injury..... 0
- RSD / CRPS (Mild)..... 2
- Sarcoidosis..... 3
- Multiple Myeloma..... 4
- Gout..... 6
- Lipoma..... 3
- Aberrant Muscle..... 5

Amyloidosis and Carpal Tunnel Syndrome

- ATTR patients seem to develop CTS 5-15 years prior to cardiac manifestations
- Once cardiac involvement is diagnosed, the disease is typically quite advanced with a median untreated survival of **2-4 years for ATTR** and **6 months for AL**
- Prior studies have demonstrated that amyloid deposition may be found on biopsy specimens at the time of CTR for 'Idiopathic' CTS

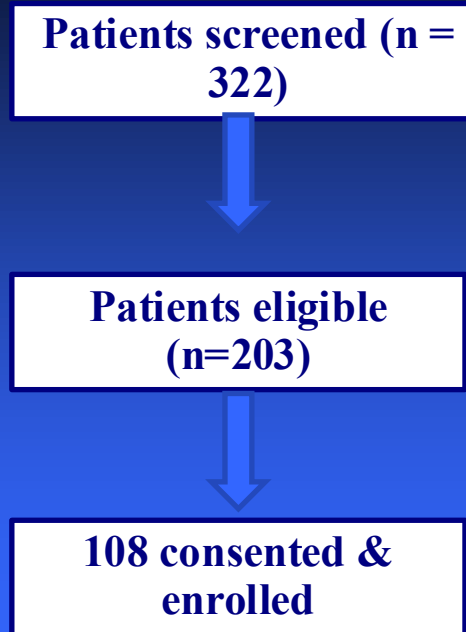


Hypotheses

1. A significant amount of older patients undergoing surgery for 'idiopathic' CTS may be diagnosed with amyloidosis through tenosynovial biopsy
2. In these patients, early detection of amyloid cardiomyopathy using advanced cardiac imaging techniques may be possible

Methods

- Prospective, longitudinal study
- Screened consecutive patients (from May 2016 – May 2017) undergoing carpal tunnel release by participating surgeons in the Cleveland Clinic Department of Orthopaedic Surgery
- Included males ≥ 50 years and females ≥ 60 years
- Excluded patients with known diagnosis of amyloidosis and rheumatoid arthritis

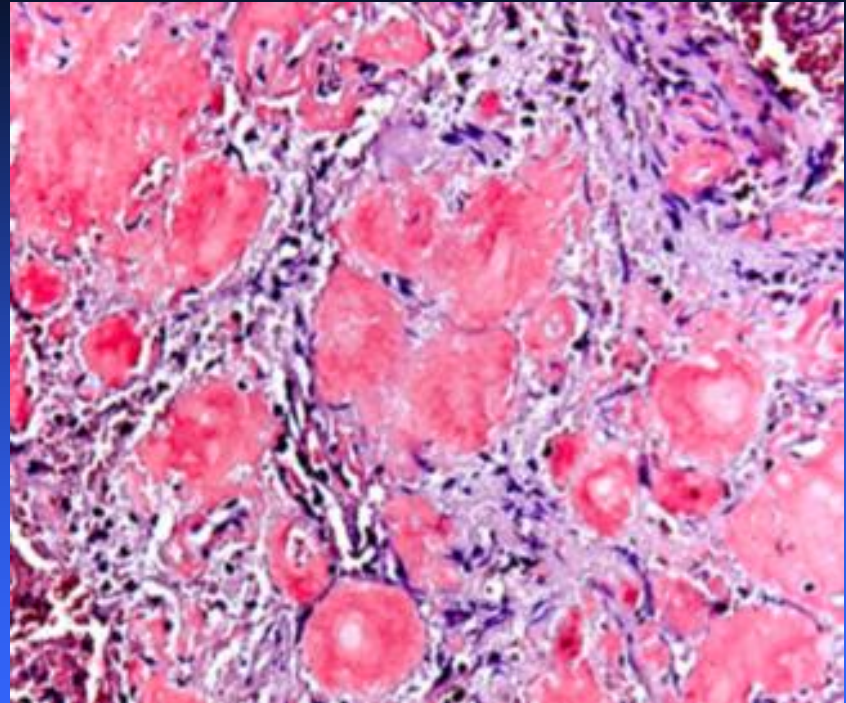


119 excluded at screening:
a) Age: M>50 yrs; F>60 yrs (n=101)
b) Other exclusion criteria (n=18)

95 excluded during consenting:
a) Declined to participate (n=57)
b) Logistic issues (n=16)
c) Unreachable (n=22)

Methods

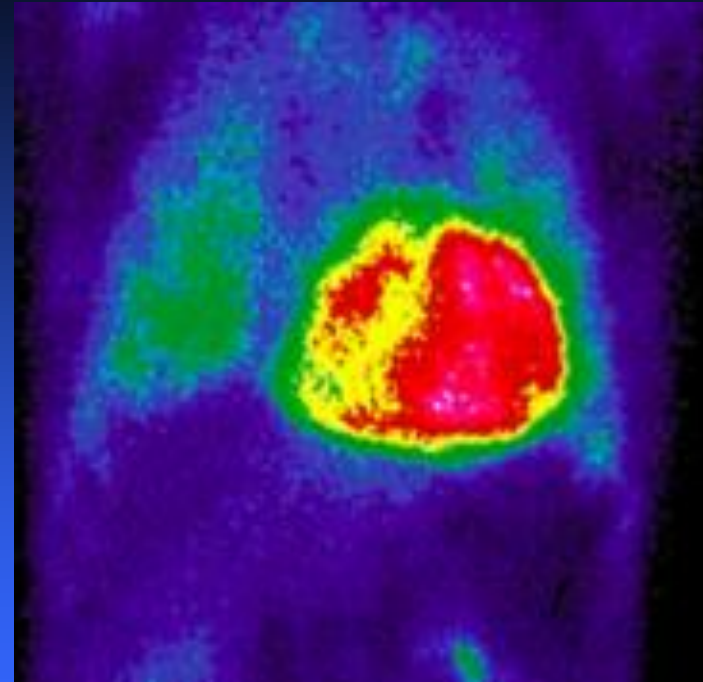
- Tenosynovial biopsy during carpal tunnel release
- Congo-red staining
 - Detects amyloid deposits



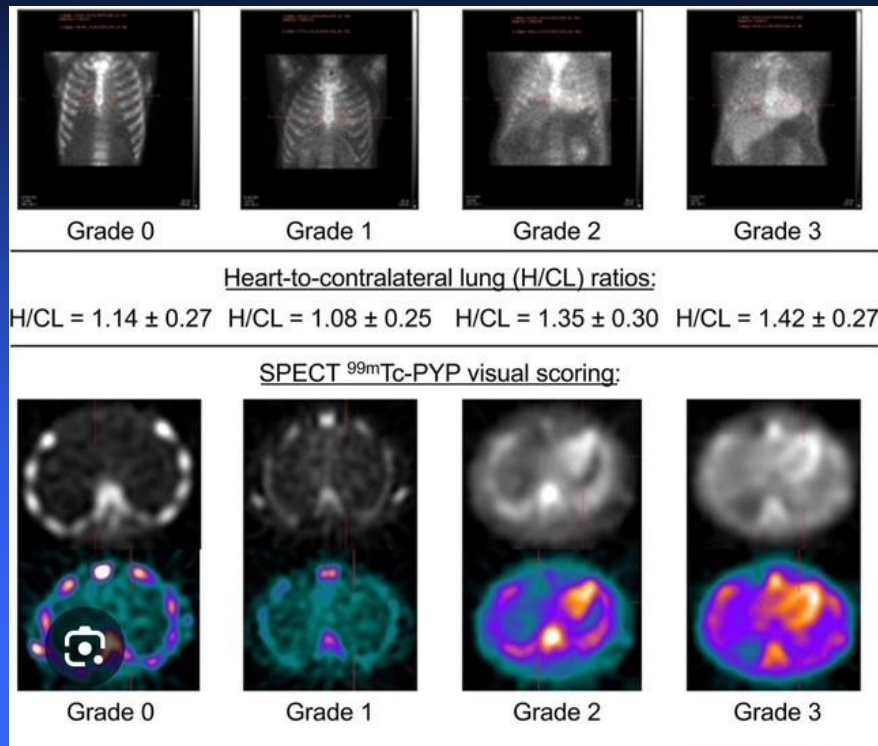
Methods

If positive for amyloid

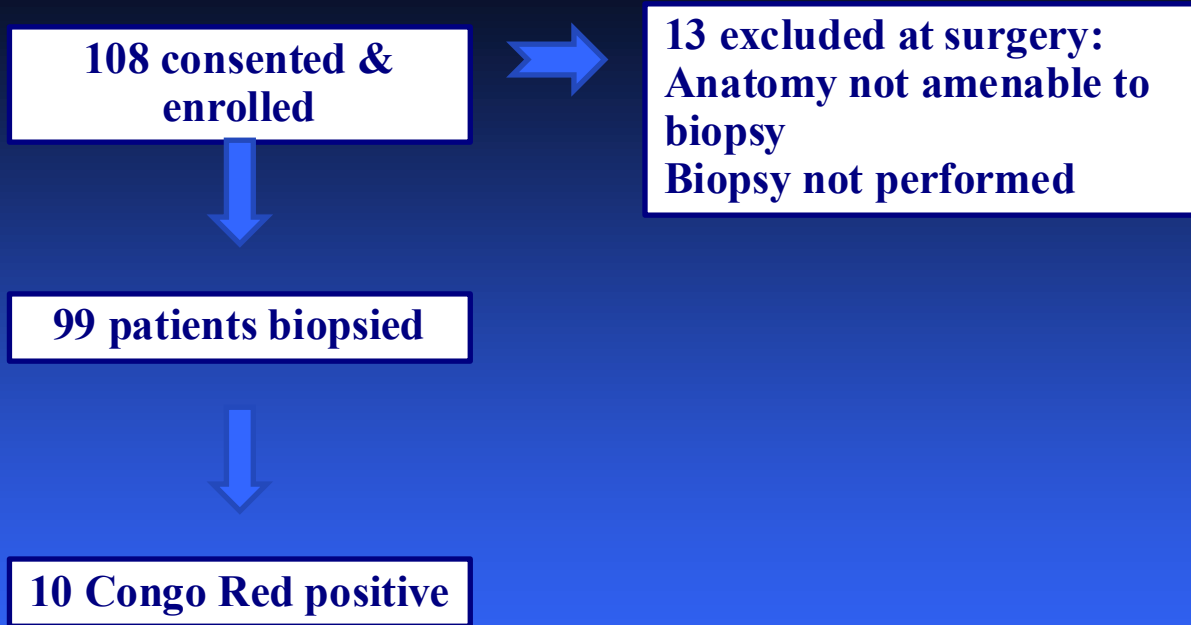
- Further tissue-sample testing to determine amyloid subtype
 - Mass spectrometry
 - Immunohistochemistry
- Cardiology workup:
 - Physical examination
 - Laboratory studies
 - EKG
 - Echocardiography with strain imaging
 - ^{99m}-technetium pyrophosphate nuclear scintigraphy



Amyloid-Specific Imaging

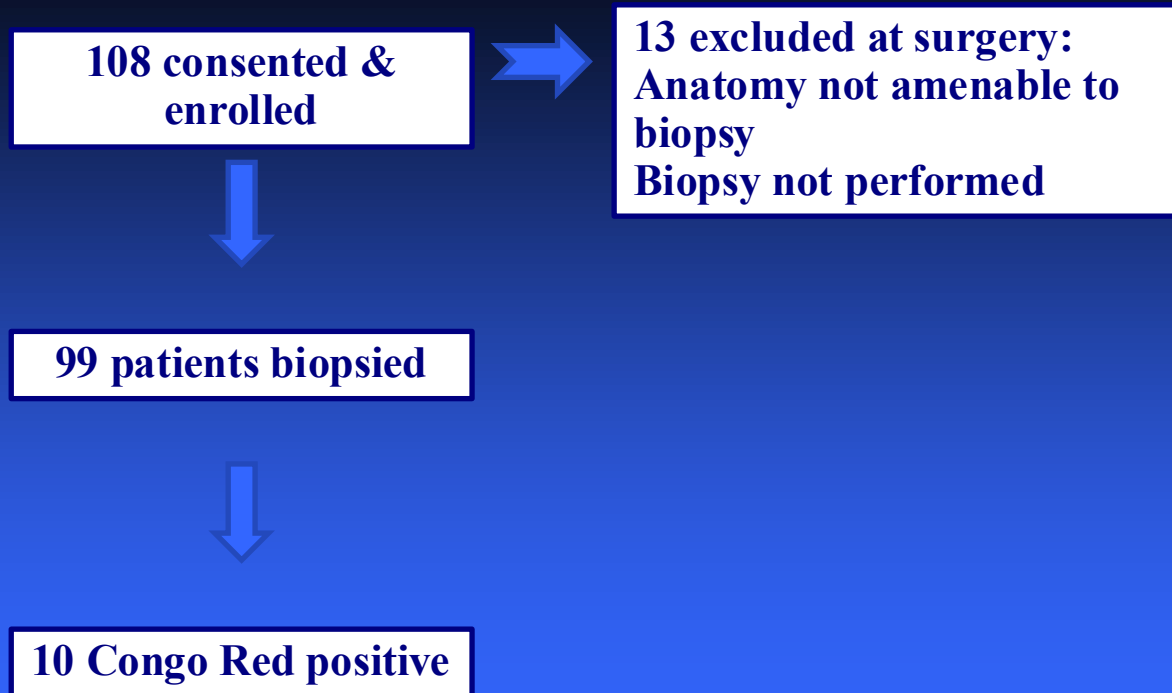


Results

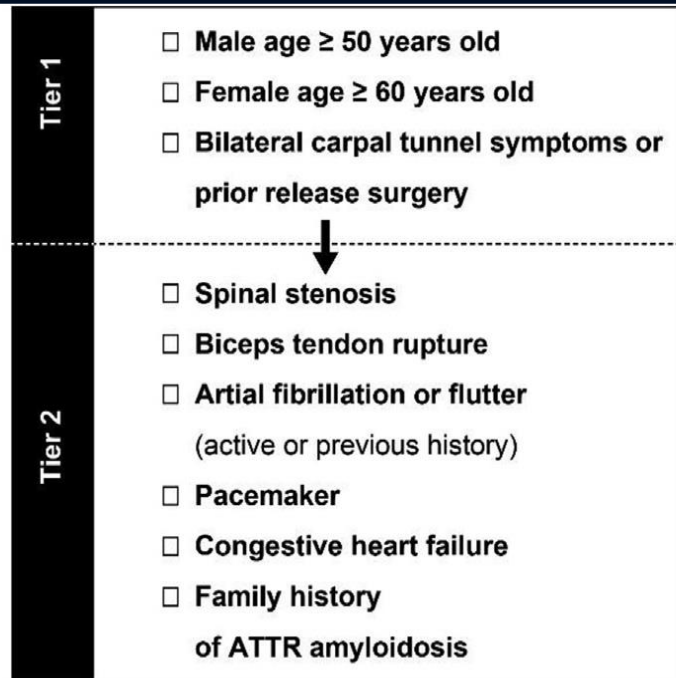


Results Pilot Study...

- 10% (10/99) prevalence of amyloidosis
 - 8 ATTR subtype
 - 2 AL subtype
- 2 found to have cardiac involvement, upon further workup
- All amyloid + patients had bilateral CTS



Also**Increasing Levels of Positivity with Associated Ortho Diagnoses / History



- Spinal Stenosis
- Trigger Finger
- Biceps Rupture
- Rotator Cuff Tear
- Achilles Rupture
- Recurrent CTS Disease

TWO characteristics from Tier 1
OR
ONE characteristic from Tier 1 *PLUS* any ONE from Tier 2

↓
Tenosynovial and/or TCL tissue biopsy
with Congo red (or Thioflavin-S) staining

****Amyloid Typing****
(mass spectrometry)

Amyloid (+)

Referral to
amyloid expert

Conclusions

- Hand surgeons should be aware of the association between carpal tunnel syndrome and amyloidosis
- Tenosynovial biopsy at the time of CTR is a low risk procedure that may lead to early diagnosis of amyloidosis, thereby allowing for timely intervention in this life-threatening disease
- Men ≥ 50 and women ≥ 60 with idiopathic carpal tunnel syndrome (particularly with bilateral disease) should be considered for screening for amyloidosis with tenosynovial biopsy and Congo-red staining

2023 CTS Updated Data CCF...

- 1100 Patients Studied
- 159 Positive for Amyloid...!!!
- Need DATA for All Other
Ortho Associations...!!!

Think About It...!!!

Take a Careful History...!!!

Patients are Grateful...!!!

We Can Save Their Lives...!!!

2 minutes / 0 Complications / \$25

14.45%

CCF 2026 Latest Update

Tenosynovial Biopsies at CTS

Total Biopsies = Aprox. 3000

512 Congo Red+ = 17%

266 TTR

215 untyped

25 AL

5 AL & TTR

191 PYP*

126 PYP

10 cardiac testing

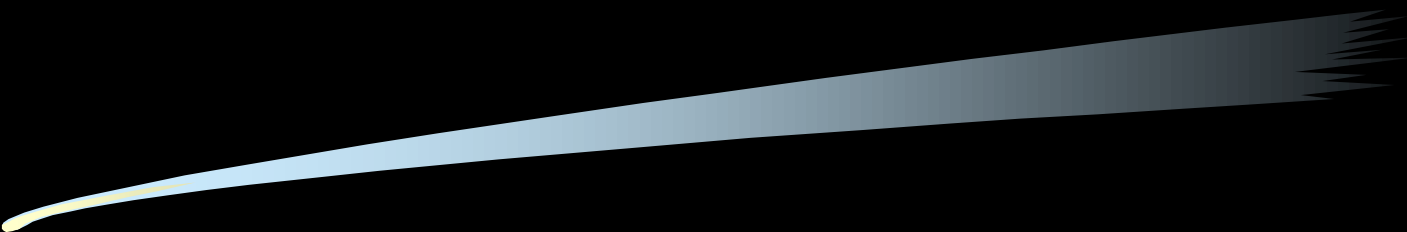
4 cardiac testing

$39/191 = 20\%$

$17/126 = 13\%$

$1/10 = 10\%$

$1/4 = 25\%$



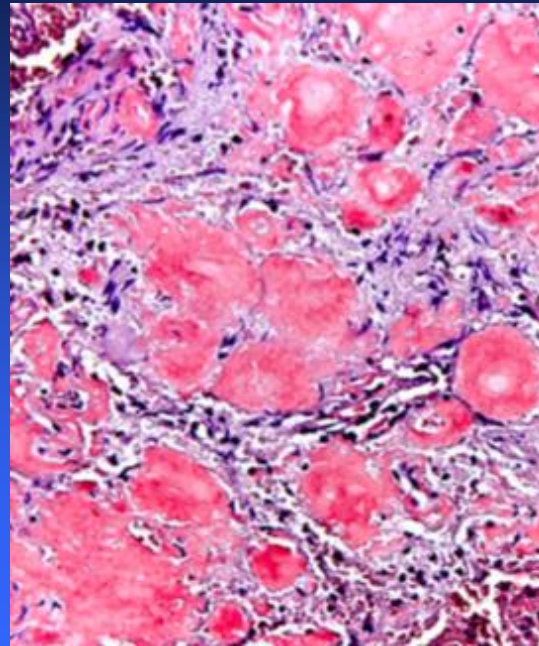
New Horizons...

- Emerging Medications ...Arrest Deposition / Disease
- Newly Recognized Associations:
- Spinal Stenosis
- Tendinopathies (Biceps, RCT, Achilles, Trigger Finger)
- Peripheral Neuropathy
- **Endoscopic CTS Biopsy Techniques
(Grandizio, et. al.... JHS, 2024)

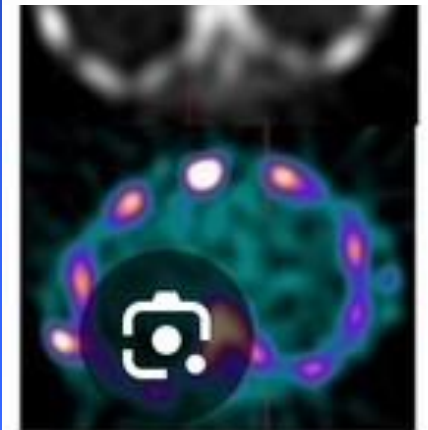
Case:

75 Y/O Healthy Male Surgeon...

- Mild Bilat CTS
- Intermittent Trigger Finger
- Hx. Rupture Achilles
- RCT & Biceps Rupture
- CTArthropathy → RTSA
- Pre-op W/U: AFIB
- FH: + AFib / CHF / RTC
- NO Cardiac Sx.
- Biceps, Rot Cuff, Labrum
+++Amyloid...



Grade 0



Grade 0

But...It's "Yours Truly...
So, Now It's More Personal...!!!
Monitor... Surveillance...
Live On...

Surgeons, PCPs, Patients...
Consider, Biopsy, Diagnose, Treat

- Wake Up...!!! Carpe Diem...!!!



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Every life deserves world class care.