Treating Wild-Type ATTR Cardiac Amyloidosis Today

SATURDAY, APRIL 18 / 12:00 p.m. - 12:45 p.m.

CHFS SCIC
Canadian Heart Failure Society
Société canadienne d'insuffisance cardiaque

Welcome and Introductions

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MD, SM, FRCPC, FACC, FCCS, FASE, FHFSA

Faculty

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Director of Echocardiography, Heart Failure Cardiologist
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Nurse Clinician/ Cardio-Oncology Clinic
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Calgary, AB

John Pasternak (Patient)
MD
Medicine Hat, AB

Disclosures: Dr. Nowell Fine

- **Consultancy/speaking fees**: Akcea, Alnylam, Pfizer, Sanofi

- **Clinical trial participation**: Pfizer

Disclosures: Ms. Debra Bosley

- **Consultancy/speaking fees**: None

- **Clinical trial participation**: None

Disclosures: Dr. Margot Davis

- **Consultancy/speaking fees**: Janssen, Novartis, Boehringer-Ingelheim, Takeda, Pfizer, Akcea, Alnylam, Amgen, Ferring

- **Grant funding**: Pfizer, Takeda, Boehringer-Ingelheim, Servier, Akcea

Disclosures: Dr. Michael Heffernan

- **Consultancy/speaking fees**: AstraZeneca, Boehringer Ingelheim, BMS/Pfizer Alliance, Novartis, Pfizer, Sanofi, Servier, Amgen, Bayer, Bristol-Myers Squibb

- **Clinical trial participation**: AstraZeneca, Boehringer Ingelheim, Novartis, Pfizer, Amgen, Bayer, Merck

- **Fiduciary Role**: Oakville Cardiologist Inc, Oakville Cardiovascular Research LP

- **Ownership/Partnership/Principal**: Oakville Cardiologist Inc, Oakville Cardiovascular Research LP

Disclosures: Dr. John Pasternak

- **Consultancy/speaking fees**: None

- **Clinical trial participation**: Pfizer

Disclosure of Commercial Support

Specific details of relationship:

- This program has received financial support from Pfizer Canada Inc. in the form of an educational grant
- This program has received in-kind support from Canadian Heart Failure Society in the form of logistical support

Potential for conflict(s) of interest:

- Speakers have received honoraria from Canadian Heart Failure Society
- Pfizer Canada Inc. is the manufacturer of a product that will be discussed in this program

Mitigating Potential Bias

Potential biases are acknowledged and are mitigated by presenting data supported by national and international guidelines, and as follows:

- Information presented is evidence-based
- Material has been developed and reviewed by a Planning Committee

Off-label uses of drugs may be discussed and will be identified as such by the speaker

Accreditation

This event is an accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians & Surgeons of Canada and approved by the Canadian Cardiovascular Society. You may claim a maximum of 0.75 hours.

Learning Objectives

- Recognize the challenges patients face prior to obtaining an ATTR amyloidosis diagnosis and the importance of early diagnosis
- Review the clinical presentation, treatment, and guidelines for wild-type ATTR amyloidosis and highlight the importance of a multidisciplinary team approach
- Integrate contemporary guidelines and treatment options in the care of patients with wild-type ATTR amyloidosis, whether managed in an academic centre or in community practice

Agenda

Topic	Facilitator
Welcome and Introductions	Dr. Nowell Fine
wtATTR Amyloidosis: A Distinct Disease to Diagnose and Treat	Dr. Margot Davis
Diving into the Reality of Managing wtATTR Amyloidosis	Dr. Nowell Fine Ms. Debra Bosley Dr. John Pasternak (Patient)
Managing wtATTR in your Own Clinic	Dr. Michael Heffernan
Q&A	ALL
Closing Remarks	Dr. Nowell Fine

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Send in your questions!

- Submit your questions for the symposium Q&A by clicking on the Q&A icon on your screen

- To direct your question to a specific speaker, please **include his/her name at the beginning of your question**

wtATTR Amyloidosis: A Distinct Disease to Diagnose and Treat

Margot K. Davis
MD, MSc, FRCPC

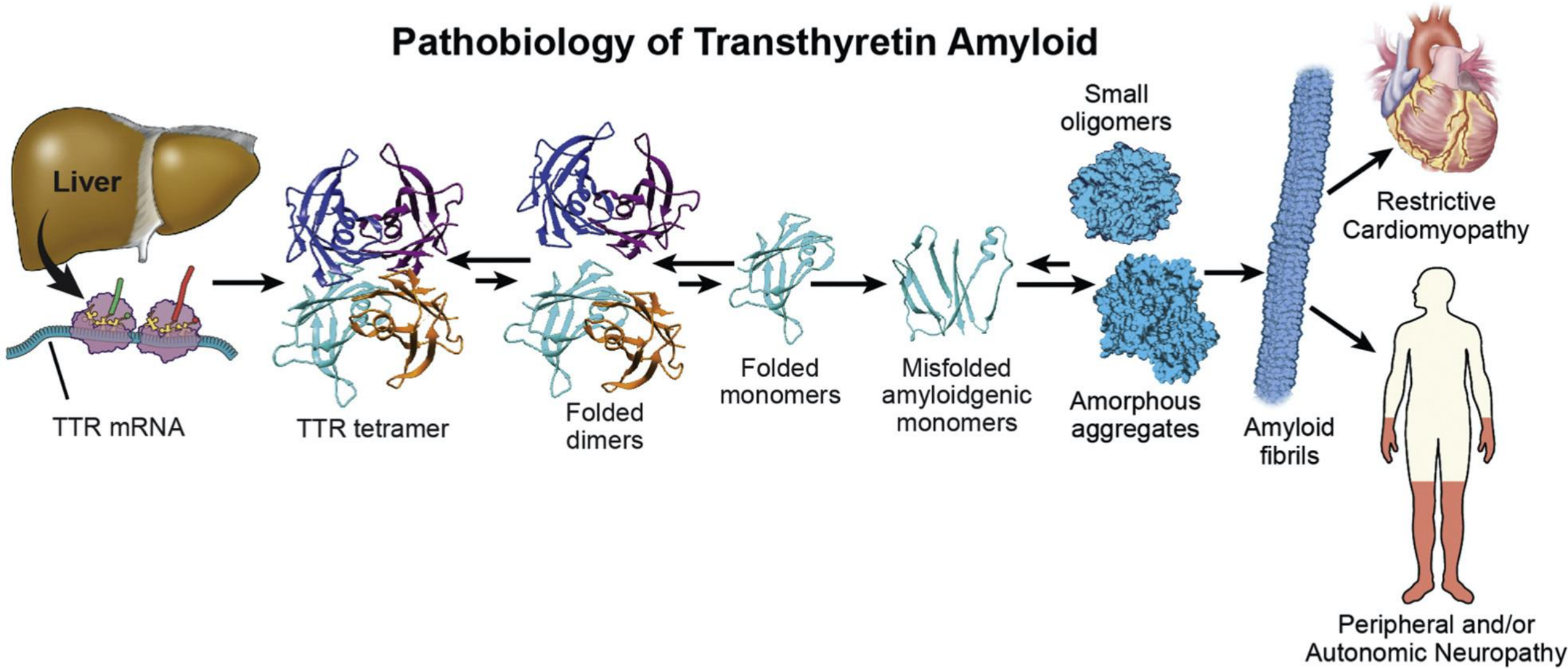
Epidemiology of wtATTR

- Accurate population data are limited
- Wild-type disease is far more common than mutant
- Estimated that at least 25% of individuals >80 years of age have histological evidence of amyloid deposits in the heart
- ATTRwt accounts for ~13% of HFpEF cases in elderly patients (≥60 years old)
- Clinical features mimic other cardiac pathologies that frequently co-exist in advanced age, such as hypertensive heart failure and aortic stenosis

ATTR, transthyretin amyloidosis; ATTR-CA, transthyretin cardiac amyloidosis; ATTRwt, wild-type form of transthyretin amyloidosis; CA, cardiac amyloidosis; HFpEF, heart failure with preserved ejection fraction; TAVR, transcatheter aortic valve replacement.

Connors LH et al. Circulation 2016;133(3):282-290; González-López E et al. Eur Heart J 2015;36(38) 2585-2594; Castaño A et al. Eur Heart J 2017;38(38):2879-2887.

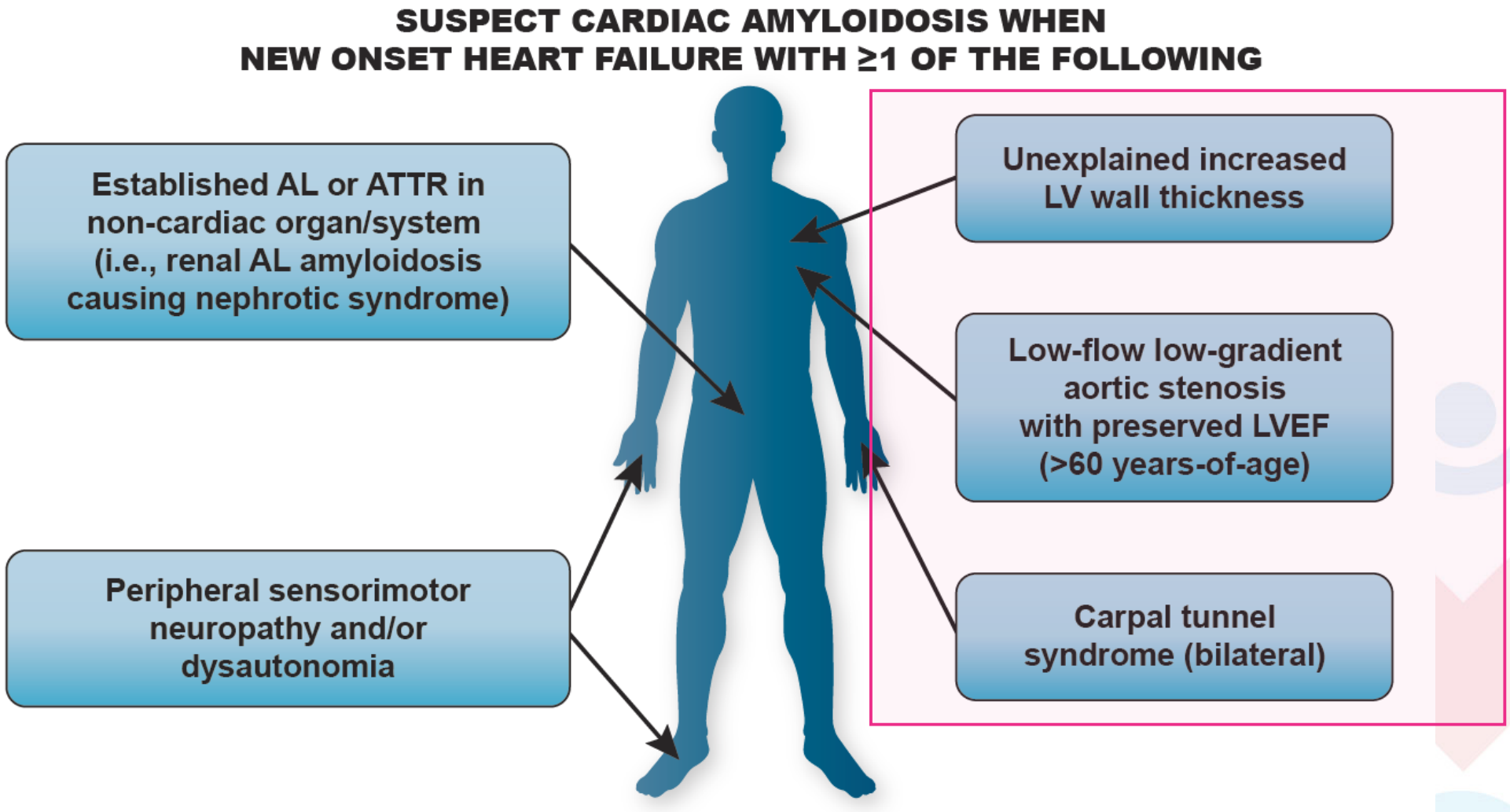
Pathobiology of Transthyretin Amyloid



Cardiac Manifestations

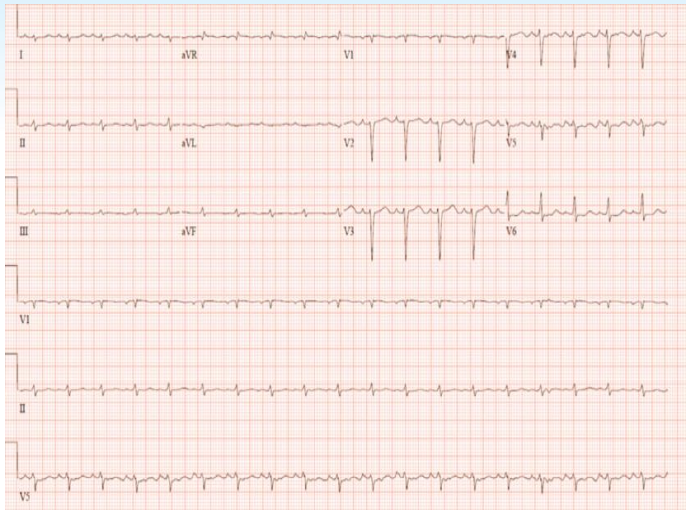
- Heart failure - frequently biventricular, typically preserved LVEF
- Atrial fibrillation
- Conduction system disease
- Ventricular arrhythmia - may be asymptomatic
- Aortic stenosis - low-flow low-gradient for wtATTR, typically with preserved LVEF

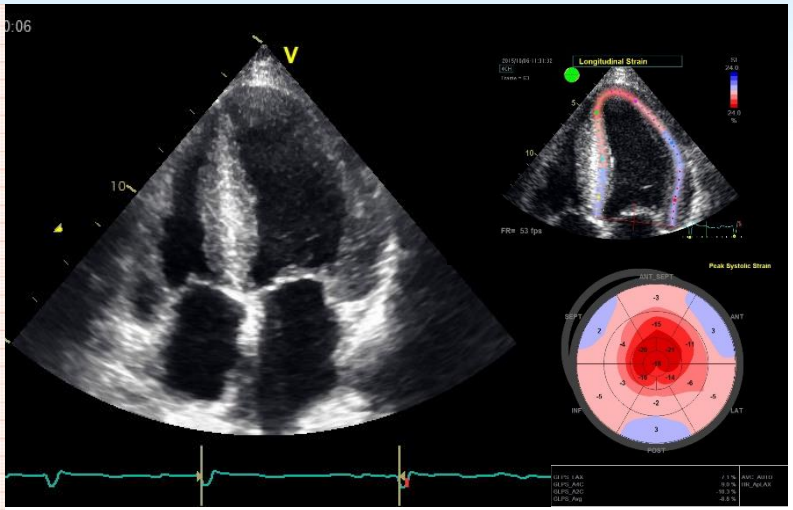
Index of Suspicion – Key Features



ECG

- Low voltage (especially limb leads)
- Pseudo-infarct pattern
- Atrial fibrillation
- Conduction system disease
- Ventricular ectopy



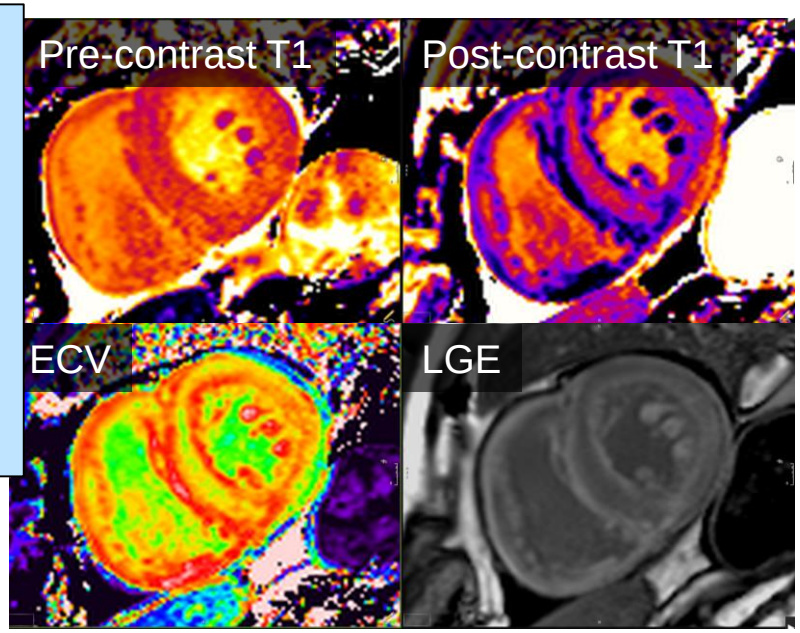


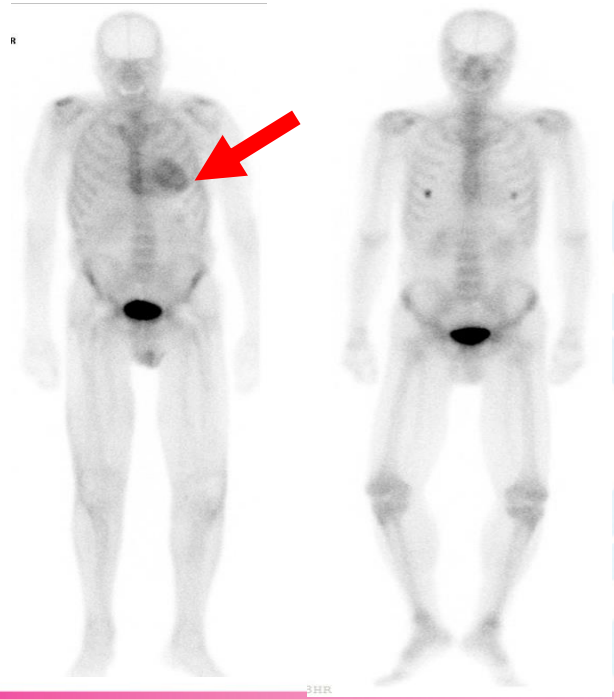
Echo

- Increased LV and RV wall thickness
- Preserved ventricular size, biatrial enlargement
- Diastolic dysfunction
- Increased valvular and interatrial septum thickness
- Small pericardial effusion
- Reduced LV GLS, preserved apical strain (basal-apical strain gradient)

- Diffuse transmural or subendocardial pattern LGE
- Left atrial LGE
- Elevated native (non-contrast) T1 mapping time
- Extracellular volume expansion (post-contrast T1 mapping)

CMRI



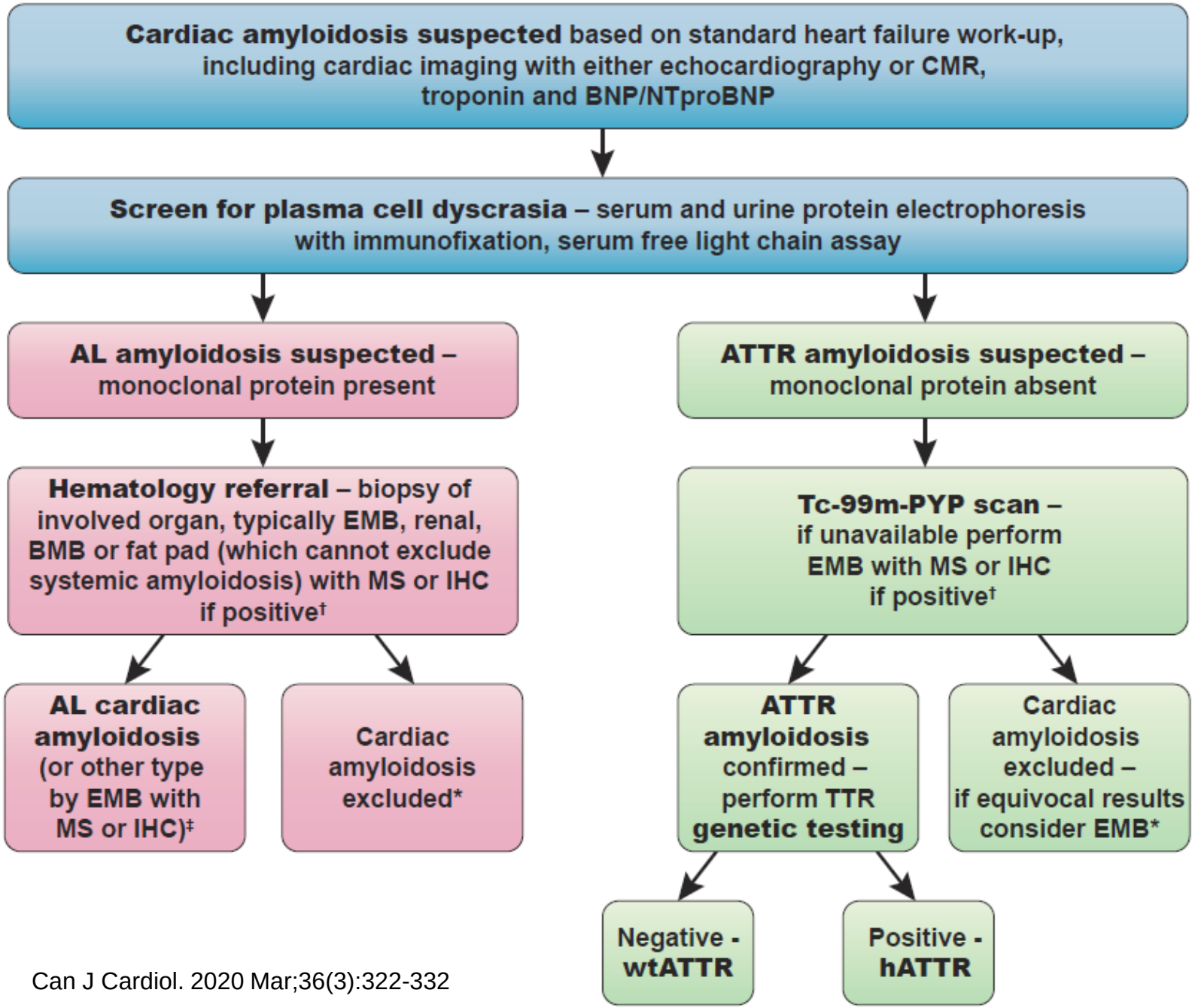


- Increased myocardial radiotracer uptake equal to or greater than bone (≥Grade 2), or in quantitative comparison with the contralateral lung (HCL ratio ≥1.5)

Tc-99m-PYP

Courtesy Dr. James White, Dr. Denise Chan, University of Calgary

CCS/CHFS Joint Position Statement



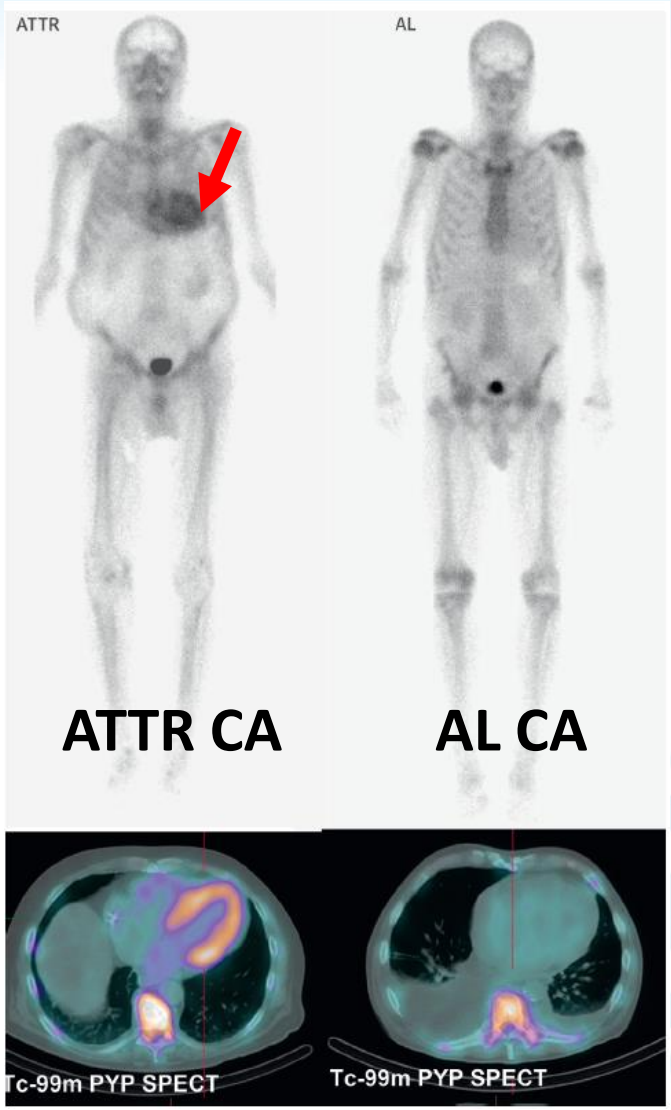
Can J Cardiol. 2020 Mar;36(3):322-332

Tc99m-PYP SPECT in Cardiac Amyloidosis

Intense diffuse myocardial uptake in a patient with ATTR cardiac amyloidosis, grade 2-3 compared with bone

No/minimal myocardial uptake in a patient with AL cardiac amyloidosis, or other causes of LVH

Heart : Contralateral lung ratio >1.5 highly sensitive (>95%) and specific (>85%) for ATTR cardiac amyloidosis



Planar whole body scan

With SPECT

ATTR, transthyretin amyloidosis; SPECT, single photon emission computed tomographyTc99m-PYP, ^{99m}technetium pyrophosphate.
J Am Coll Cardiol, 68(12), Falk RH et al., 1323-1341, (2016)

Tc99m-PYP (Bone) Scintigraphy Enables the Diagnosis of Cardiac ATTR Amyloidosis Without the Need for Histology

Study Design

- 1217 patients with suspected cardiac amyloidosis
- Bone scintigraphy and biochemical investigations

Results

- 857 patients – histologically proven amyloid (374 with endomyocardial biopsies)
- 360 patients – nonamyloid cardiomyopathies
- Myocardial radiotracer uptake on bone scintigraphy was **>99% sensitive** and **86% specific** for cardiac ATTR amyloid
    - False positives almost exclusively from uptake in patients with cardiac AL amyloidosis
- Combined findings of grade 2 or 3 myocardial radiotracer uptake on bone scintigraphy + absence of a monoclonal protein in serum or urine:
    - **Specificity and positive predictive value** for cardiac ATTR amyloidosis: **100%** (CI 98.0-100)

AL, light-chain amyloidosis; ATTR, transthyretin amyloidosis; Tc99m-PYP, ^{99m}technetium pyrophosphate.

Gillmore JD et al. Circulation 2016;133:2404-2412.

Overview of Management

MANAGEMENT OF CARDIAC SEQUELAE

- Cautious use or avoidance of beta-blockers, calcium channel blockers, ACEI/ARBs and digoxin
- Diuresis
- Anticoagulation for atrial fibrillation/flutter
- Pacemaker implantation for symptomatic bradycardia
- Defibrillator implantation for secondary prevention in appropriate patients
- Consideration of heart transplantation for highly selected patients

DISEASE MODIFYING THERAPY

- Chemotherapy ± autologous stem cell transplantation for AL
- Tafamidis for hATTR or wtATTR cardiomyopathy with NYHA I-III symptoms
- Inotersen or patisiran for hATTR with ambulatory polyneuropathy symptoms
- Liver transplant for hATTR

Supportive Care in Cardiac Amyloidosis

Recommendation

- We recommend that heart transplantation be considered for select patients with advanced HF due to cardiac amyloidosis, in whom significant extra-cardiac manifestations are absent and the risk of disease progression is considered low and/or amenable to disease modifying therapy (Strong Recommendation, Moderate-Evidence Quality).

Recommendation

- In the absence of contraindications, we recommend therapeutic anticoagulation in patients with cardiac amyloidosis and AF, regardless of calculated risk of stroke or systemic embolism. (Strong Recommendation, Low-Quality Evidence).

Disease-Modifying Therapy in Cardiac Amyloidosis

Recommendation

- We recommend tafamidis (if available) for patients with ATTR cardiac amyloidosis and NYHA class I-III symptoms. (Strong Recommendation, High-Quality Evidence).

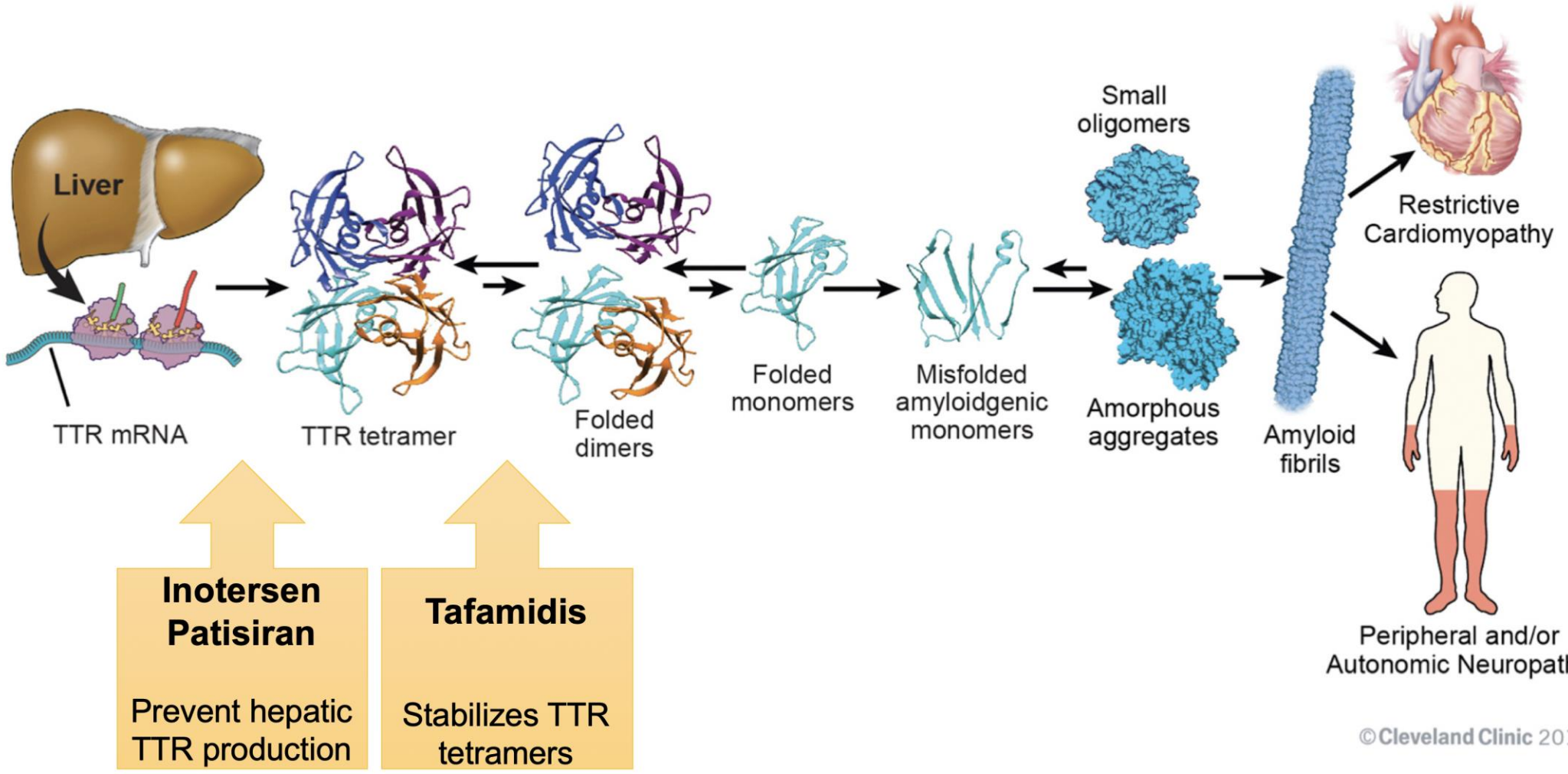
Recommendation

- We recommend treatment with a TTR RNA silencing agent (patisiran or inotersen) for patients with hereditary ATTR amyloidosis with ambulatory polyneuropathy (Strong Recommendation, High-Quality Evidence).

Summary of Evidence Deficiencies

- Use of beta blockers, ACE/ARB, MRA, (ARNI), CCB, digoxin
- Role of liver transplant in era of ATTR disease-modifying therapy
- Role of LVAD
- Rate vs. rhythm control
- Warfarin vs DOAC
- Role of prophylactic pacemakers
- Role of CRT
- Criteria for primary prevention ICD

Emerging Therapeutic Targets of the Amyloidogenic TTR Cascade



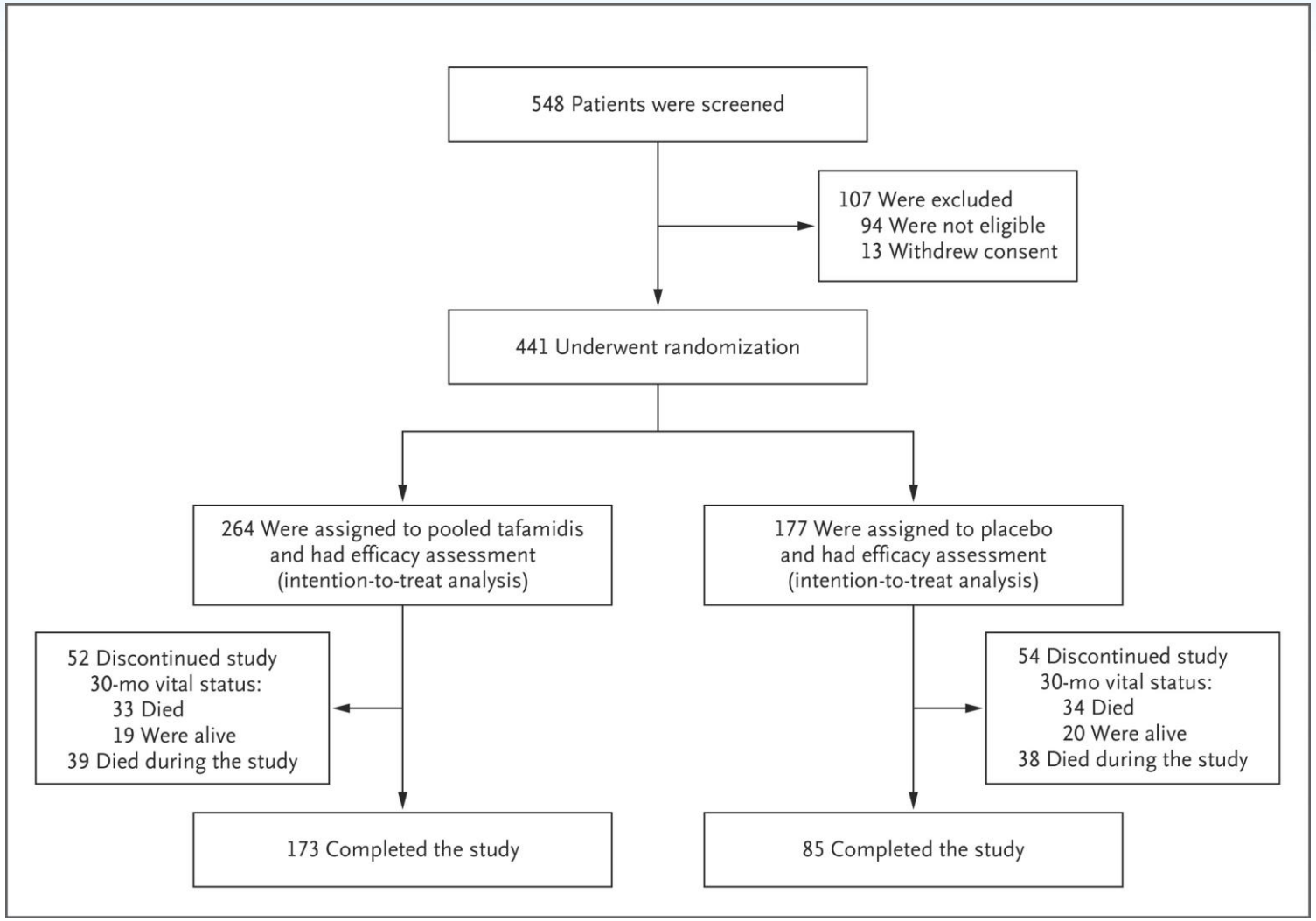
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 13, 2018 VOL. 379 NO. 11

Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

Mathew S. Maurer, M.D., Jeffrey H. Schwartz, Ph.D., Balarama Gundapaneni, M.S., Perry M. Elliott, M.D., Giampaolo Merlini, M.D., Ph.D., Marcia Waddington-Cruz, M.D., Arnt V. Kristen, M.D., Martha Grogan, M.D., Ronald Witteles, M.D., Thibaud Damy, M.D., Ph.D., Brian M. Drachman, M.D., Sanjiv J. Shah, M.D., Mazen Hanna, M.D., Daniel P. Judge, M.D., Alexandra I. Barsdorf, Ph.D., Peter Huber, R.Ph., Terrell A. Patterson, Ph.D., Steven Riley, Pharm.D., Ph.D., Jennifer Schumacher, Ph.D., Michelle Stewart, Ph.D., Marla B. Sultan, M.D., M.B.A., and Claudio Rapezzi, M.D., for the ATTR-ACT Study Investigators*

Randomization, Evaluation, & Outcomes



Maurer MS et al. N Engl J Med 2018;379:1007-1016

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Tafamidis (N=264)	Placebo (N=177)
Age — yr		
Mean	74.5±7.2	74.1±6.7
Median (range)	75 (46–88)	74 (51–89)
Sex — no. (%)		
Male	241 (91.3)	157 (88.7)
Female	23 (8.7)	20 (11.3)
Race — no. (%)		
White	211 (79.9)	146 (82.5)
Black	37 (14.0)	26 (14.7)
Asian	13 (4.9)	5 (2.8)
Other	3 (1.1)	0
TTR genotype — no. (%)		
ATTRm	63 (23.9)	43 (24.3)
ATTRwt	201 (76.1)	134 (75.7)
Blood pressure — mm Hg		
Supine		
Systolic	115.4±15.4	115.1±15.7
Diastolic	70.4±10.3	70.2±9.5
Standing		
Systolic	115.5±15.5	115.9±15.9
Diastolic	70.6±9.9	71.0±10.3
Heart rate, mean — beats per minute		
Supine	70.7±12.3	69.9±11.7
Standing	72.9±12.9	73.8±12.2
NYHA Class — no. (%)		
Class I	24 (9.1)	13 (7.3)
Class II	162 (61.4)	101 (57.1)
Class III	78 (29.5)	63 (35.6)
Modified BMI†	1058.8±173.8	1066.4±194.4
NT-proBNP level — pg/ml		
Median	2995.9	3161.0
Interquartile range	1751.5–4861.5	1864.4–4825.0

Primary Analysis and Components

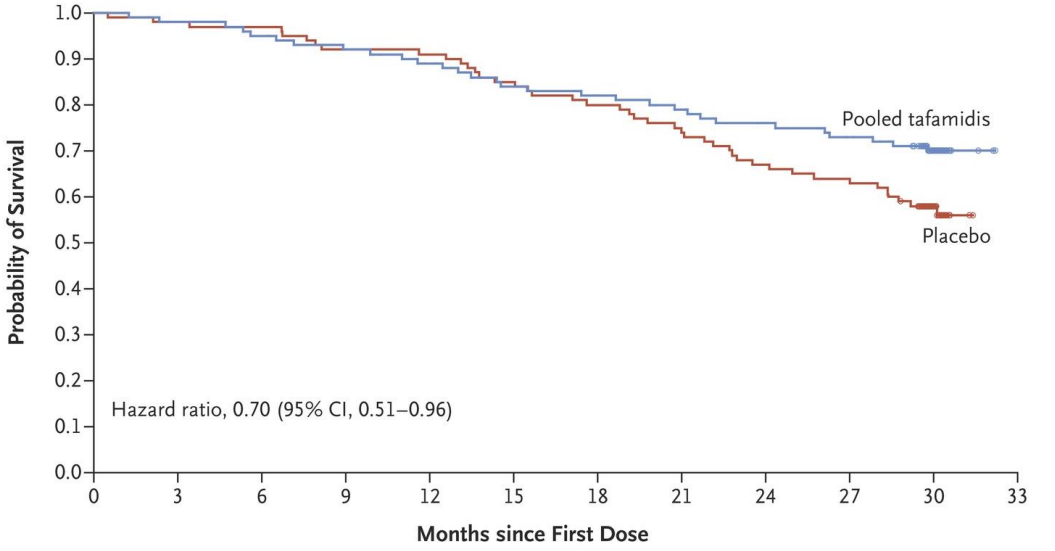
A Primary Analysis, with Finkelstein–Schoenfeld Method

	No. of Patients	P Value from Finkelstein–Schoenfeld Method	Win Ratio (95% CI)	Patients Alive at Mo 30	Average Cardiovascular-Related Hospitalizations during 30 Mo among Those Alive at Mo 30
				no. (%)	*per patient per yr*
Pooled Tafamidis	264	<0.001	1.70 (1.26–2.29)	186 (70.5)	0.30
Placebo	177			101 (57.1)	0.46

C Frequency of Cardiovascular-Related Hospitalizations

	No. of Patients	No. of Patients with Cardiovascular- Related Hospitalizations	Cardiovascular- Related Hospitalizations	Pooled Tafamidis vs. Placebo Treatment Difference
		total no. (%)	*no. per yr*	*relative risk ratio (95% CI)*
Pooled Tafamidis	264	138 (52.3)	0.48	0.68 (0.56–0.81)
Placebo	177	107 (60.5)	0.70	

B Analysis of All-Cause Mortality

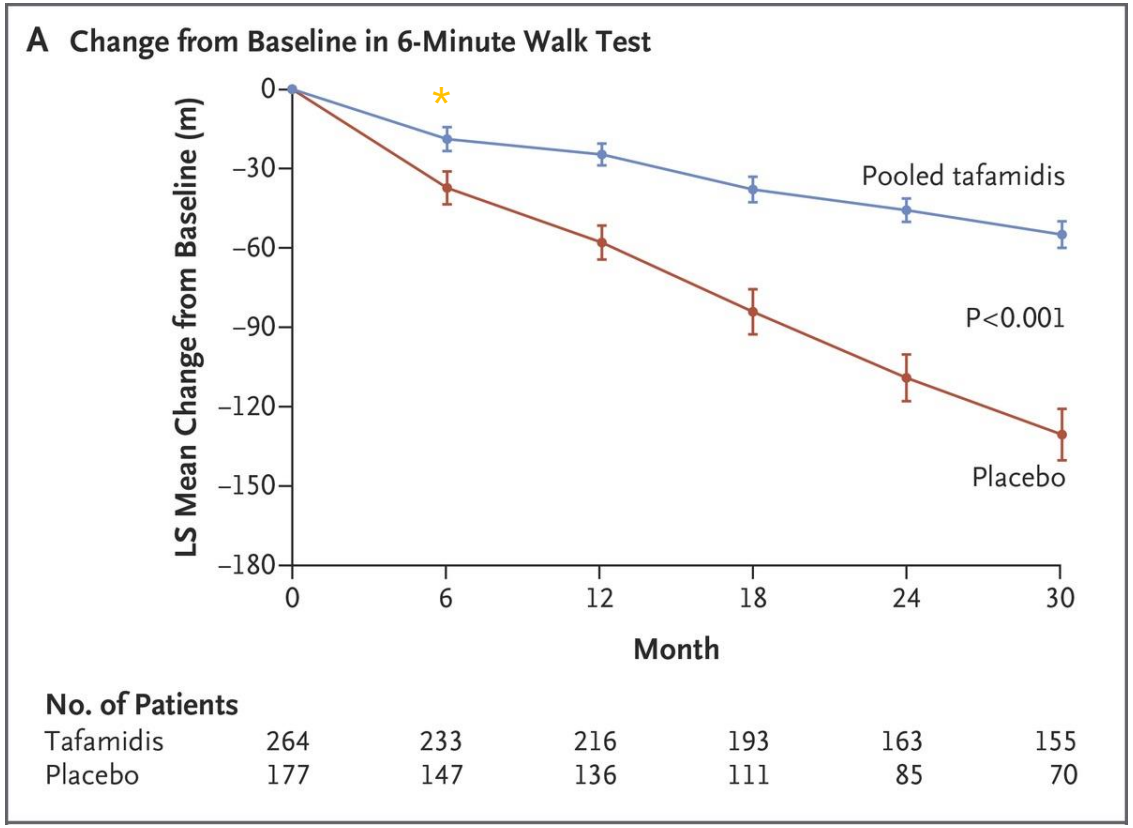


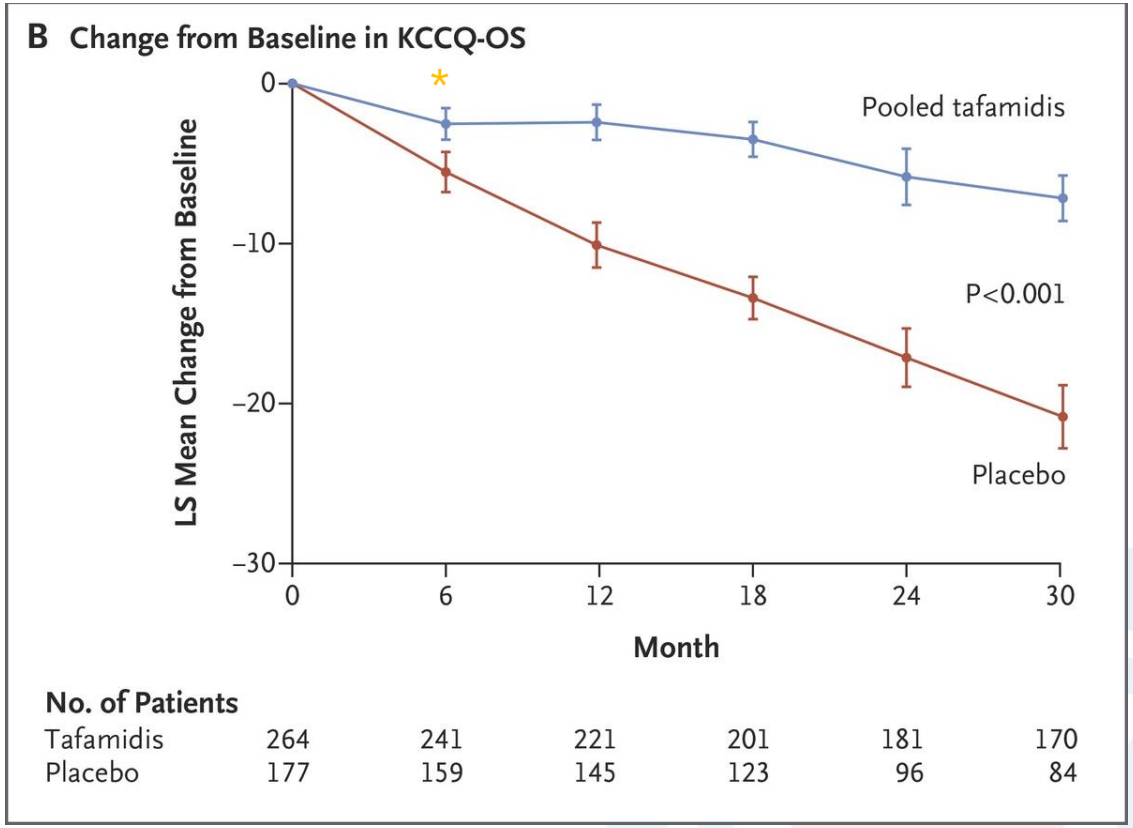
No. at Risk (cumulative no. of events)

Pooled tafamidis	264 (0)	259 (5)	252 (12)	244 (20)	235 (29)	222 (42)	216 (48)	209 (55)	200 (64)	193 (71)	99 (78)	0 (78)
Placebo	177 (0)	173 (4)	171 (6)	163 (14)	161 (16)	150 (27)	141 (36)	131 (46)	118 (59)	113 (64)	51 (75)	0 (76)

Maurer MS et al. N Engl J Med 2018;379:1007-1016

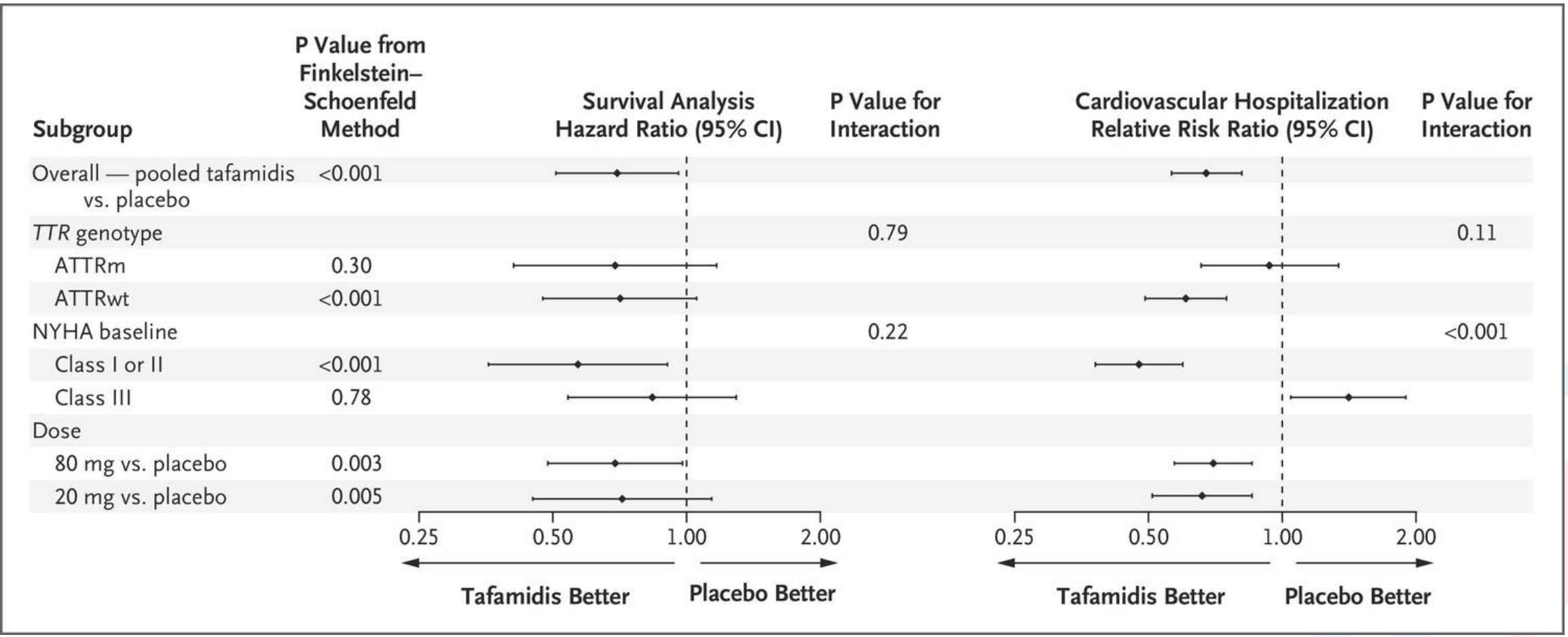
Key Secondary End Points





Maurer MS et al. N Engl J Med 2018;379:1007-1016

Tafamidis: Subgroup Analysis



CI, confidence interval.

Adapted from Maurer MS et al. N Engl J Med 2018; Epub ahead of print doi: 10.1056/NEJM/Moa1805689.

Conclusions

- ATTR-CM is an underdiagnosed cause of heart disease

- Emerging therapeutic options act at different point in the amyloidogenic TTR cascade:
  - Silencers: Agents target suppression of amyloidogenic TTR
  - Stabilizers: TTR-stabilizing agents
  - Degraders: Removal of already deposited fibrils

- Tafamidis is the first HC-approved disease-modifying therapy for wtATTR-CM with the ability to prolong survival and improve symptoms in ATTR patients

- Additional therapies and advances in the diagnosis will continue to improve the care of this challenging and complex population

ATTR, transthyretin amyloidosis; ATTRm, mutated form of transthyretin amyloidosis; TTR, transthyretin.

Q&A

Diving into the Reality of Managing wtATTR Amyloidosis

Nowell Fine
MD, SM, FRCPC, FACC, FCCS, FASE, FHFSA

Debra Bosley
RN, BScN

John Pasternak (Patient)
MD

Caring for the wtATTR Patient: Clinic and Patient Perspectives

Debra Bosley, Nurse Clinician
Cardiac Amyloidosis Clinic, University of Calgary

- **Multidisciplinary 'team' approach** to patient care
  - Nurse clinician, cardiologist
  - Other medical subspecialties – Calgary Amyloidosis Working Group

- **Referral review and triage**
  - Client phone interview
  - Review investigations with cardiologist, determine appropriate pre-appointment testing
    - Imaging, AL urine/serum screening

Cardiac Amyloidosis Clinic
University of Calgary

- **Initial appointment**
  - Need for subsequent investigations – genetic testing
  - Management plan – heart failure care, subspecialty referrals, disease-modifying therapy
  - Patient/client education
    - Disease course, subtype, symptoms, progression
    - Clinic protocols and procedures

Cardiac Amyloidosis Clinic
University of Calgary

- **Follow-up care**
  - Monitor and interpret follow-up testing, labs, symptoms
  - Follow-up on medical subspecialty referrals
  - Ongoing education and support for clients/families
  - Liaise and coordinate with research team regarding clinical trials

Dr. John Pasternak
Family Physician, wtATTR Patient

- **What are the important considerations from the patient perspective of?**
  - Initial consultation and diagnostic work-up
  - Follow-up management and care
  - What other advice do you have for healthcare providers of ATTR patients?

Q&A

Managing wtATTR in your own Clinic

Michael Heffernan
MD, PhD, FRCPC, FACC

Translating Canadian Guidelines into Practice

Canadian Journal of Cardiology 36 (2020) 322–334

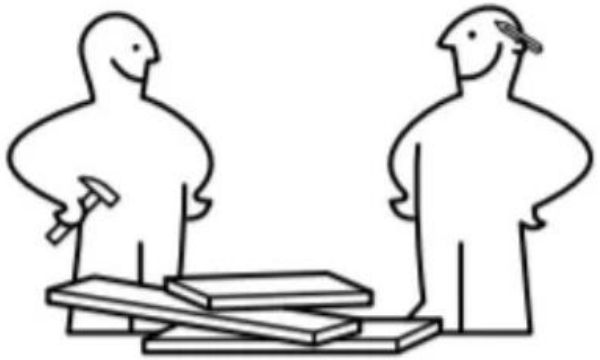
Society Position Statement

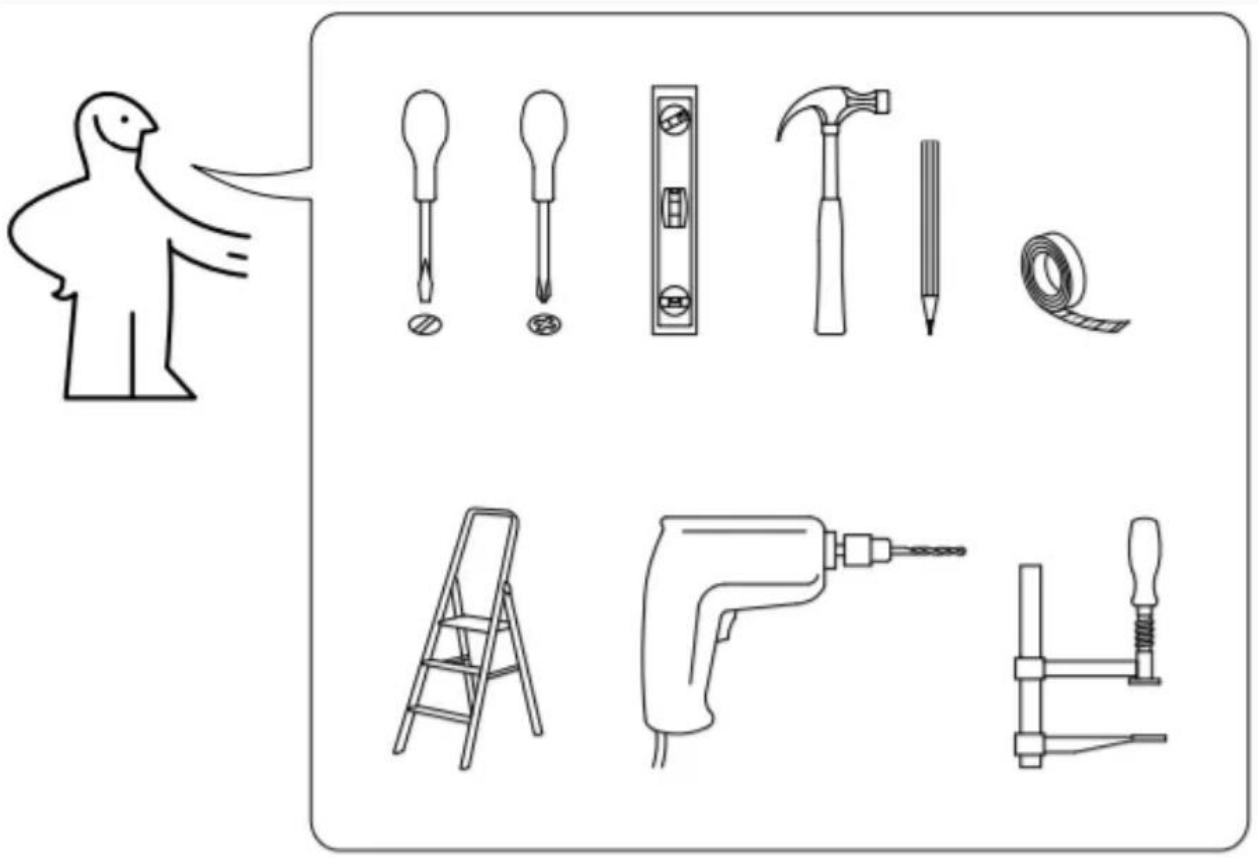
Canadian Cardiovascular Society/Canadian Heart Failure Society Joint Position Statement on the Evaluation and Management of Patients With Cardiac Amyloidosis

Primary Panel: Nowell M. Fine, MD, SM (Co-chair),[a] Margot K. Davis, MD, SM (Co-chair),[b] Kim Anderson, MD,[c] Diego H. Delgado, MD,[d] Genevieve Giraldeau, MD,[e] Abhijat Kitchlu, MD,[d] Rami Massie, MD,[f] Jane Narayan, NP,[b] Elizabeth Swiggum, MD,[g] Christopher P. Venner, MD,[h]

Secondary Panel: Anique Ducharme, MD, MSc,[e] Natalie J. Galant, PhD,[d] Christopher Hahn, MD,[a] Jonathan G. Howlett, MD,[a] Lisa Mielniczuk, MD,[i] Marie-Claude Parent, MD,[e] Donna Reece, MD,[d] Virginie Royal, MD,[j] Mustafa Toma, MD,[b] Sean A. Virani, MD,[b] and Shelley Zieroth, MD[k]

Implementing The Guidelines At Your Centre



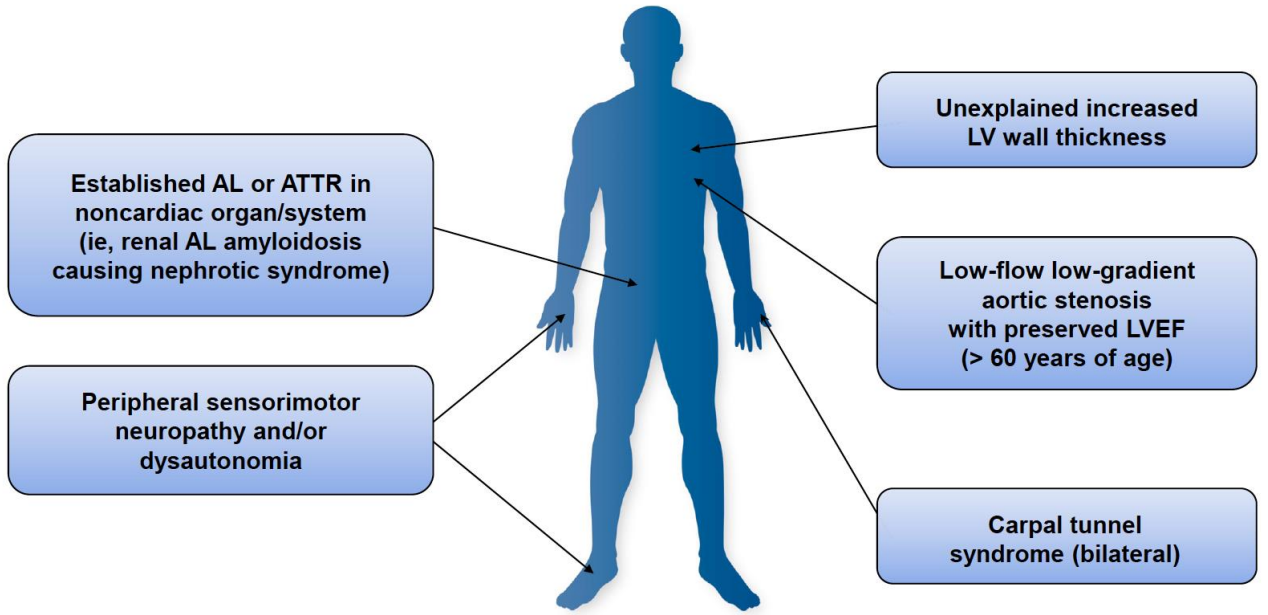


Diagnosis: It Begins With An Index of Suspicion

If amyloidosis is not in your differential diagnosis you will not make the diagnosis

Awareness of the ATTR Red Flags

Consider using search algorithms in your EMR to identify patients with Red Flag features that may have been overlooked in the past several years



AL Amyloid: Ruling Out A Medical Emergency

- AL amyloidosis, a multiorgan disease commonly affecting the kidney, resulting in nephrotic syndrome
- Cardiac involvement is the second most common presenting manifestation
- Other organ systems that may be involved include
  - Peripheral and autonomic nervous system
  - Vasculature
  - Liver
  - Gastrointestinal tract
  - Soft tissues.

Untreated, the median survival from onset of heart failure is approximately 6 months, but current therapies can induce a prolonged remission and extend life by many years

AL Amyloidosis Screen

Screening requisition in your EMR ready for use

Other Tests - one test per line

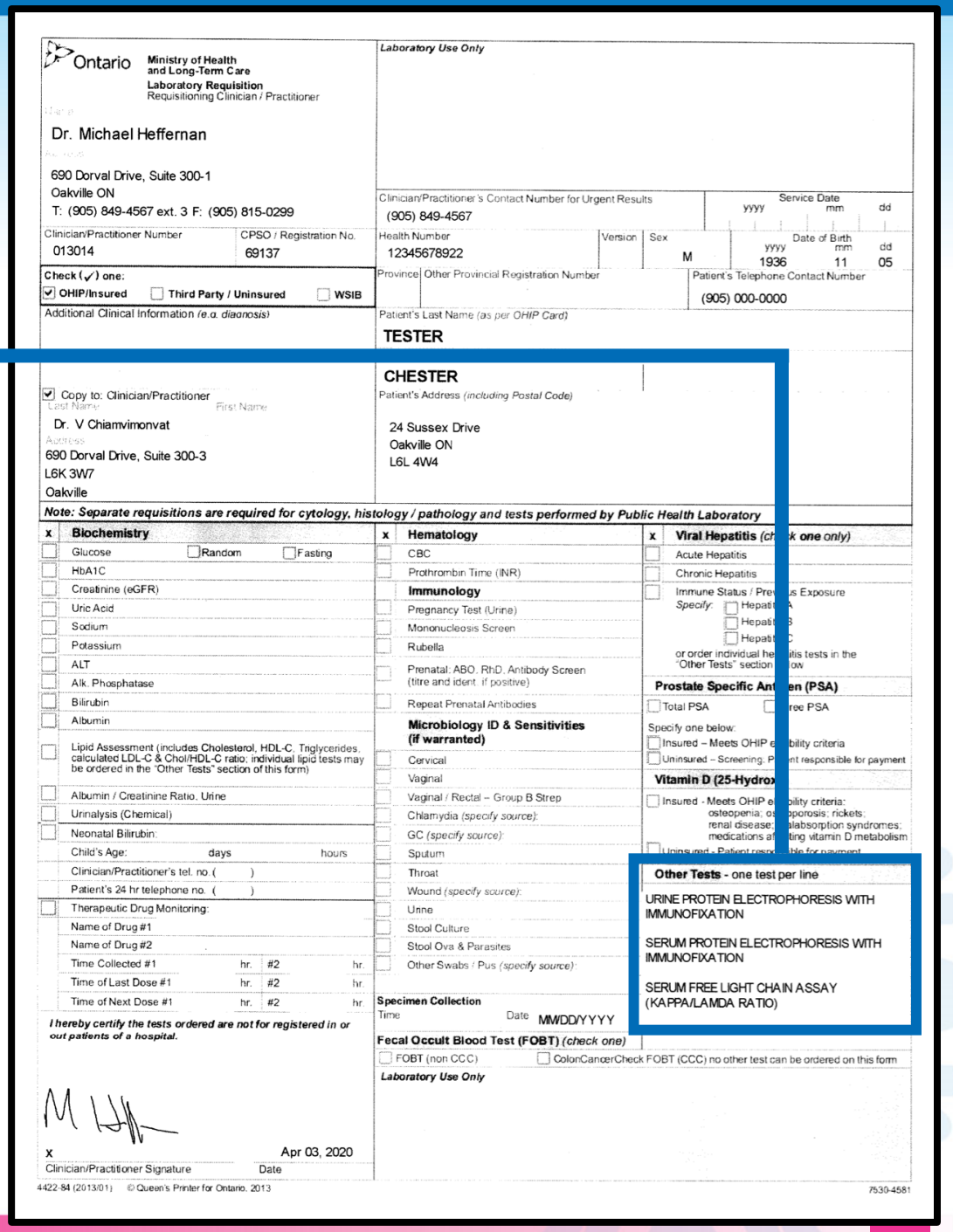
URINE PROTEIN ELECTROPHORESIS WITH IMMUNOFIXATION

SERUM PROTEIN ELECTROPHORESIS WITH IMMUNOFIXATION

SERUM FREE LIGHT CHAIN ASSAY (KAPPA/LAMDA RATIO)

Immunofixation will reveal an M-protein

sFLC will reveal an abnormal kappa-lambda ratio.
< 0.26 - monoclonal lambda light chain process
> 1.65 - monoclonal kappa light chain process.



Ontario Ministry of Health and Long-Term Care
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Clinician/Practitioner Number: 013014
CPSO / Registration No.: 69137

Check (✓) one: ☑ OHIP/Insured ☐ Third Party / Uninsured ☐ WSIB

Additional Clinical Information (e.g. diagnosis)

Laboratory Use Only

Clinician/Practitioner's Contact Number for Urgent Results: (905) 849-4567
Service Date: yyyy mm dd
Health Number: 12345678922
Version
Sex: M
Date of Birth: yyyy 1936 mm 11 dd 05
Province
Other Provincial Registration Number
Patient's Telephone Contact Number: (905) 000-0000

Patient's Last Name (as per OHIP Card): TESTER
CHESTER
Patient's Address (including Postal Code)
24 Sussex Drive
Oakville ON
L6L 4W4

☑ Copy to: Clinician/Practitioner
Dr. V Chiamvimonvat
690 Dorval Drive, Suite 300-3
L6K 3W7
Oakville

Note: Separate requisitions are required for cytology, histology / pathology and tests performed by Public Health Laboratory

x **Biochemistry**
- ☐ Glucose ☐ Random ☐ Fasting
- ☐ HbA1C
- ☐ Creatinine (eGFR)
- ☐ Uric Acid
- ☐ Sodium
- ☐ Potassium
- ☐ ALT
- ☐ Alk. Phosphatase
- ☐ Bilirubin
- ☐ Albumin
- ☐ Lipid Assessment (includes Cholesterol, HDL-C, Triglycerides, calculated LDL-C & Chol/HDL-C ratio; individual lipid tests may be ordered in the "Other Tests" section of this form)
- ☐ Albumin / Creatinine Ratio, Urine
- ☐ Urinalysis (Chemical)
- ☐ Neonatal Bilirubin: Child's Age: days hours
- Clinician/Practitioner's tel. no. ( )
- Patient's 24 hr telephone no. ( )
- ☐ Therapeutic Drug Monitoring: Name of Drug #1, Name of Drug #2, Time Collected #1 hr. #2 hr., Time of Last Dose #1 hr. #2 hr., Time of Next Dose #1 hr. #2 hr.

x **Hematology**
- ☐ CBC
- ☐ Prothrombin Time (INR)

Immunology
- ☐ Pregnancy Test (Urine)
- ☐ Mononucleosis Screen
- ☐ Rubella
- ☐ Prenatal: ABO, Rh D, Antibody Screen (titre and ident. if positive)
- ☐ Repeat Prenatal Antibodies

Microbiology ID & Sensitivities (if warranted)
- ☐ Cervical
- ☐ Vaginal
- ☐ Vaginal / Rectal – Group B Strep
- ☐ Chlamydia (specify source):
- ☐ GC (specify source):
- ☐ Sputum
- ☐ Throat
- ☐ Wound (specify source):
- ☐ Urine
- ☐ Stool Culture
- ☐ Stool Ova & Parasites
- ☐ Other Swabs / Pus (specify source):

x **Viral Hepatitis** (check one only)
- ☐ Acute Hepatitis
- ☐ Chronic Hepatitis
- ☐ Immune Status / Previous Exposure Specify: ☐ Hepatitis A ☐ Hepatitis B ☐ Hepatitis C
or order individual hepatitis tests in the "Other Tests" section below

Prostate Specific Antigen (PSA)
- ☐ Total PSA ☐ Free PSA
Specify one below:
- ☐ Insured – Meets OHIP eligibility criteria
- ☐ Uninsured – Screening; Patient responsible for payment

Vitamin D (25-Hydroxy)
- ☐ Insured - Meets OHIP eligibility criteria: osteopenia; osteoporosis; rickets; renal disease; malabsorption syndromes; medications affecting vitamin D metabolism
- ☐ Uninsured - Patient responsible for payment

Other Tests - one test per line
URINE PROTEIN ELECTROPHORESIS WITH IMMUNOFIXATION
SERUM PROTEIN ELECTROPHORESIS WITH IMMUNOFIXATION
SERUM FREE LIGHT CHAIN ASSAY (KAPPA/LAMDA RATIO)

Specimen Collection
Time Date MM/DD/YYYY

Fecal Occult Blood Test (FOBT) (check one)
☐ FOBT (non CCC) ☐ ColonCancerCheck FOBT (CCC) no other test can be ordered on this form

Laboratory Use Only

I hereby certify the tests ordered are not for registered in or out patients of a hospital.

x Clinician/Practitioner Signature
Apr 03, 2020 Date

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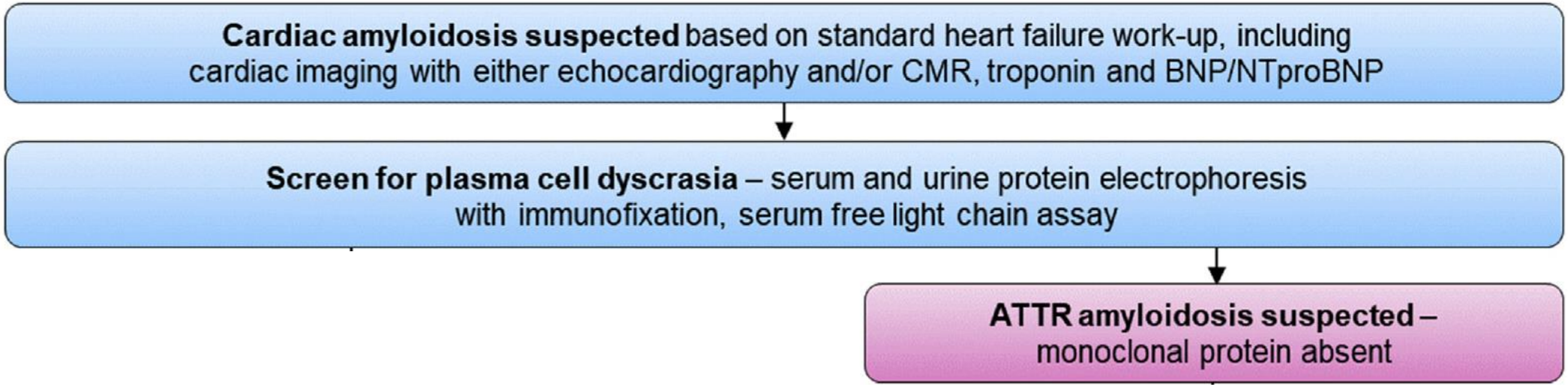
Diagnosis: Ruling in ATTR



Diagnosis: Establishing Cardiac PYP Scanning

Radiopharmaceutical and Dose: Tc99m Pyrophosphate / 15-20mCi

Imaging Time: 1 hour-post injection

May have to image at 2 hours post injection if the heart : contralateral ratio is 1.3-1.6 (equivocal range) and/or the visual grade is 1 or 2

Acquisition: Planars: Anterior, Left Lateral (8min/750kcts/Zoom 1.5)

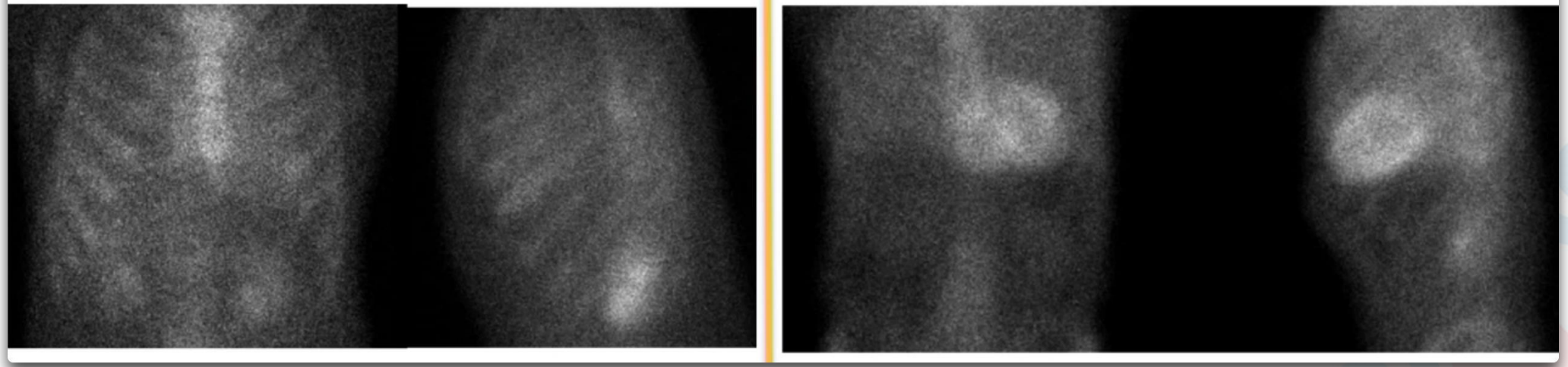
SPECT and gated planars (differentiate between myocardial uptake vs blood pool) should be performed for equivocal studies.

Visual Scoring

0 = absent cardiac uptake **1** = mild uptake less than ribs

2 = moderate uptake equal to ribs **3** = high uptake greater than ribs

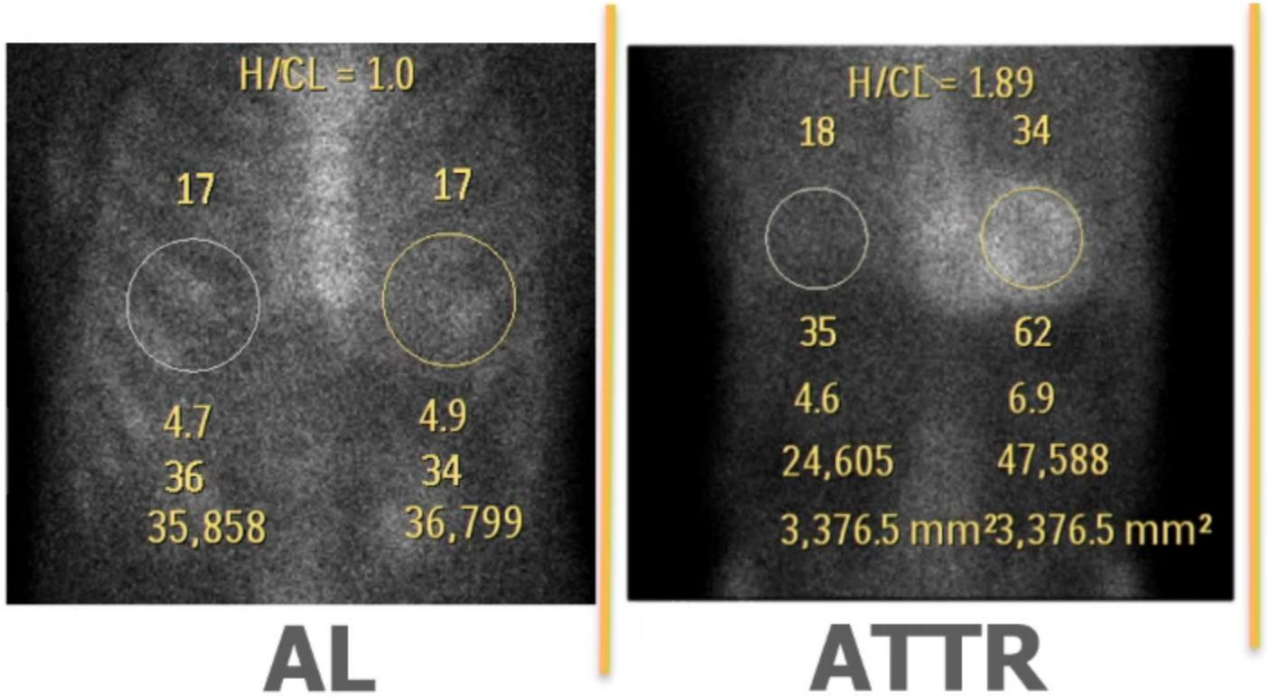
Absent cardiac uptake on planar ^{99m}Tc-PYP images

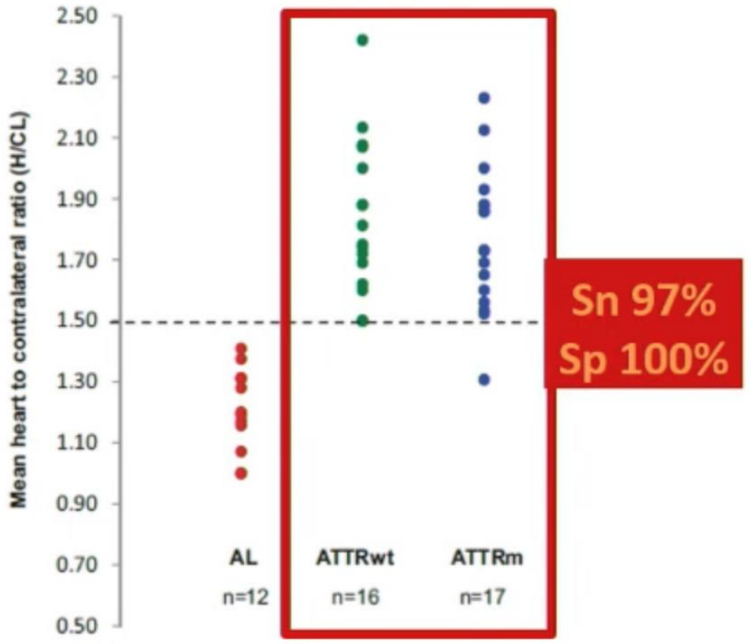


Opacity in cavity excludes blood pool

Quantitative Analysis

- Circular ROI over heart, copied, mirrored CL chest
- Mean counts/pixel corrected for background counts
- Heart-to-contralateral ratio (H/CL)





#ASNC2019

Bokhari et al: *Circ Cardiovasc Imag* 2013

Cardiac PYP: Stepwise Image Analysis

- Image quality
  - Need to see the ribs and sternum clearly
- Visual Scan interpretation
  - Note focal hotspots and agreement with sampling windows
- Semi-quantatative interpretation in relation to rib uptake
  - Grade 0 to 3
- Quantitative scoring of heart to contralateral lung ratio
- SPECT analysis for equivocal studies
  - Rule in or out blood pool false positive

Responding to the PYP Result

Positive

Refer to regional centre for treatment until this is more widely available

Would expect local initiation of therapy in the future

Equivocal

Rescan PYP with SPECT

Perform cardiac MRI

Biopsy

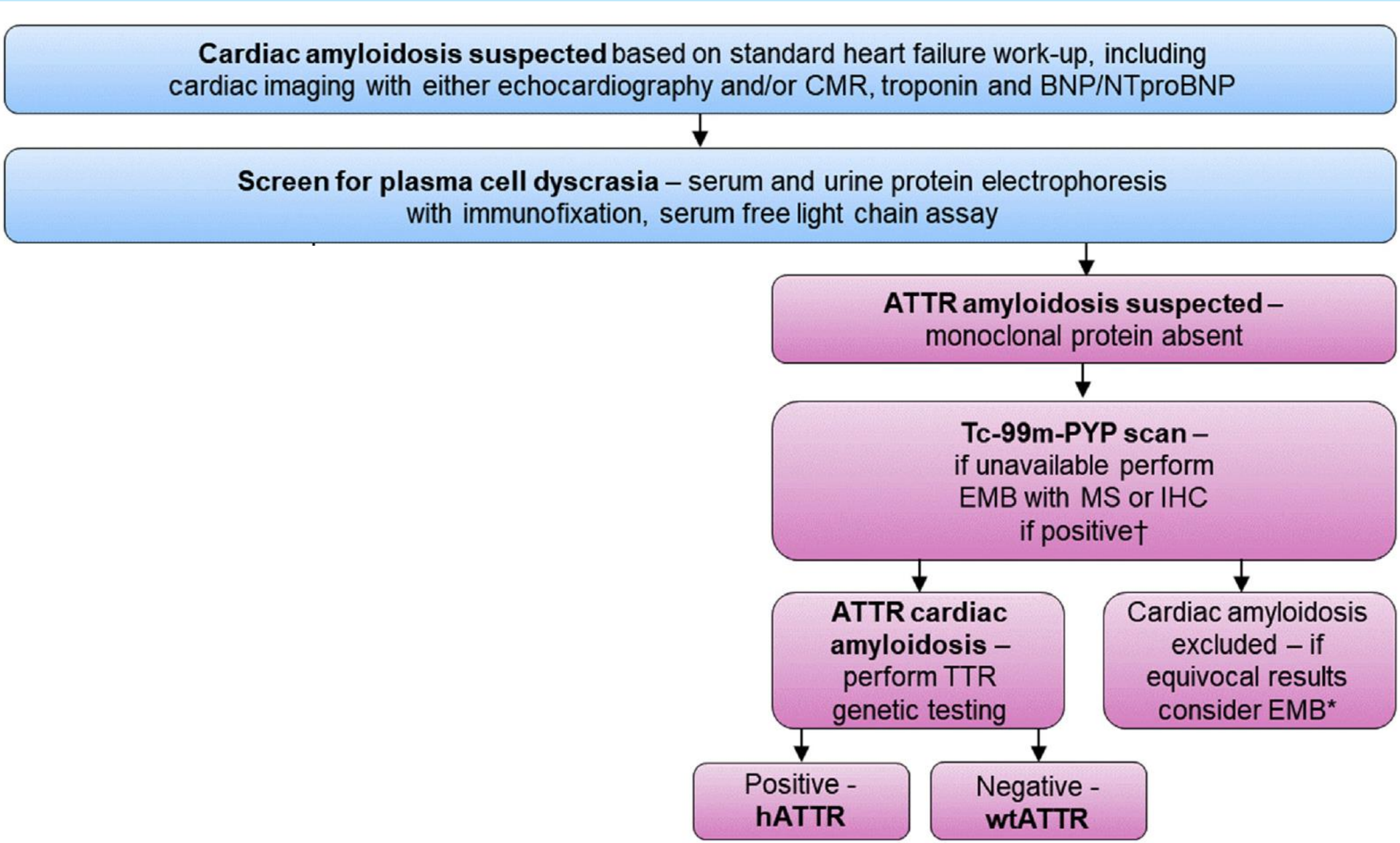
Negative

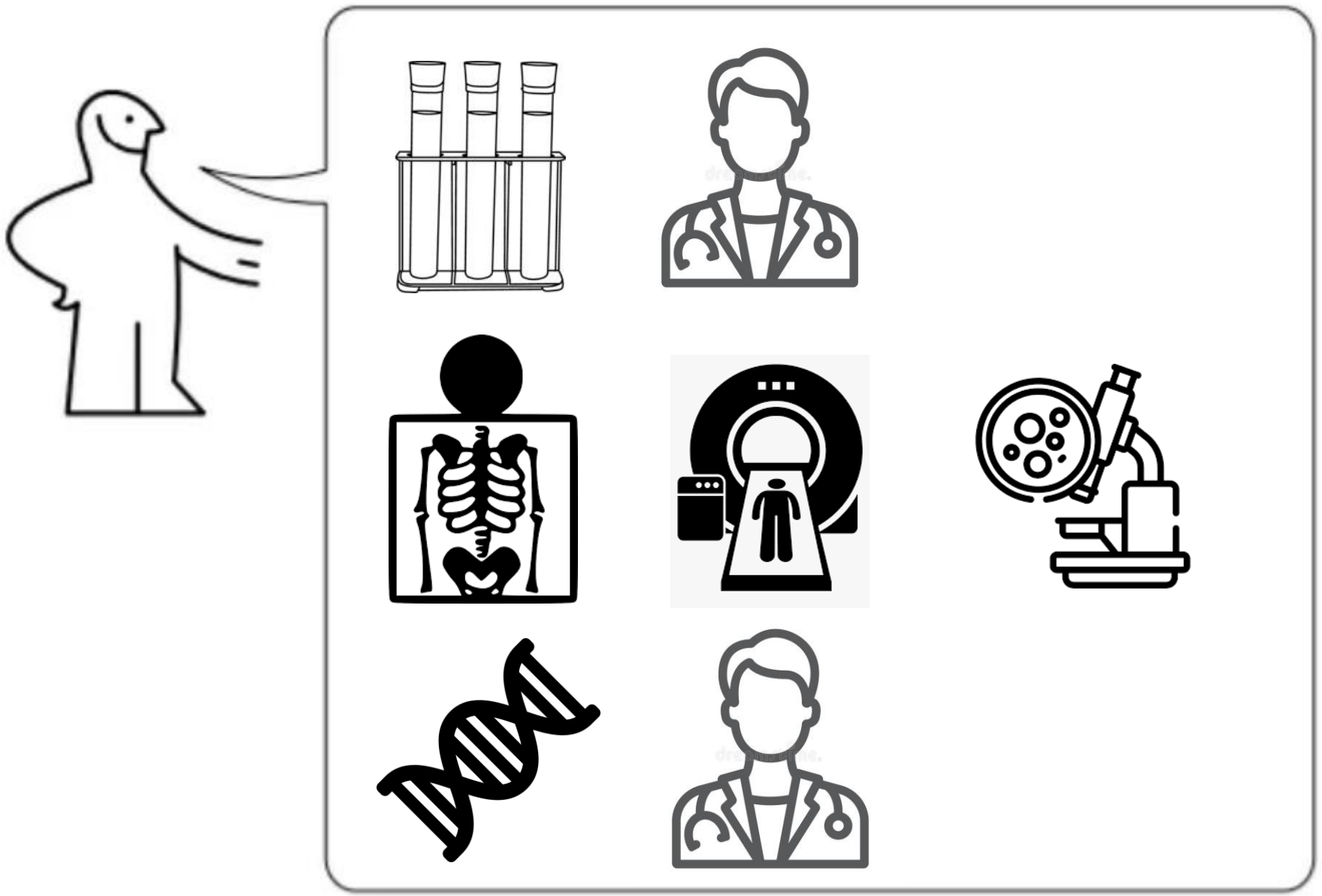
Consider another etiology

A full-length variant (Phe64Leu and Thr59Lys) is an important false negative and will require a biopsy if your clinical suspicion is high

Diagnosis: Genetic Analysis

- A positive ATTR patient will require genetic testing
- Genetic tests are readily available (similar to the 23andMe home kit)
- Wide regional variation of accessibility to genetic counselling
- Recognized mutations (hATTR) and wild type (wATTR) are definitive
- Mutations of unknown significance are just that
  - Input of a geneticist is helpful


Cardiac amyloidosis suspected based on standard heart failure work-up, including cardiac imaging with either echocardiography and/or CMR, troponin and BNP/NTproBNP
Screen for plasma cell dyscrasia – serum and urine protein electrophoresis with immunofixation, serum free light chain assay
ATTR amyloidosis suspected – monoclonal protein absent
Tc-99m-PYP scan – if unavailable perform EMB with MS or IHC if positive†
ATTR cardiac amyloidosis – perform TTR genetic testing
Cardiac amyloidosis excluded – if equivocal results consider EMB*
Positive - **hATTR**
Negative - **wtATTR**


Rx

Q&A

Evaluations and Certificates

- Here's how to access evaluations:
  - Congress APP: "Evaluation Forms" icon
  - You'll also get a notification and email each day with evaluation links

- Information regarding certificates to be emailed next week

Next Up…A Break

- Don’t disconnect!! – Plenary Session #4 is coming up in a few minutes
- Remember to complete **all evaluations** – Go to congress APP or your email
  - To Download the app: Search **CrowdCompass AttendeeHub**; Find **Heart Failure Update**
- Visit the VIRTUAL EXHIBIT HALL on HFupdate.ca - Uber Eats gift cards offered!

Thank you!