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Amyloidosis Screening by Biopsy During Carpal Tunnel Release: A Systematic Review and Meta-analysis

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Background: Cardiac amyloidosis (CA) is an underdiagnosed cause of heart failure with newly available effective therapies. Carpal tunnel syndrome is a common early manifestation of amyloidosis, and tissue obtained during carpal tunnel release (CTR) can be screened for amyloid, allowing for early CA diagnosis and treatment. However, neither screening criteria nor diagnostic yield are well defined. We estimated the prevalence of amyloid within the tenosynovium or transverse carpal ligament and occult CA among patients undergoing screening biopsy during CTR based on the results of published studies.

Methods: We conducted a systematic review and meta-analysis of studies that analyzed screening biopsies obtained at the time of CTR for the presence of amyloid.

Results: Of 21 articles meeting inclusion criteria, 14 included biopsies from a general population undergoing CTR, 5 reported biopsies from a prescreened population at elevated risk for amyloidosis undergoing CTR, and 2 included patients undergoing CTR with suspected amyloidosis. The pooled prevalence of amyloid within the tenosynovium/transverse carpal ligament was 11% (95% confidence interval: 5%–18%) in American and European studies without prescreening, 20% (95% confidence interval: 13%–29%) in studies of screened patients, and 88%–100% in studies of patients suspected of having amyloidosis preoperatively. Overall, 5%–20% of patients with amyloid-positive biopsies who underwent cardiac screening were eventually diagnosed with CA, of whom 33% were started on transthyretin tetramer stabilizers.

Conclusions: Biopsies for amyloid during CTR demonstrate a high rate of positivity among at-risk populations and an opportunity for early detection of occult CA. Future studies should further refine diagnostic criteria to optimize cost-effectiveness of widespread screening. *(Plast Reconstr Surg Glob Open 2025;13:e6816; doi: 10.1097/GOX.0000000000006816; Published online 28 May 2025.)*

INTRODUCTION

Amyloidosis is defined by extracellular deposition of misfolded precursor proteins.[1] There are more than 30 subtypes with manifestations varying by the pathological protein and organs affected.[1] The most common subtypes include AL and ATTR amyloidosis (Table 1), whose earliest clinical manifestation is often carpal tunnel syndrome (CTS).[6] This pathology likely results from a combination of compression and microvascular obliteration causing ischemia,[7] and its prevalence varies by amyloid subtype (Table 1). Amyloid-associated CTS generally precedes the more serious manifestations of the disease, including cardiac amyloidosis (CA), often by several years.[6,8] Until recently, this observation was not of great clinical utility due to a lack of effective interventions. Newly available treatments can slow disease progression, but their benefit relies on early diagnosis, and recent data indicate that amyloidosis remains drastically underdiagnosed.[9,10] For

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instance, among patients without known amyloidosis, amyloid was detected in the myocardium of 12% of older patients requiring admission for diastolic heart failure,[11] and up to 85% of a general population of patients older than 85 years.[12]

Modern diagnosis of CA is now typically established by technetium pyrophosphate scintigraphy (PYP scan) and extracardiac tissue biopsy demonstrating amyloid deposition (including tissue obtained during carpal tunnel release [CTR]).[1] In general, tissue diagnosis is required in most countries for insurance coverage of medical therapy, as the treatments are costly.[2,13,14] Amyloidosis detection through screening biopsy of the transverse carpal ligament (TCL) or tenosynovium, which can be performed at the time of CTR with minimal added procedural time or risk, provides an opportunity for earlier diagnosis and initiation of medical therapy to reduce morbidity and mortality.[9,15–18] Recent investigations have attempted to risk-stratify patients undergoing CTR to identify patients with a high likelihood of amyloidosis to maximize the yield of screening programs,[3,15,16,19–21] and multiple algorithms have been proposed to guide patient selection for biopsy.[5,21] However, there is no consensus regarding which patients should undergo a screening biopsy during CTR. We performed a systematic review of the literature and meta-analysis to assess the criteria used for screening and the likelihood of a positive screening biopsy in different populations.

Takeaways

Question: What is the prevalence of amyloid within the tenosynovium or transverse carpal ligament and occult cardiac amyloidosis among patients undergoing screening biopsy during carpal tunnel release?

Findings: This systematic review and meta-analysis found that the pooled prevalence of amyloid was 11% in American and European studies without prescreening, versus 20% in studies of screened patients.

Meaning: The use of clinical criteria to identify high-risk patients increases the yield of biopsy during carpal tunnel release for the detection of amyloid, and screening algorithms should, therefore, be applied to determine the necessity for intraoperative screening biopsy.

MATERIALS AND METHODS

A comprehensive search of PubMed, Ovid, and Embase was conducted according to preferred reporting items for systemic reviews and meta-analyses guidelines[22] for complete articles published through August 2023 for studies investigating the detection of amyloid via biopsy in patients undergoing CTR. Search terms were "carpal tunnel," "carpal tunnel syndrome," "carpal tunnel release," "amyloid," "amyloidosis," "screening," "biopsy," "transverse carpal ligament," and "tenosynovium" and the medical subject heading/EMTREE headings "Amyloidosis," "Amyloid," "Decompression, Surgical," "Nerve Compression Syndromes," "Carpal Tunnel Syndrome," and "Biopsy." Abstracts, review articles, meta-analyses, case reports, and articles in languages other than English were excluded. The resulting 349 unique articles were individually reviewed by 2 separate reviewers. Studies that conducted biopsy of any tissue during carpal tunnel surgery that was investigated for amyloid deposition were included. Discrepancies between reviewers were reconciled with discussion.

Meta-analysis was performed using a random-effect model to pool the Freeman-Tukey transformed proportions prevalence of positive biopsy and to obtain the related 95% confidence intervals (CIs). Statistical analysis was performed using the statistical software Stata 18.0 (StataCorp LLC, College Station, TX).

RESULTS

Of 860 records identified and after the exclusion of nonjournal articles and duplicates, 334 abstracts were screened for relevance. Of those, 47 were retrieved and

Table 1. Overview of Most Common Amyloidosis Subtypes Frequently Affecting the Myocardium

	AL	ATTRm	ATTRwt
Pathological protein	Immunoglobulin light chain	Transthyretin	Transthyretin
Hereditary/acquired	Acquired	Hereditary	Acquired
Commonly affected organ systems	ANS, heart, kidneys, liver, MSK, PNS	ANS, CNS, eye, heart, MSK, PNS	ANS, heart, PNS, MSK
Percent of patients who develop CTS	30%[2]	10%–29%[3]	33%–68%[2,4]
Screening methodology	Biopsy TCL or tenosynovium, place in formalin, send to Congo red stain, mass spectrometry for confirmation and subtyping	Biopsy TCL or tenosynovium, place in formalin, send to Congo red stain, mass spectrometry for confirmation and subtyping	Biopsy TCL or tenosynovium, place in formalin, send to Congo red stain, mass spectrometry for confirmation and subtyping
Cardiac involvement?	Very common[5]	Variable depending on mutation[5]	Very common[5]
Will patients benefit from early diagnosis via screening biopsy?	Yes	Yes	Yes
Possible medical therapies	Bortezomib, dexamethasone, cyclophosphamide, bone marrow transplant	Tetramer stabilizers (tafamidis, diflunisal), transthyretin synthesis inhibitors (patisiran, inotersen), liver transplant	Tetramer stabilizers (tafamidis, diflunisal)

ANS, autonomic nervous system; CNS, central nervous system; MSK, musculoskeletal system; PNS, peripheral nervous system.

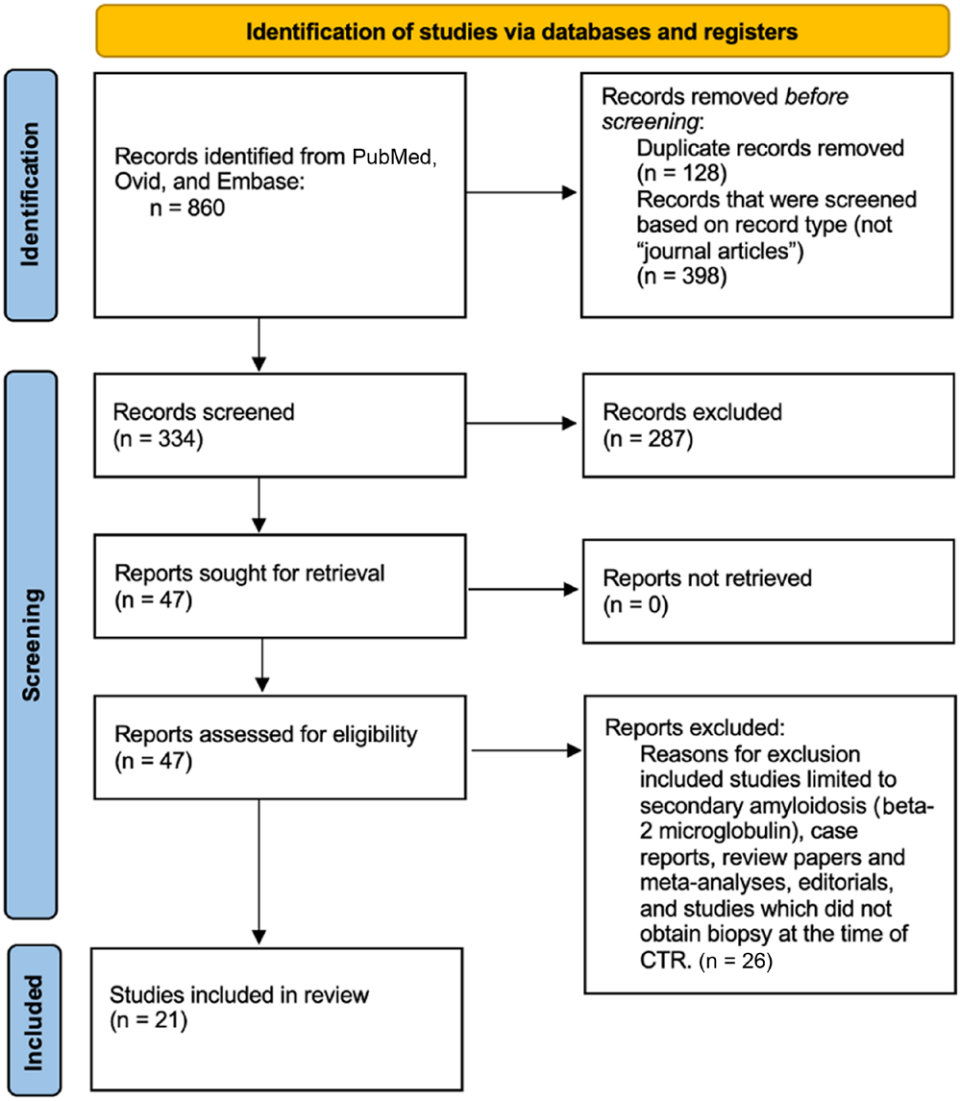

Fig. 1. Search strategy based on PRISMA guidelines. PRISMA, preferred reporting items for systemic reviews and meta-analyses.

assessed for review in full. Twenty-one original research articles met the inclusion criteria, with biopsy of the TCL or tenosynovium during CTR to screen for the presence of amyloid, comprising a total of 4611 wrists from 4482 patients (Fig. 1, Tables 2 and 3). For articles that did not distinguish between the number of patients and the number of wrists, it was assumed that each wrist represented a distinct patient.

Biopsy Technique

Biopsies were taken from the TCL (3 studies, 14%), tenosynovium (13 studies, 62%), either the TCL or tenosynovium (2 studies, 10%), or both the TCL and the tenosynovium (3 studies, 14%). Although most studies did not comment on the amount of tissue obtained, those that did specified a minimum of 0.3 cm^2 of tissue from the TCL or 0.5 cm^2 of tissue from the tenosynovium. Two studies compared biopsies from the TCL and the tenosynovium and found comparable prevalence of amyloid deposition between the 2 tissue types.[16,28,35,36] All studies that described their amyloid screening technique used immediate formalin fixation, paraffin embedding, and Congo red staining, with apple-green birefringence indicating the presence of amyloid. Four studies used further immunohistochemical staining to confirm and subtype the amyloid deposition found on Congo red stain,[17,18,31,32] and 5 studies used mass spectrometry for confirmation and subtyping.[3,15,16,19,30]

Biopsy Results

Of the 21 included studies, 14 (67%) included biopsies from a general population of primary CTS patients (CTS-general) (Table 2). In 5 (24%) studies, a screening algorithm was used to select patients who were at increased likelihood of having amyloidosis (CTS-screened) (Table 3). Two studies (10%) included patients who were

Table 2. Included Studies With Biopsies From a General Population of Patients with Primary CTS Undergoing CTR

Authors	Year	Country	Study Design	Patients, n	Men, %	Mean Age, y	Black Race, %	CTR Approach	Biopsy Location	Amyloid-positive Biopsy, n (%)
Short and Palmer[23]	1981	United States	RC	21	Nr	Nr	Nr	Open	TCL	5 (24)
Bjerrum et al[24]	1984	Denmark	CS	26	23	53	Nr	Open	Tenosynovium and TCL	1 (4)
Scelsi et al[25]	1989	Italy	CS	80	25	Nr	Nr	Open	Tenosynovium	2 (3)
Stein et al[26]	1987	Germany	CS	108	Nr	Nr	Nr	Open	Tenosynovium or TCL	27 (19)
Kyle et al[27]	1989	United States	CS	1500	Nr	Nr	Nr	Open	Tenosynovium	152 (10)
Nakamichi and Tachibana[28]	1998	Japan	CS	130	12	58	Nr	Nr	Tenosynovium and TCL	14 (8)
Alizadeh and Tavangar[29]	2002	Iran	CS	209	0	Nr	Nr	Nr	Tenosynovium or TCL	31 (15)
Sekijima et al[30]	2011	Japan	CC	100	25	67	Nr	Nr	Tenosynovium	34 (34)
Sueyoshi et al[31]	2011	Japan	CS	111	50	65	Nr	Nr	Tenosynovium	38 (37)
Uchiyama et al[32]	2014	Japan	PC	107	22	68	Nr	Open or endoscopic	Tenosynovium	38 (36)
Fernandez Fuertes et al[33]	2017	Spain	PC	147	21	58	Nr	Nr	TCL	29 (20)
Sugiura et al[18]	2021	Japan	CS	79	41	72	Nr	Nr	Tenosynovium	27 (34)
Bäcker et al[34]	2022	Ireland	CS	699	37	67	Nr	Open	Tenosynovium	10 (1.4)
Takashio et al[17]	2023	Japan	CS	700	36	64	Nr	Nr	Tenosynovium	261 (37)
Total				4017						669 (17)

CC, case control; CS, cross sectional; NR, not reported; PC, prospective cohort; RC, retrospective cohort.

Table 3. Included Studies With Biopsies From Screened Populations at High Risk of Amyloidosis or Suspected Amyloidosis Undergoing CTR

	Authors	Year	Country	Study Design	Patients, n	Men, %	Mean Age, y	Black Race, %	CTR Approach	Amyloid Screening Algorithm Used	Biopsy Location	Amyloid-positive Biopsy, n (%)
CTS-suspected	Samões et al[13]	2017	Portugal	CS	16	19	46	Nr	Nr	Known ATTRm amyloidosis (genetically confirmed)	TCL	14 (88)
	Elzinga et al[35]	2023	Canada	CS	13	85	83	Nr	Extended open	Suspected ATTR (without tissue confirmation)	Tenosynovium and TCL	18 (100)
CTS-screened	Sperry et al[15]	2018	United States	CS	98	52	68	5	Open	Age: men > 50 y; women > 60 y	Tenosynovium	10 (10)
	Scott et al[3]	2019	United States	CS	35	46	72	Nr	Open	Revision CTR	Tenosynovium	9 (26)
	DiBenedetto et al[19]	2022	United States	CS	185	52	71	Nr	Mini open	Age: men > 50 y; women > 60 y	Tenosynovium	55 (29)
	Gannon and Ward[16]	2023	United States	CS	62	53	Nr	Nr	Open	Cleveland Clinic algorithm*	Tenosynovium	14 (23)
	Gray et al.[20]	2023	United States	CS	56	43	66 male; 68 female	7	Open or Endoscopic	Men age ≥ 50 and women ≥ 60 with bilateral CTS, multiple trigger digit or bilateral CTS + multiple TD	Tenosynovium	9 (16)
			Total: 465									129 (28)

*Screening algorithm proposed by Donnelly et al.[1]
CS, cross sectional; NR, not reported.

suspected of having amyloidosis based on preoperative cardiac or genetic screening tests but did not have a formal tissue diagnosis at the time of CTR (CTS-suspected) (Table 3). Pooled data from studies within the CTS-general group demonstrated an 18% (95% CI = 11%–27%) prevalence of positive screening biopsy (Fig. 2A). We additionally stratified the studies into Japanese and non-Japanese studies, given the higher

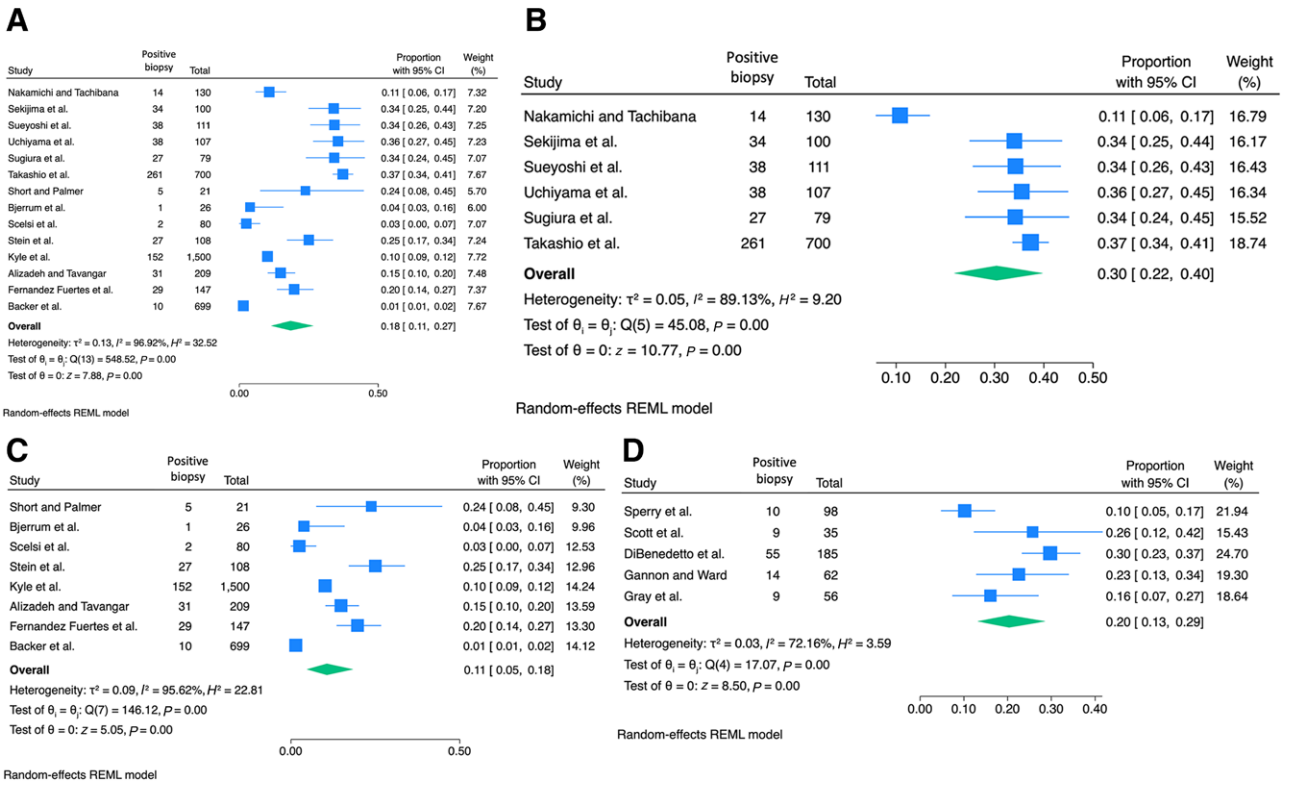

Fig. 2. Prevalence of amyloid-positive biopsy by study. Prevalence of amyloid-positive biopsy among all CTS-general articles (A), CTS-general articles from Japan (B), CTS-general studies from the United States, Europe, and the Middle East (C), and from CTS-screened populations (D). REML, restricted maximum likelihood.

Table 4. Included Studies That Reported Workup for CA in Patients With Amyloid-positive Biopsies

Authors	Year	Patients, n	Amyloid Screening Algorithm Used	Amyloid-positive Biopsy, n (%)	Cardiac Amyloid Diagnosis Modality	Patients Diagnosed With CA, n (% of Biopsy + Patients, % of Total Cohort)	Patients Started on CA Medical Treatment, n	CA Follow-up Duration, mo
Sperry et al[15]	2018	98	Age: men >50 y, women >60 y	10 (10)	Echo, EKG, biomarkers. PYP scan for confirmation	2 (20, 2)	2	0
Sugiura et al[18]	2021	79	None	27 (34)	Echo, EKG, biomarkers. PYP scan for confirmation	3 (11, 4)	0	0
Gannon and Ward[16]	2023	62	Cleveland Clinic algorithm*	14 (23)	Referral to cardiology and hematology for further workup, PYP scan for confirmation	1 (7, 2)	1	0
Takashio et al[17]	2023	700	None	261 (37)	Echo, EKG, biomarkers, PYP scan for confirmation	6 (2, 1)	1	0

*Proposed screening algorithm in supplemental materials of Donnelly et al.[1]
EKG, electrocardiogram.

described prevalence of amyloidosis in Japan compared with Europe and North America.[36–39] All Japanese studies were from the CTS-general group, and the pooled prevalence of amyloid-positive biopsy in this group was 30% (95% CI = 22%–40%, Figure 2B), versus 11% (95% CI = 5%–18%, Figure 2C) in the non-Japanese CTS-general group. The pooled prevalence of positive biopsy among the CTS-screened group was 20% (95% CI = 13%–29%, Figure 2D). Among the CTS-screened studies, DiBenedetto et al[19] reported the highest rate of biopsy positivity (29%) by including men older than 50 and women older than 60 in the biopsy cohort. However, Sperry et al[15] used the same screening criteria and reported the lowest prevalence of positive biopsy among the included CTS-screened studies (10%). The prevalence of amyloid among biopsies from the CTS-suspected group ranged from 88% to 100%. Eleven studies reported the amyloid subtype for positive biopsies.[3,13,15–19,30–32,35] Across all studies that reported subtypes, the aggregate percentages were 82% ATTRwt, 11% indeterminate, 5% ATTRm, and 1% AL. One study enrolled only patients with suspected ATTRm amyloidosis, of whom 88% had a biopsy positive for amyloid.[13]

Four studies included evaluation for asymptomatic CA in patients whose CTR biopsy was positive for amyloid: 2

from the CTS-general population[17,18] and 2 from the CTS-screened population (Table 4).[15,16] All patients found to have amyloid deposition in the TCL/tenosynovium were offered CA screening with electrocardiogram, and biomarkers were used as an additional CA screening modality in 3 studies.[15,17,18] Final diagnosis of CA was made with a PYP scan in all studies. Of note, none of the patients required an endomyocardial biopsy for tissue diagnosis, as that requirement was satisfied by the biopsy during CTR. Overall, 5%–20% of patients with amyloid-positive biopsies who underwent cardiac screening were eventually diagnosed with CA. All 12 patients diagnosed with CA had the ATTRwt subtype, and 4 were started on transthyretin tetramer stabilizers.[15–17] Two patients were diagnosed with AL amyloidosis and were started on chemotherapy,[3,15] and 1 patient was diagnosed with ATTRm amyloidosis and was started on diflunisal for the treatment of progressive polyneuropathy.[15] Overall, the proportion of patients who were ultimately diagnosed with CA was 1% of the CTS-general population (11% of whom were started on medical therapy for CA), and 2% of the CTS-screened population (100% of whom were started on medical therapy).

DISCUSSION

Data from published studies of amyloid screening during CTR suggest that in a general, unscreened population of idiopathic CTS patients, biopsies are expected to return positive for amyloid deposition within the TCL or tenosynovium in 11% (95% CI: 5%–18%) of American and European populations and in 30% (95% CI: 22%–40%) of Japanese populations, and 1%–4% of the CTS-general population may have asymptomatic CA. This higher rate in Japan is consistent with previously published findings of a higher prevalence of ATTR amyloidosis in Japan compared with Europe and North America,[36–39] and is likely due to a combination of factors including higher prevalence of ATTR genetic variants in Japan as well as Japan's older population.[40,37] Selecting which patients to biopsy using one of a number of strategies based on factors that increase the risk of amyloidosis is associated with a higher yield of screening biopsy in American, European, and Middle Eastern populations to 20% (95% CI: 13%–29%) and may increase the detection of underlying asymptomatic CA; however, the optimal screening paradigm has yet to be defined, reflected by the heterogenous criteria used in the studies reported to date. The included studies also reflect several key areas that must be studied further to develop consensus criteria and optimize amyloidosis screening practices.

Serial Cardiac Evaluation

The studies to date have not followed biopsy-positive patients whose initial CA workup is negative to determine the incidence of CA development over time. Only a small percentage of patients with positive biopsies have cardiac involvement identified during workup in the immediate postoperative period, though some patients with tenosynovial amyloid and an initially negative cardiac workup may go on to develop CA. The incidence of CA within biopsy-positive cohort is, therefore, likely to be higher than that of the general population and higher than the prevalence of CA reported in the included studies. Two recent studies performed delayed CA screening of a population of general CTS patients who had previously undergone CTR and found a 4%–8% prevalence of CA in that population, supporting the theory that a considerable number of patients who do not show signs of CA at the time of CTR may develop it in a delayed fashion and would benefit from surveillance.[4,41] Patients with confirmed amyloidosis who do not yet have clinically significant cardiac involvement will also derive the greatest benefit from early medication initiation. Studies following biopsy-positive patients with a negative initial CA evaluation over time will help define the true screening utility as well as appropriate surveillance parameters, which are currently undefined.

Risk Factors for Positive Biopsy

Studies to date that have examined the prevalence of positive biopsy in selected populations have used variable criteria for screening and have been limited to small single-institution cohorts, precluding robust identification of clinical factors predictive of positive biopsy. Although the screening nomogram proposed by Sood et al[21] leveraged a large clinical data set to identify risk factors for the development of amyloidosis after CTR, it was not based on clinical biopsy data and has not been validated in a prospective cohort. Large multi-institutional prospective studies are, therefore, required to obtain sufficient clinical data to define and validate optimal criteria for screening. For instance, there has been a paucity of Black patients screened in the included studies relative to the US composition (13.6% Black),[42] a population that is at disproportionately high risk of heart failure mortality and risk of ATTRm amyloidosis.[21] Neither of the included studies that specifically investigated race found Black race to be a significant risk factor for positive biopsy, though both of these study cohorts were composed of less than 8% Black patients.[15,20] Indeed, Black race has been shown to be a significant risk factor for amyloidosis development after CTR in a cohort with a racial composition more similar to that of the United States overall.[21] Of the 9 articles that did attempt to analyze other risk factors for positive biopsy, 6 found age to be a significant risk factor,[3,17–19,30,31] and 5 found male gender to be a significant risk factor.[3,17–19,30] Further studies are required to study the association of other potential risk factors with positive biopsy (including but not limited to race, monoclonal gammopathy of undetermined significance or multiple myeloma, rheumatoid arthritis, atrial fibrillation, spinal stenosis, and bilateral CTS) and to develop a validated prediction model.

Biopsy Technique

The optimal technique for obtaining a screening biopsy has yet to be defined. The studies that have compared TCL to tenosynovium found similar rates of amyloid positivity between the 2 tissue types;[28,35] however, these were in relatively small cohorts, which involved different sample sizes from the different tissue types, and 1 was in

the CTS-suspected population,[35] which may affect its generalizability. A recent study compared biopsies from both the TCL and the tenosynovium from the same patients during open CTR and found a 93% correlation.[43] Of the subjects with discordant biopsy results, a similar number were positive in only the TCL compared with only the tenosynovium, suggesting that biopsy of either tissue type is likely acceptable.[43] Another recent study found a significantly lower prevalence of amyloid positivity in biopsies performed endoscopically compared with open in a screened population raising the question of whether CTR technique may influence biopsy yield.[44] Relatedly, in 1 included study, authors advocate for an extended open approach for patients with suspected amyloidosis in need of tissue diagnosis to ensure adequate release due to concern that this patient population may be more likely to require external neurolysis.[35] However, further studies are needed to confirm whether high suspicion of amyloidosis necessitates this more invasive approach, as it is not known whether patients with amyloidosis have inferior outcomes if treated with conventional open or endoscopic CTR compared with extended open release.

Cost-effectiveness

The cost of screening CTR patients for amyloidosis must also be considered. Although Congo red stain for histology is a relatively inexpensive screening test, a positive result may generate multiple, more expensive tests, including mass spectrometry, and cardiac workups, including echocardiogram and PYP scan. Although the screening algorithms applied by the included studies varied, applying a screening algorithm to identify patients at the highest risk is an important first step toward minimizing cost and inadvertent harm. The psychological impact on the 80%–95% of patients who have amyloid present in their TCL/tenosynovium and undergo extensive cardiac workup without findings of CA must also be considered, especially when surveillance parameters are uncertain. Even for patients who are identified to have CA, the proportion of patients being started on therapy is relatively low. Tafamidis is expensive, and a recent cost analysis found that its use to treat CA greatly exceeds conventional cost-effectiveness thresholds for treatment.[2] Surveillance adds additional cost but will also likely increase the percentage of screened patients ultimately started on therapy. Although the cost is currently high, the potential benefit gained by patients is also great considering the high morbidity and mortality associated with CA. As screening algorithms are further refined, cardiac surveillance protocols are optimized, and drug prices are reduced, the cost-effectiveness of screening and treatment should improve. A formal cost analysis of the implementation of amyloidosis screening is needed.

Although ATTRwt is the most prevalent amyloidosis subtype found via screening biopsy, patients with other types also benefit from early diagnosis when they are otherwise asymptomatic. At least 1 ATTRm patient diagnosed by screening biopsy was initiated on diflunisal for polyneuropathy.[15] Although CTS is a less common manifestation of AL amyloidosis than it is for ATTRwt, up to 30% of patients with AL do experience CTS.[45] These patients also benefit from early detection and initiation of chemotherapy. Indeed, among the included articles, 2 patients from the screening population were diagnosed with AL amyloidosis and were started on therapy.[3,15]

Clinical Pathway for Surgeons

At the senior authors' institutions, the nomogram from Sood et al[21] is used to calculate a risk score for patients undergoing CTR, and biopsy is offered to patients with a score of 100 or more. The algorithm proposed by Sperry et al[15] is another common tool currently being used for risk stratification. It is our practice to biopsy the tenosynovium at the time of either open or endoscopic CTR. Biopsy through the endoscopic incision is performed by flexing the wrist to relax the tendons, retrieving an ulnar-sided flexor tendon with a nerve hook, drawing it up through the endoscopic incision, and excising the tenosynovial specimen from the flexor tendon. Though no specific guideline exists for biopsy size, at least a 1 × 1 cm sample of tenosynovium is recommended by our pathologists to ensure there is enough tissue for Congo red stain and confirmatory mass spectrometry when indicated. Biopsy specimens are immediately fixed in formalin and sent to pathology for Congo red stain. The presence of apple-green birefringence triggers confirmation and amyloid subtyping via mass spectrometry. Patients diagnosed with ATTRwt and ATTRm are referred to cardiology, and patients with AL are referred to hematology for further workup and treatment initiation. Referral to a provider with experience treating amyloidosis specifically is recommended if possible, as is care of these patients in a multidisciplinary amyloidosis program where available. Figure 3 outlines a suggested workflow for managing these patients.

Limitations

The included studies investigated heterogenous populations, used various screening criteria, and utilized different surgical and biopsy techniques. This heterogeneity is an inherent limitation of meta-analyses, highlighting the need for large prospective studies.

CONCLUSIONS

Due to the recent availability of therapeutics to halt the progression of amyloidosis, increasing awareness of CA as being underdiagnosed, and the potential for early diagnosis with biopsy at CTR, hand surgeons have an opportunity to facilitate early initiation of life-saving therapy. Our analysis of available data suggests that the use of clinical criteria to identify high-risk patients increases the yield of biopsy during CTR for the detection of amyloid. Screening algorithms should, therefore, be applied to adult patients undergoing CTR to determine the necessity for intraoperative screening biopsy. Further studies, ideally prospective and multi-institutional in nature, should focus on delineating factors predicting positive biopsy and include patients of diverse racial backgrounds, ascertaining the optimal biopsy technique; defining the role and method of serial cardiac evaluation in amyloid-positive patients

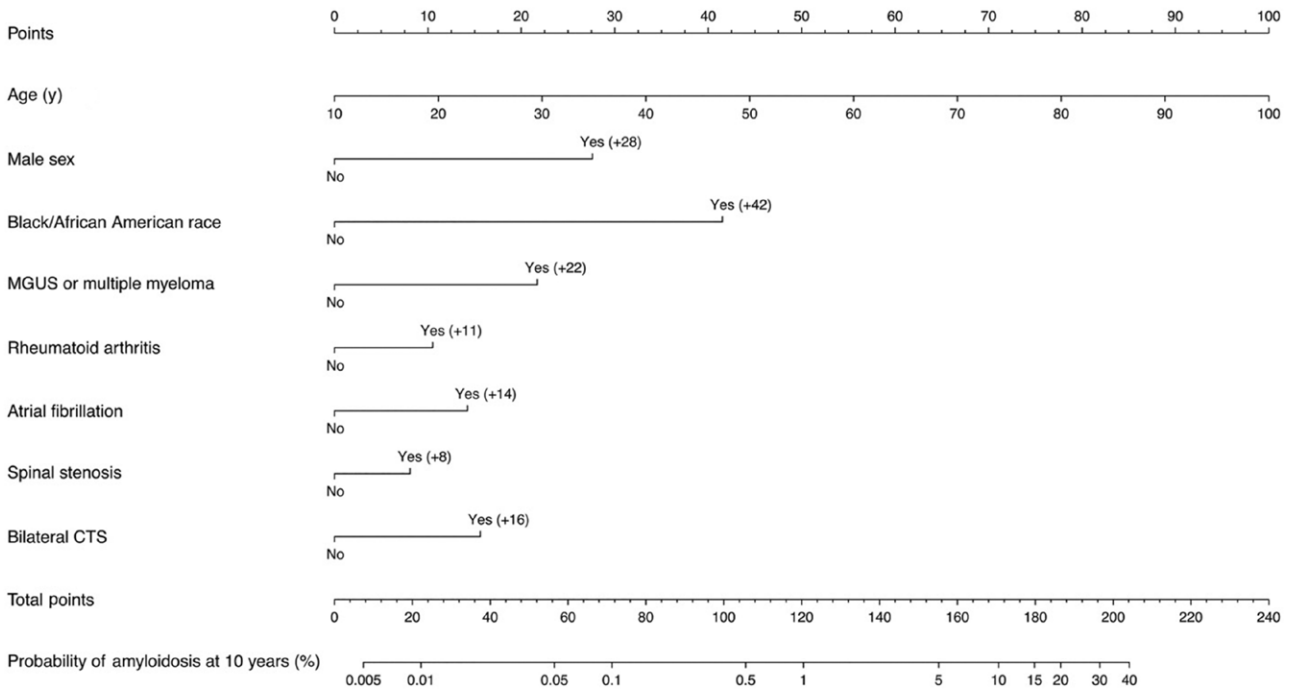

Fig. 3. Workflow for CTS patients at high risk for amyloidosis. MGUS, monoclonal gammopathy of undetermined significance.

with initially negative cardiac workup; and developing unified, validated screening criteria whose cost-effectiveness should be directly assessed. As we work to reach consensus on evidence-based screening practices, all surgeons who perform CTR should be familiar with the available evidence and consider biopsy in patients at elevated risk.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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