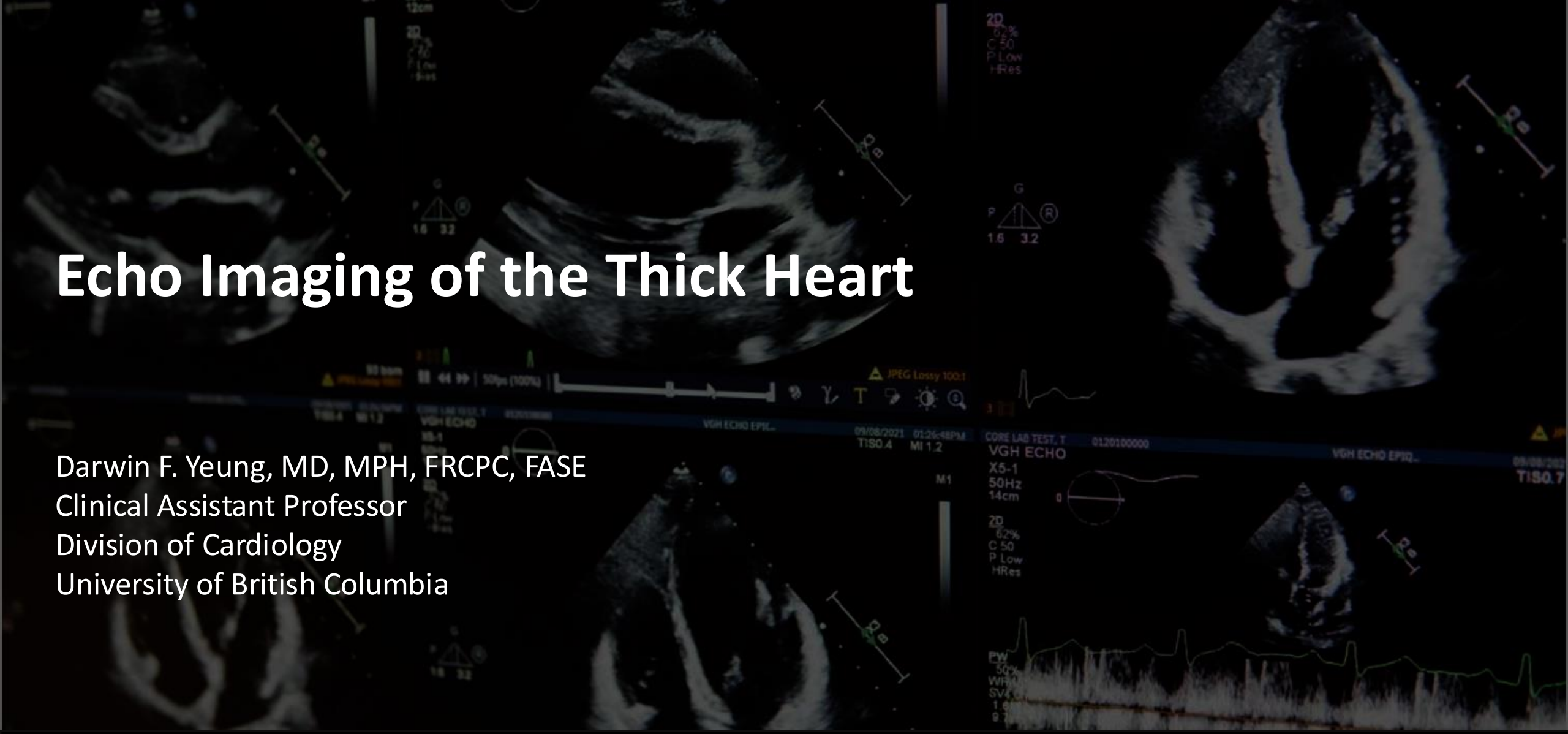

Echo Imaging of the Thick Heart

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Healthier lives through discovery

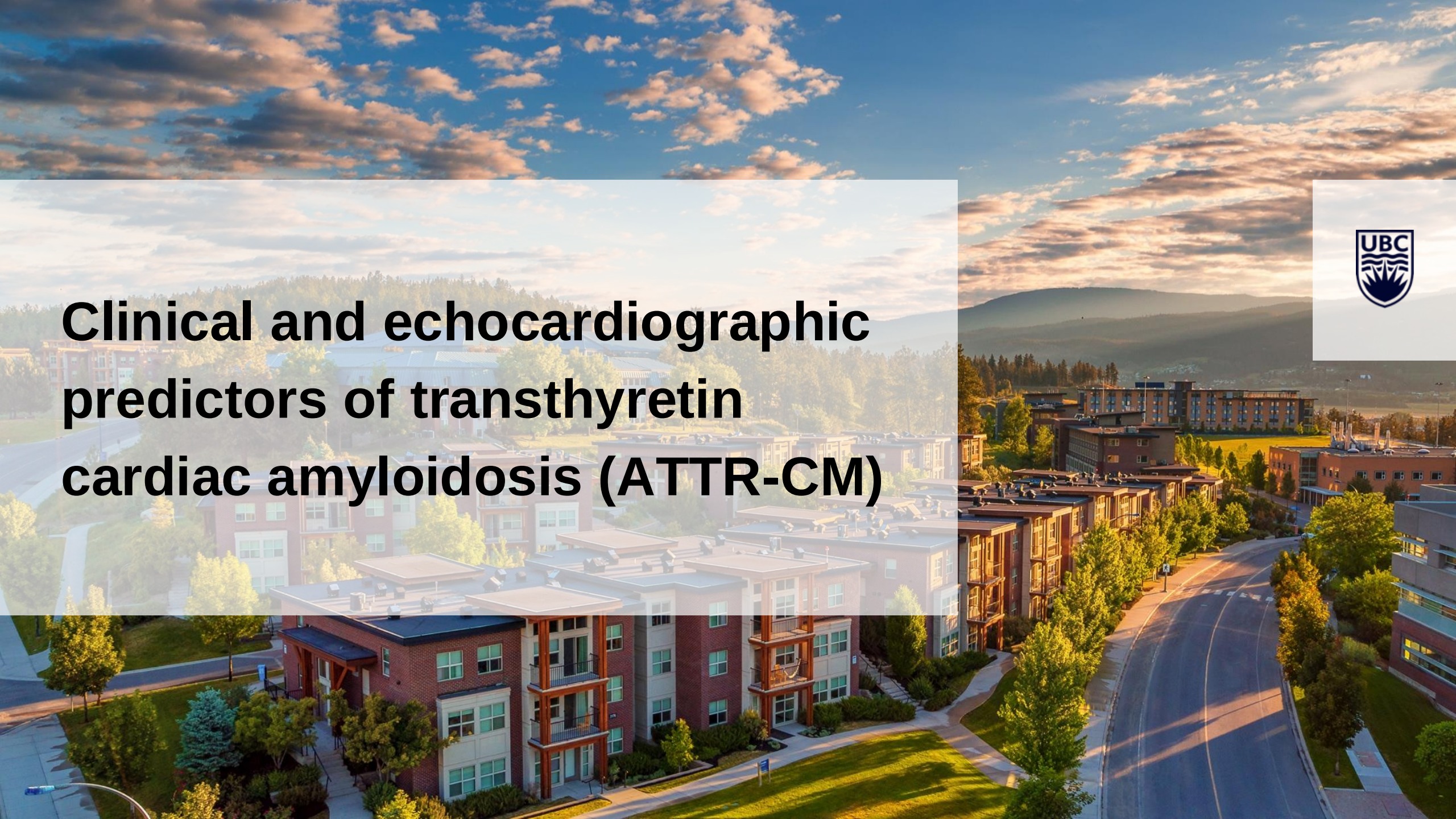
CCI-CIC Centre for Cardiovascular Innovation
Centre d'Innovation Cardiovasculaire

UBC

Overview of Research Program and Current Projects

Echo Assessment of Non-Ischemic Cardiomyopathies

Echo Imaging of the Thick Heart	Echo Insights into Valvular Heart Disease	Refining Diastolic Function Assessment
Hypertrophic Cardiomyopathy	**Severe Aortic Stenosis**	**LA strain vs. PCWP correlation**
• Echo predictors of genetic yield	• Myocardial mechanics pre-/post- AVR	• LA strain to predict invasive PCWP
Cardiac Amyloidosis	**Tricuspid Regurgitation**	**LA strain vs. LVEDP correlation**
• Echo predictors of ATTR-CM	• TR severity vs. AF burden association	• LA strain to predict invasive LVEDP
Fabry Cardiomyopathy	**Carcinoid Heart Disease**	**AI score vs. LVEDP correlation**
• Prevalence of apical HCM/aneurysm	• Contemporary prevalence in NET cohort	• AI score to predict invasive LVEDP
Hypertensive Heart Disease	**Severe Mitral Regurgitation**	**AI score vs. outcomes correlation**
• Prevalence of LVH / LVH regression	• Optimizing patient selection for TEER	• AI score to predict HF outcomes



Clinical and echocardiographic predictors of transthyretin cardiac amyloidosis (ATTR-CM)

Disclosures

Grants/Research Support: Vancouver Coastal Health Research Institute, Sanofi

Honoraria: Pfizer, Takeda, Sanofi, Bristol Myers Squibb

Background

Heart failure is a leading cause of hospitalization and is associated with high mortality.

Transthyretin amyloid cardiomyopathy (ATTR-CM) is an under-recognized cause of heart failure caused by the deposition of misfolded proteins in the heart.

Certain clinical and echocardiographic characteristics can be suggestive but by themselves not definitively diagnostic of ATTR-CM.

While the diagnosis of ATTR-CM previously depended on a cardiac biopsy, due to recent advances in nuclear imaging, the diagnosis can now be made non-invasively.

Furthermore, a novel disease-modifying therapy has recently been shown to improve survival in patients with ATTR-CM; therefore, timely diagnosis is now even more important.

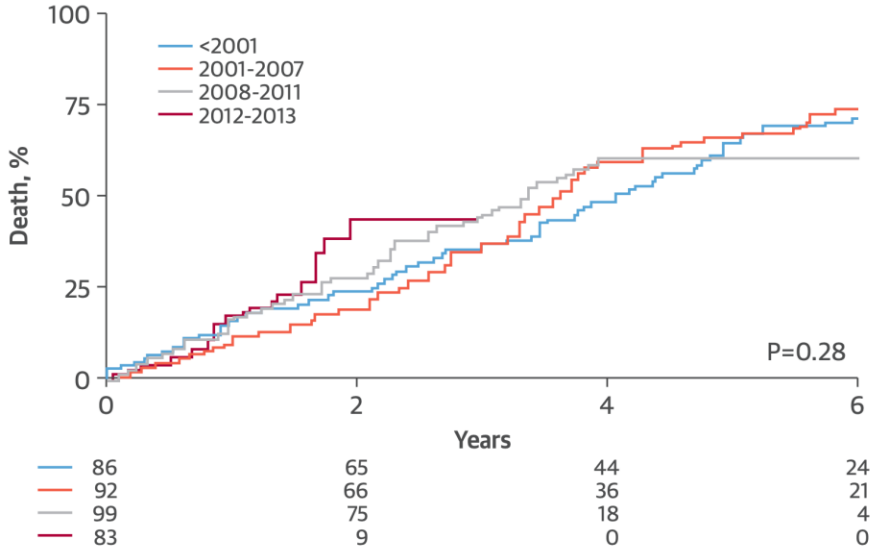
ATTR-CM prognosis and treatment

ATTR-CM has a median overall survival of 3.6 years if left untreated.

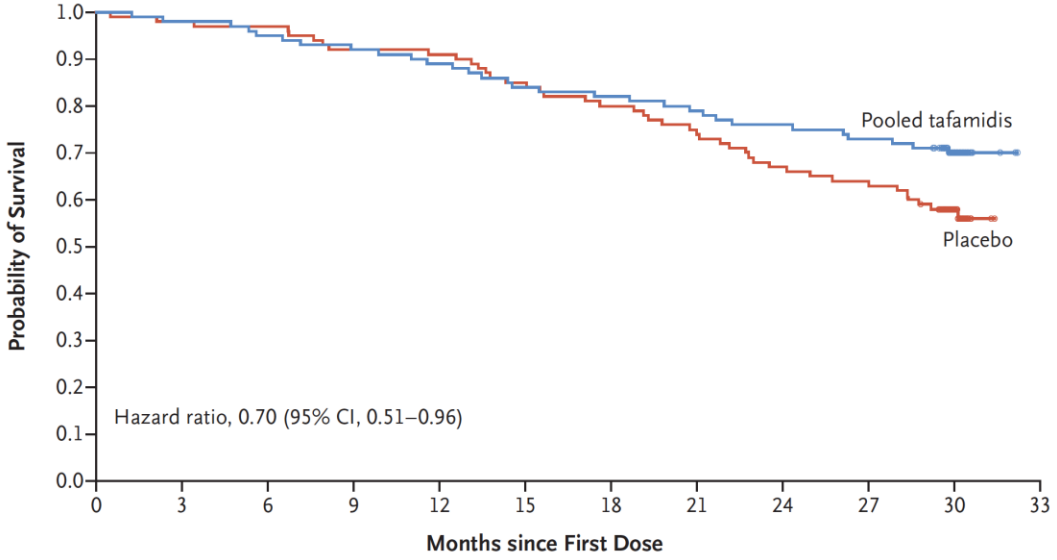
Prior to 2018, there were no effective disease-modifying therapies available.

Since then, tafamidis has been shown to reduce all-cause mortality and CV-related hospitalizations.

Natural history of wild-type ATTR-CM



Survival in ATTR-CM patients treated with tafamidis vs. placebo



Grogan et al (*J Am Coll Cardiol*, 2016); Maurer et al (*NEJM*, 2018)

How common is ATTR-CM?

In an autopsy series of 256 patients aged ≥85 years, 25% had wild-type ATTR organ involvement.

In a prospective study of 120 patients >60 years with heart failure with preserved ejection fraction and left ventricular wall thickness >12 mm, 16 (13%) were found to have wild-type ATTR-CM.

In 150 patients (mean age 67.4 ± 1.0 years) undergoing aortic and mitral valve surgery, ATTR deposits were found in 83 (55%) of them.

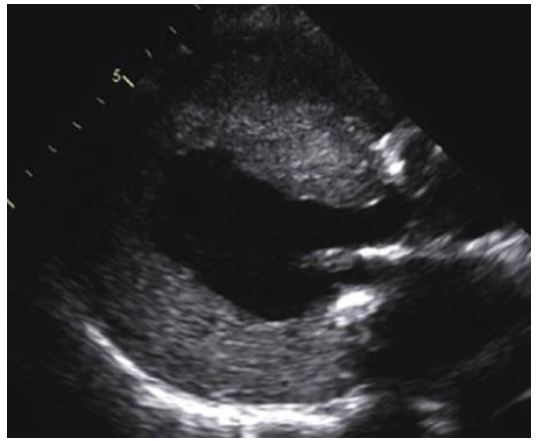
In a cohort of 151 patients with severe symptomatic aortic stenosis who underwent transcatheter aortic valve replacement, 24 (16%) of them were eventually found to be positive for ATTR-CM.

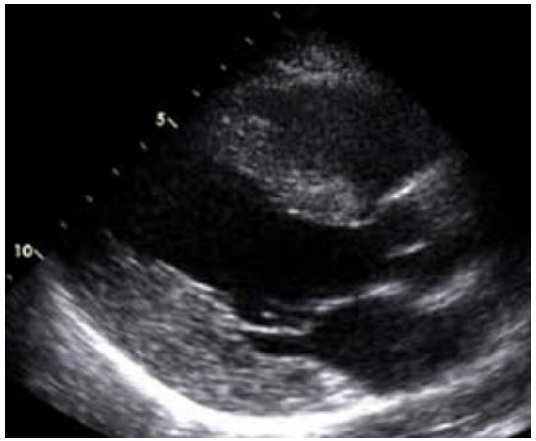
Among 98 patients (men aged ≥50 years and women aged ≥60 years) undergoing carpal tunnel release, 10% had amyloid deposits in their surgical specimens.

Kristen (*Cardiovasc Path*, 2010); Gonzalez-Lopez (*Eur Heart J*, 2015); Castaño (*Eur Heart J*, 2017); Tanskanen (*Ann Med*, 2008); Sperry (*J Am Coll Cardiol,* 2018)

Other causes of increased left ventricular wall thickness

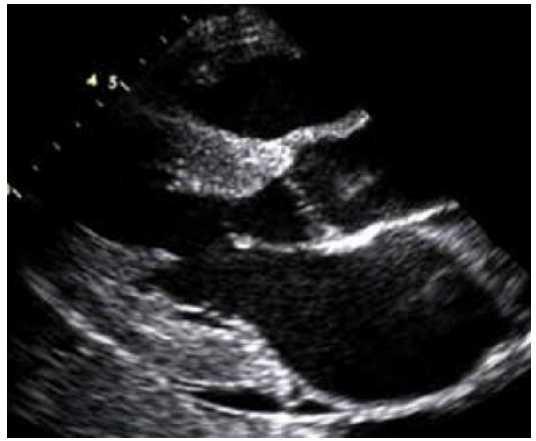
Fabry disease

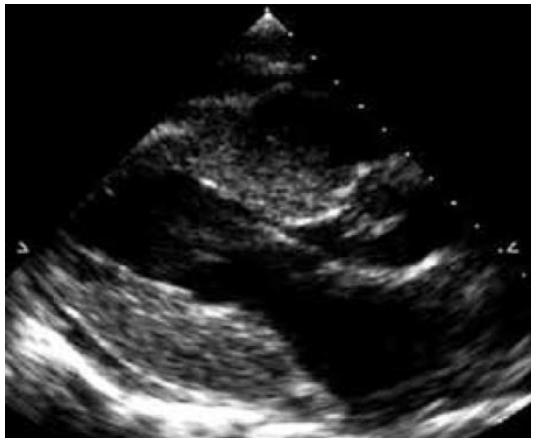




Hypertrophic cardiomyopathy

Amyloidosis

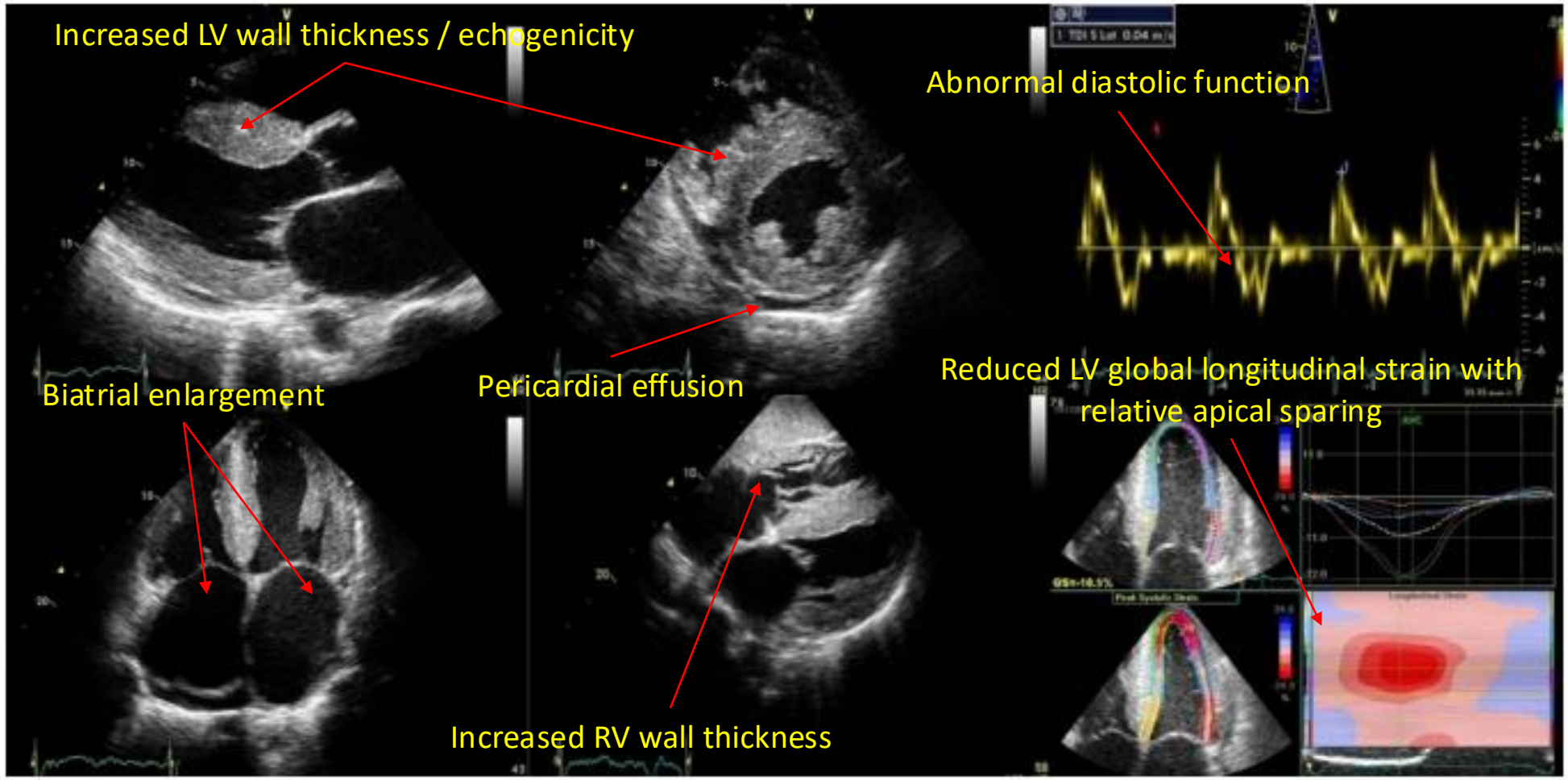




Hypertension

Seward (*J Am Coll Cardiol*, 2010) / Geske et al (*J Am Coll Cardiol*, 2014)

Classic echo features of cardiac amyloidosis

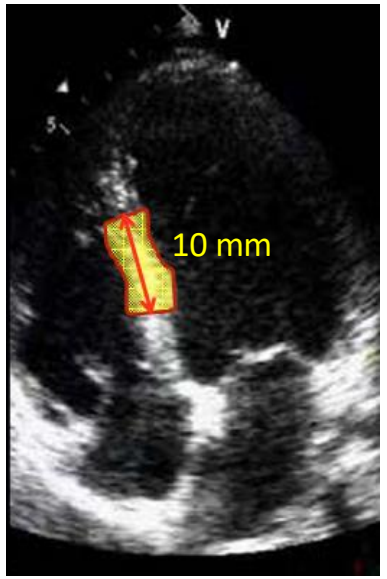


Dungu et al (*Heart*, 2012)

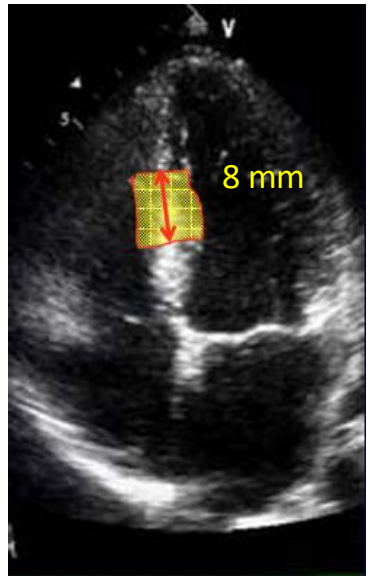
A primer on strain imaging

$$\text{Strain} = \frac{L - L_0}{L_0} = \frac{\Delta L}{L_0}$$

$$= \frac{8 - 10}{10} = -20\%$$



End Diastole



End Systole

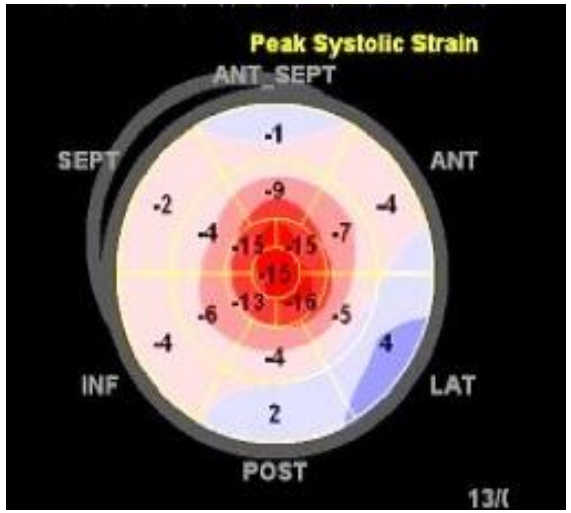
Strain measures the % change in fiber length when the heart contracts compared to its original length when relaxed.

Longitudinal strain is a negative value since muscle fibers shorten during myocardial contraction.

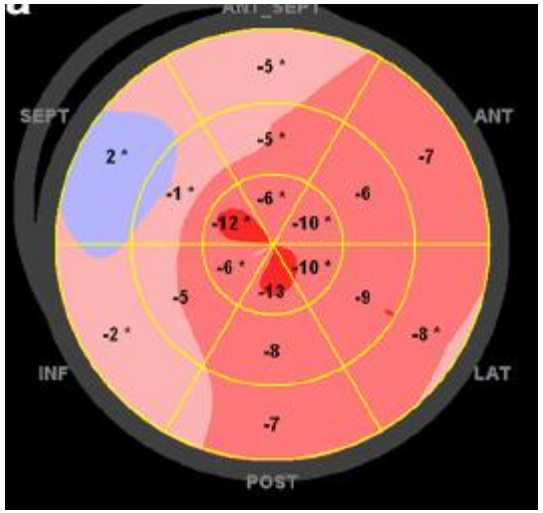
A value more negative than -18% is considered normal in our echo lab (-16% to -18% considered borderline).

Slide contents courtesy of Dr. Michael Tsang and Dr. Teresa Tsang; Gorcsan (ASE, 2017)

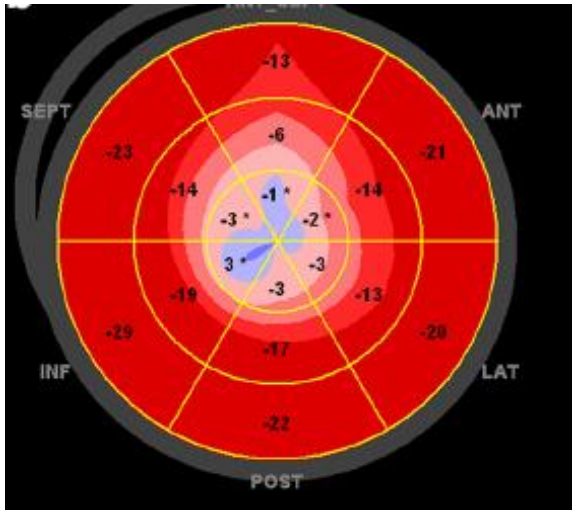
Strain patterns could provide clues to the diagnosis



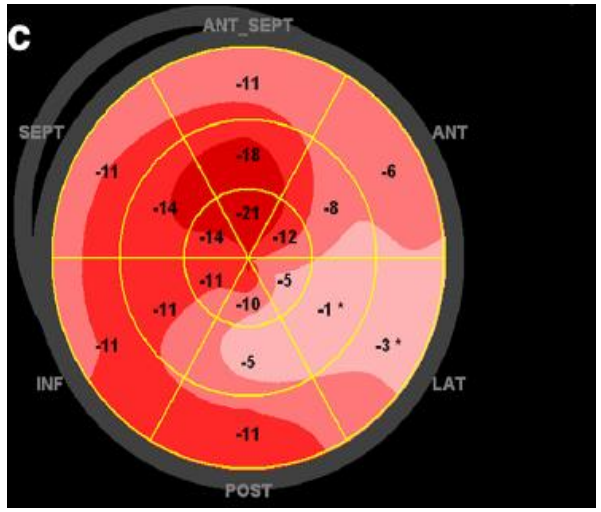
Cardiac amyloidosis



Hypertrophic cardiomyopathy (asymmetric septal hypertrophy)



Hypertrophic cardiomyopathy (apical variant)



Fabry disease

Liu et al (*Eur J Med Res*, 2016)

How do we quantify relative apical sparing?

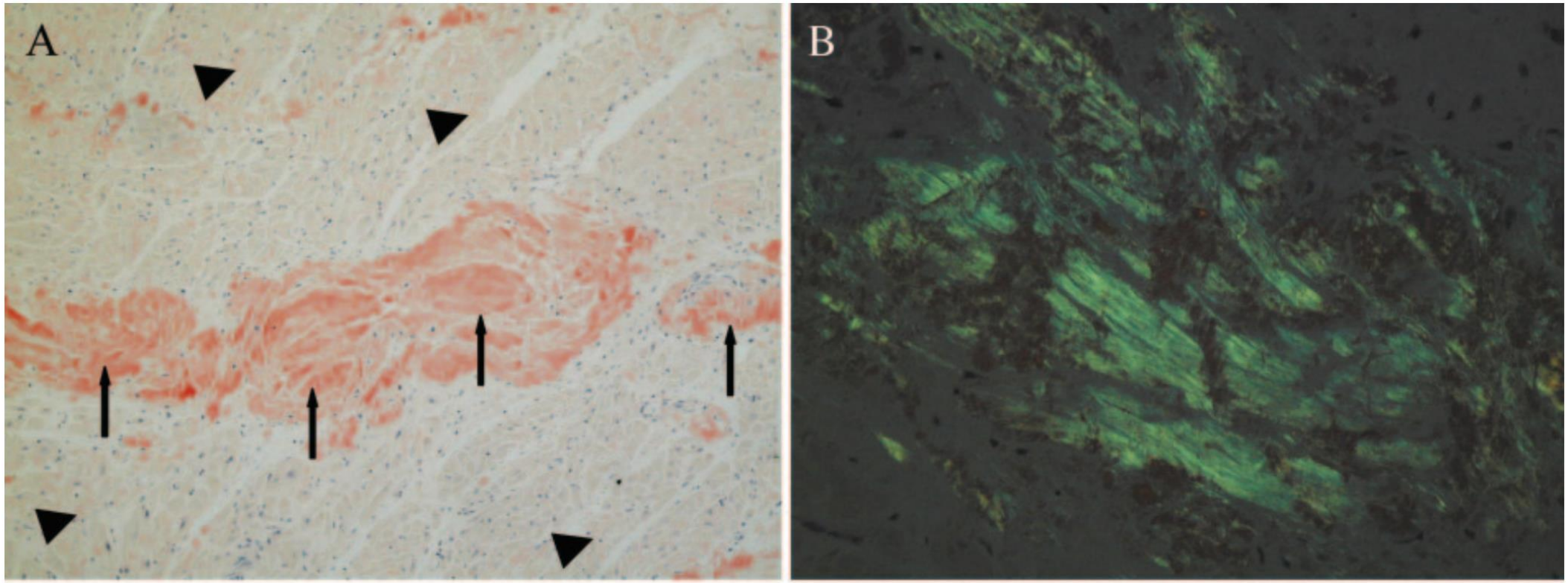
$$\text{Relative apical LS} = \frac{\text{Average apical LS}}{\text{Average basal LS} + \text{Average mid LS}}$$

The initial study that proposed relative apical sparing of longitudinal strain as a potential sign of cardiac amyloidosis compared 55 consecutive patients with cardiac amyloid to 30 controls (15 with hypertrophic cardiomyopathy, 15 with aortic stenosis).

A relative apical longitudinal strain (RALS) >1.0 had a 93% sensitivity and 82% specificity in differentiating cardiac amyloidosis from controls in that small study.

Phelan D et al (*Heart*, 2012)

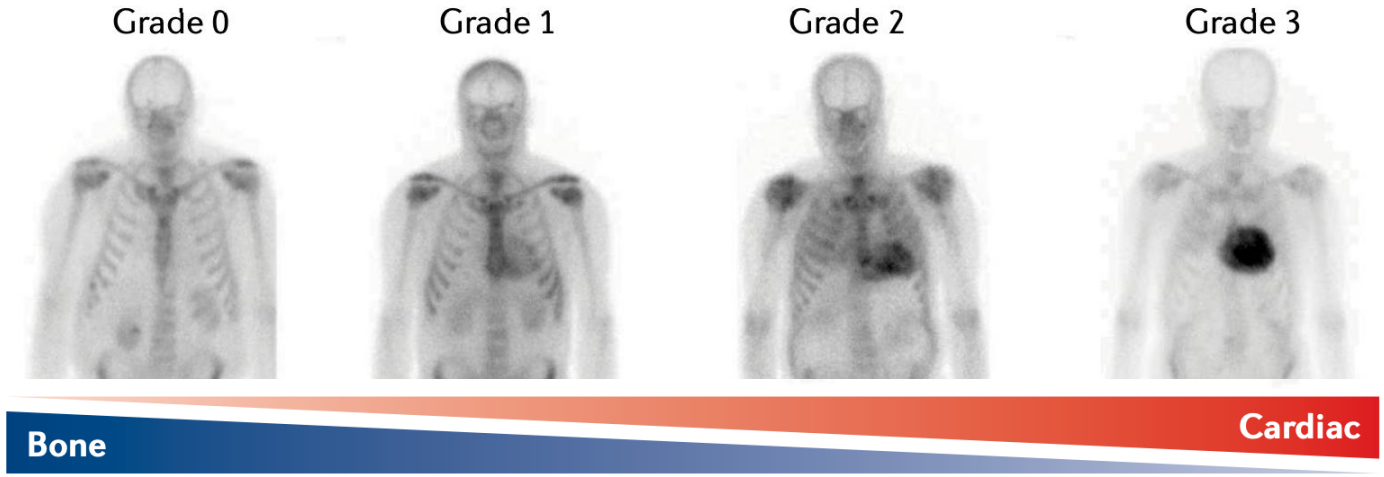
Cardiac biopsy for pathologic diagnosis



Congo red staining of amyloid tissue produces apple-green birefringence under polarized light.

Maceira AM et al (*Circulation*, 2005)

Pyrophosphate scan as an alternative to cardiac biopsy



Grade	Myocardial ^{99m}Tc-PYP Uptake
Grade 0	no uptake and normal bone uptake
Grade 1	uptake less than rib uptake
Grade 2	uptake equal to rib uptake
Grade 3	uptake greater than rib uptake with mild/ absent rib uptake

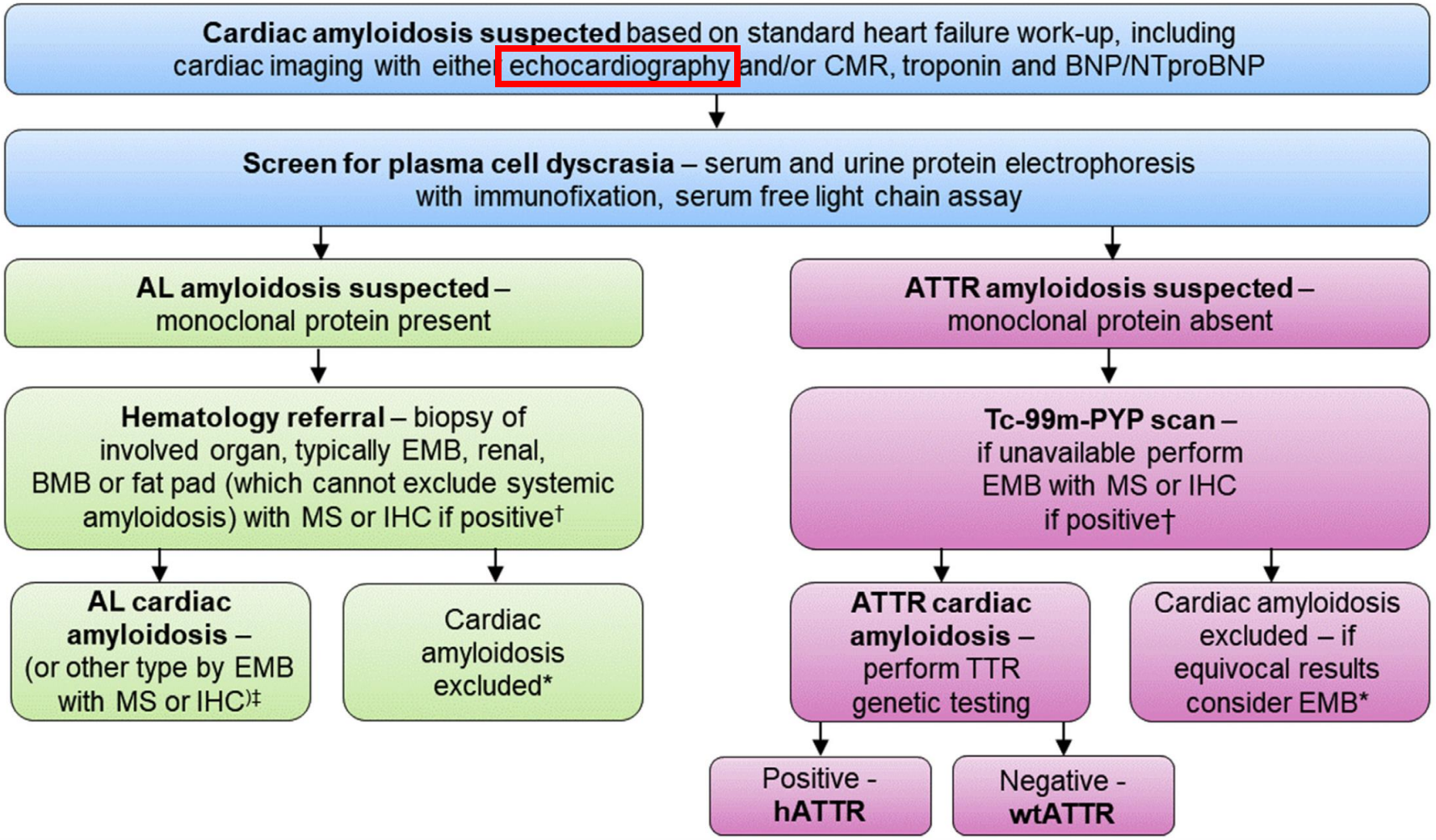
Bone-seeking radiotracers accumulate in the myocardium of patients with amyloid (especially ATTR-CM).

Grade 2 or 3 is considered positive.

In the absence of monoclonal protein in serum or urine, a PYP scan demonstrates >99% sensitivity and specificity for diagnosis of ATTR-CM.

Martinez-Naharro A et al (*Nature Reviews*, 2020); Gillmore et al (Circulation, 2016)

Current diagnostic algorithm



Fine NM, Davis MK et al (*Can J Cardiol*, 2020)

Study aims

1. To compare the clinical and echo characteristics between patients with and without ATTR-CM in a cohort of patients referred for PYP scan for suspected ATTR-CM.

2. To assess the test characteristics of the relative apical longitudinal strain ratio and similar longitudinal strain metrics to differentiate patients with or without ATTR-CM in a diverse real-world cohort of patients with suspected ATTR-CM.

3. To develop a scoring system based on clinical and/or echo parameters to predict ATTR-CM derived from the local cohort of patients with suspected ATTR-CM.

Hypotheses

1. There will be significant differences in clinical and echo characteristics between patients with and without ATTR-CM in the cohort of patients referred for PYP scan with suspected ATTR-CM.

2. The relative apical longitudinal strain ratio and similar longitudinal strain metrics will perform less well to differentiate patients with or without ATTR-CM in this diverse real-word cohort of patients with suspected ATTR-CM (compared to in their previously published derivation and validation cohorts).

3. A scoring system based on clinical and/or echo parameters to predict ATTR-CM derived from the local cohort of patients with suspected ATTR-CM will provide incremental predictive value compared to individual parameters alone.

Study design

This is a retrospective diagnostic accuracy cross-sectional (cohort) study to identify clinical and echocardiographic predictors of transthyretin cardiac amyloidosis (ATTR-CM).

Study setting

British Columbia is the 3rd most populated province in Canada with >5 million residents (13.5%).

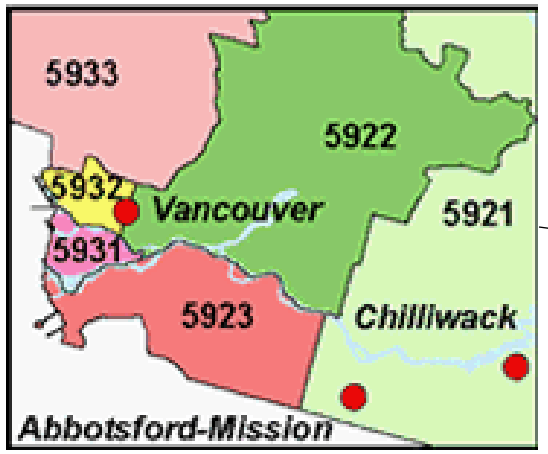
Just over half of BC residents live in Metro Vancouver area with >2.8 million (52%).

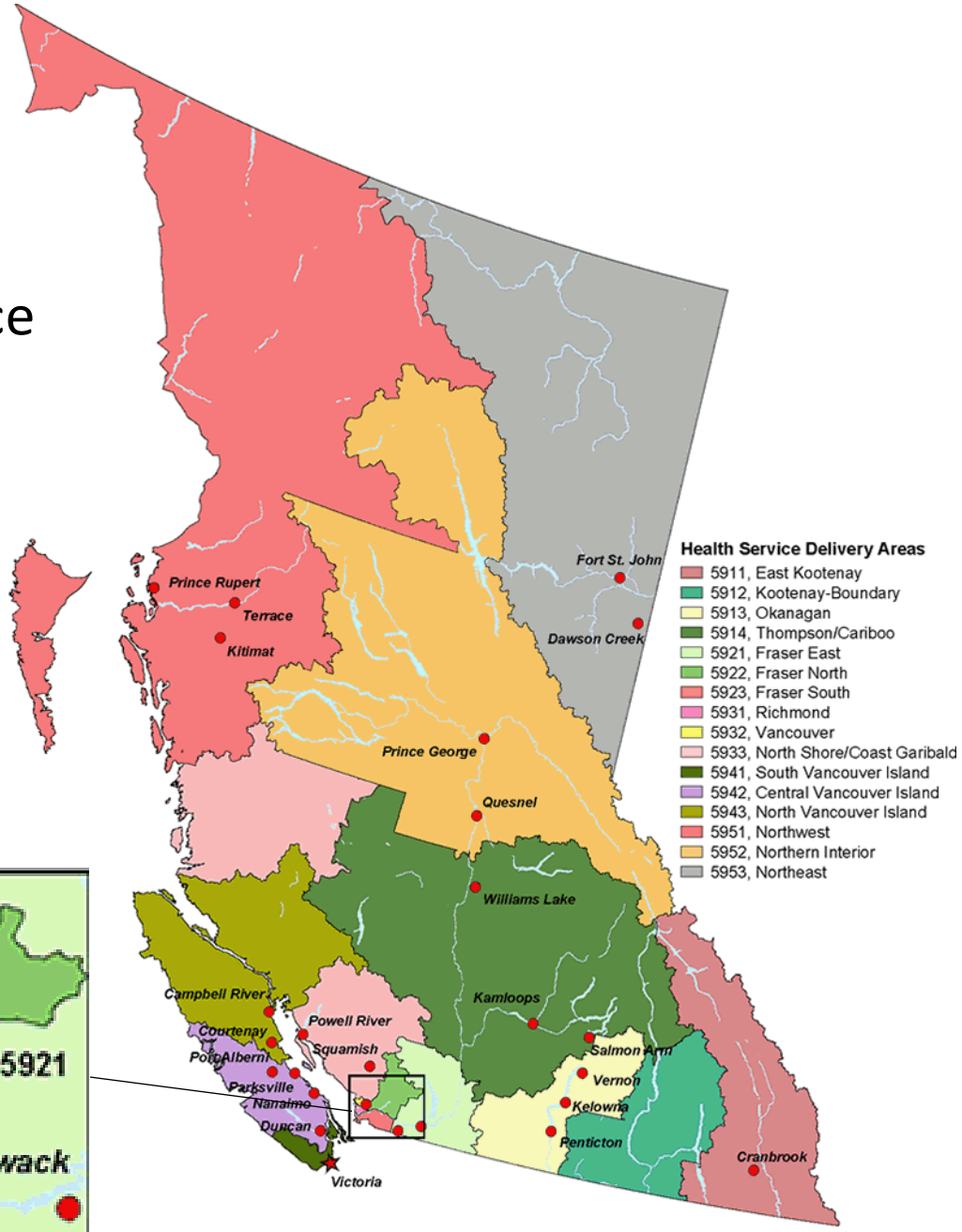
Ethnically diverse (34% visual minorities).

>12% live in rural communities.

Divided into health authorities.

Universal health care.





Statistics Canada: 2021 Census

Cohort construction

Inclusion criteria:

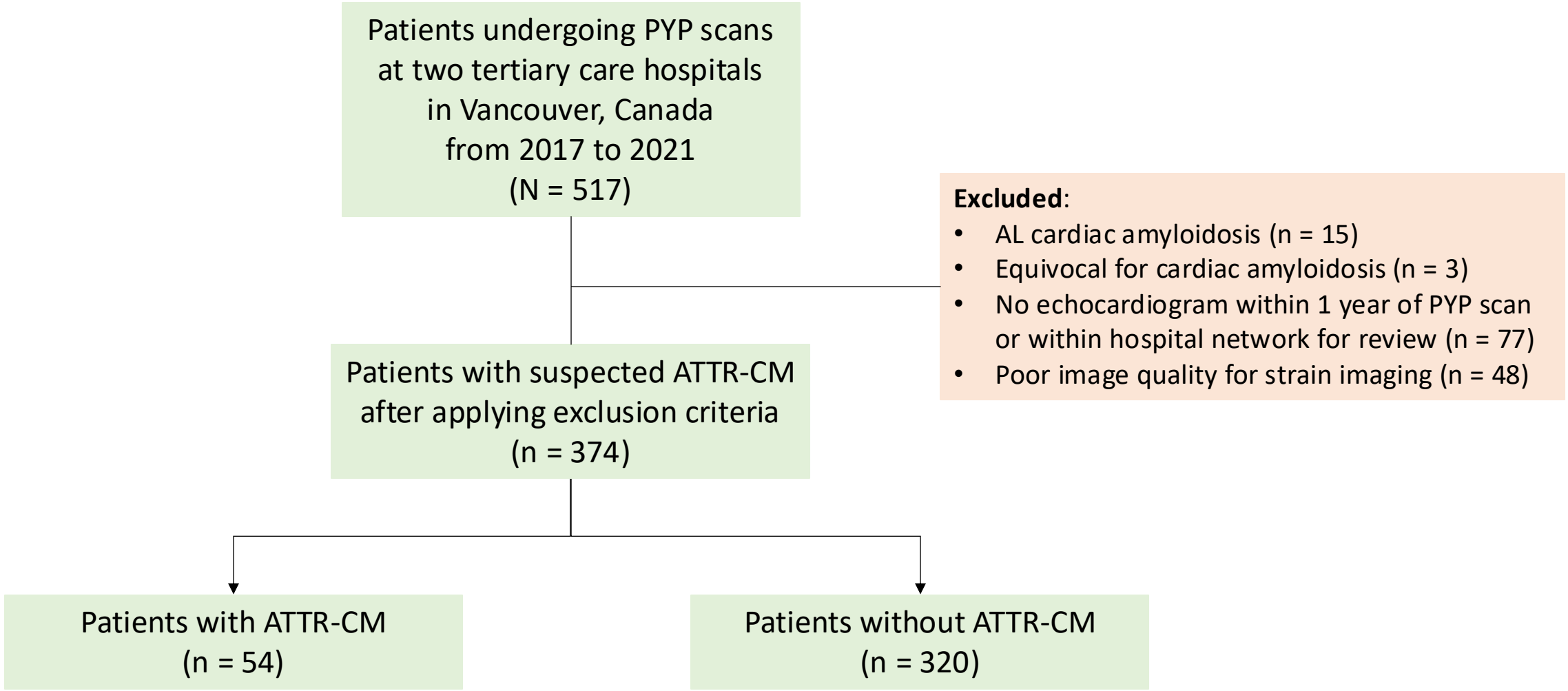
- Consecutive patients aged ≥18 years who underwent clinically indicated PYP scan for suspected ATTR-CM at the 2 largest tertiary care centers in Vancouver, Canada between January 1, 2017 and May 31, 2021.
- Clinical diagnosis of ATTR-CM (***gold standard*** in this study) based on:
  - Positive PYP scan (Grade 2 or 3) and absence of monoclonal gammopathy or multiple myeloma (which would suggest AL cardiac amyloid instead); or
  - Pathologic confirmation of ATTR-CM by endomyocardial biopsy if PYP scan equivocal.
- Echocardiogram performed within 1 year of the PYP scan in the 2 associated health authorities (reported by readers from 6 hospitals in the Metro Vancouver Area).

Cohort construction

Exclusion criteria:

- AL cardiac amyloidosis
- Equivocal for cardiac amyloidosis
- No echocardiogram performed within 1 year of PYP scan in the 6 hospitals associated with the 2 academic-affiliated health authorities
- Poor image quality (precluding the use of strain imaging)

Study cohort



Clinical and echo characteristics

The following relevant baseline clinical and echo characteristics were extracted by chart review:

Clinical characteristics:

Demographics: Age, sex, height, weight

Comorbidities: Diabetes, hypertension, heart failure, atrial fibrillation, device therapy (e.g., permanent pacemakers), prior TIA/stroke, chronic kidney disease, coronary artery disease, aortic stenosis, high-grade AV block

Echo characteristics:

Conventional: Left ventricle measurements (LVEF, IVSd, PWd, LVEDDi, LVMI, RWT);
LV diastolic function measurements (E and A velocities, e' velocities, E/e' ratio);
Right ventricle measurements (RVd, TAPSE, peak TR velocity, PASP, pericardial effusion);
Atrial measurements (LAVI, RAVI).

Advanced: LV global longitudinal strain (if available)

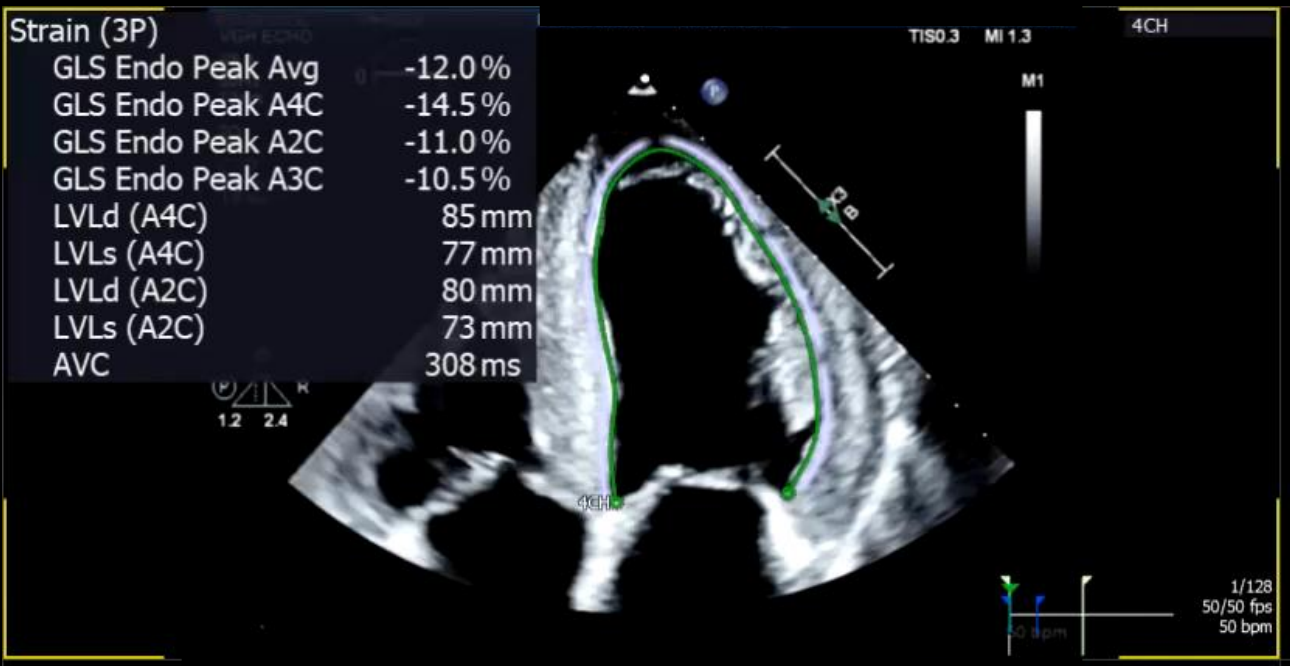
Raw echo images were reviewed and independent measurements performed if routine variables were missing on the report.

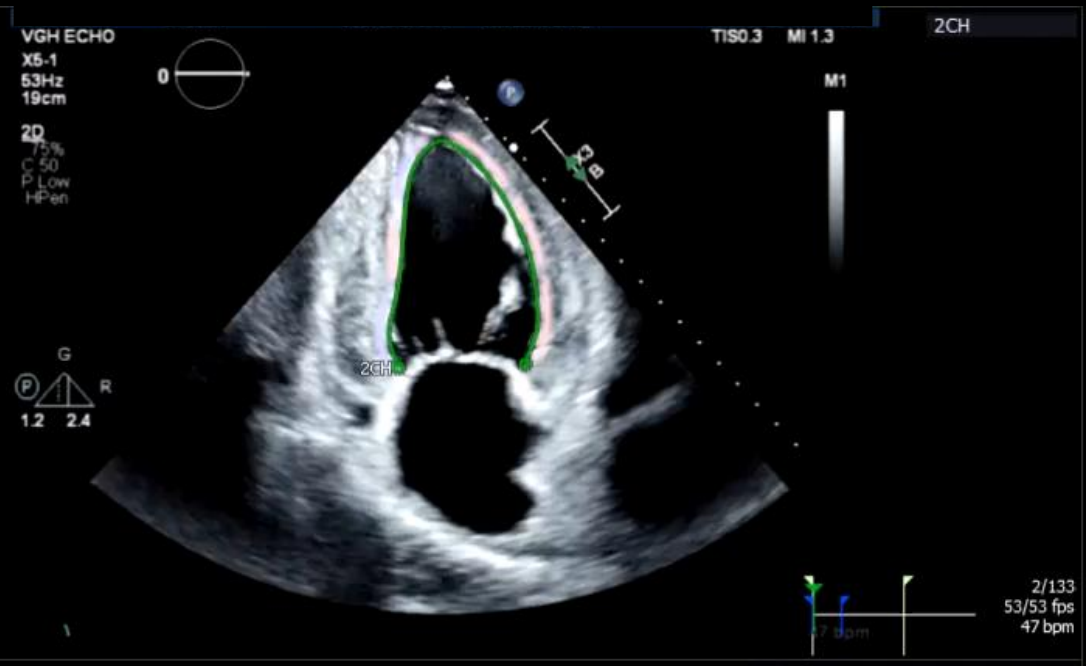
Longitudinal strain measurements

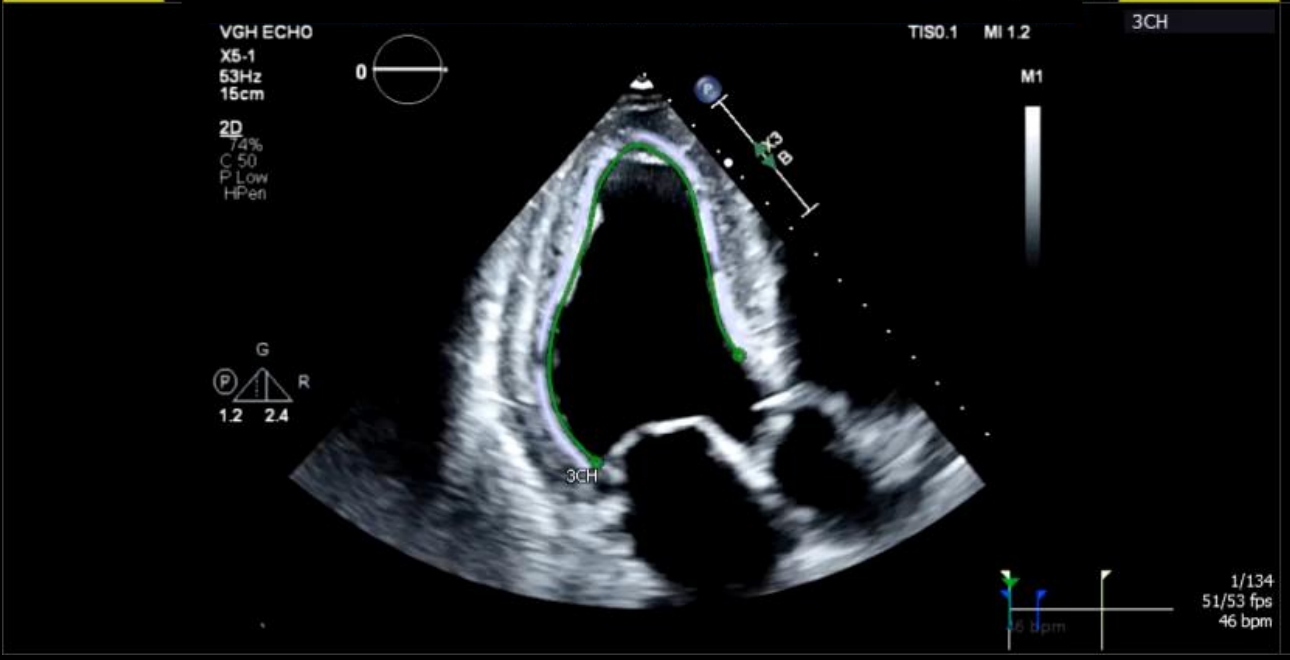
Given the lack of consistent reporting of strain measurements on the formal echo reports, LV longitudinal strain measurements were repeated in all patients in the cohort.

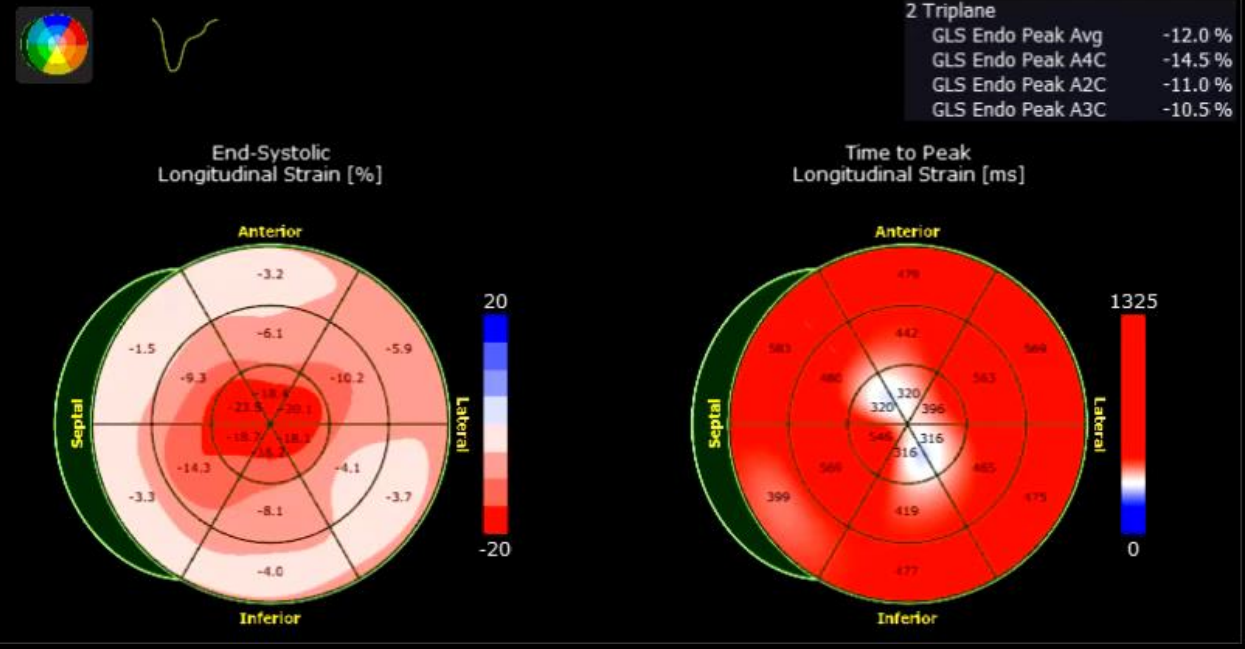
LV longitudinal strain analysis was performed using TomTec (strain analysis software):

- Highest-quality apical 4-chamber, 2-chamber, and long-axis views chosen for analysis;
- Analysis performed on a single cardiac cycle;
- Endocardial borders automatically traced by TomTec with manual adjustments made to optimize tracking;
- All measurements performed independently (blinded to the diagnosis of ATTR-CM);
- 1st echocardiographer performed repeat measurements in 20 patients for intra-observer variability;
- 2nd echocardiographer performed repeat measurements in 20 patients for inter-observer variability.


Strain (3P)
GLS Endo Peak Avg -12.0 %
GLS Endo Peak A4C -14.5 %
GLS Endo Peak A2C -11.0 %
GLS Endo Peak A3C -10.5 %
LVLd (A4C) 85 mm
LVLs (A4C) 77 mm
LVLd (A2C) 80 mm
LVLs (A2C) 73 mm
AVC 308 ms
TIS0.3 MI 1.3
4CH
M1
1.2 2.4
1/128
50/50 fps
50 bpm


VGH ECHO
X5-1
53Hz
19cm
2D
TIS0.3 MI 1.3
2CH
M1
1.2 2.4
2/133
53/53 fps
47 bpm


VGH ECHO
X5-1
53Hz
15cm
2D
TIS0.1 MI 1.2
3CH
M1
1.2 2.4
1/134
51/53 fps
46 bpm


2 Triplane
GLS Endo Peak Avg -12.0 %
GLS Endo Peak A4C -14.5 %
GLS Endo Peak A2C -11.0 %
GLS Endo Peak A3C -10.5 %
End-Systolic
Longitudinal Strain [%]
Anterior
Septal
Lateral
Inferior
20
-20
Time to Peak
Longitudinal Strain [ms]
1325
0

Statistical analysis

Between group comparisons were performed using the Student's t-test or Wilcoxon rank-sum test for continuous variables and the chi-square or Fisher exact test for categorical variables, as appropriate.

Reproducibility analysis was performed using Bland-Altman plots and intra-class correlation coefficients to evaluate the consistency of the LV longitudinal strain measurements.

Receiver operating characteristic (ROC) curves were constructed for each continuous clinical or echo variable (using the clinical diagnosis of ATTR-CM as the gold standard).

Optimal cut-off values for each parameter was determined by the Youden index on the ROC curve to maximize the combination of sensitivity and specificity.

For each resulting binary parameter, univariate logistic regression was performed to determine the odds ratios (with the variable representing the exposure and the clinical diagnosis of ATTR-CM the outcome).

Multivariate logistic regression was then performed using a backward stepwise selection process to identify the key variables that independently predicted a diagnosis of ATTR-CM.

Statistical analysis was performed using JMP and SPSS software.

Results: Baseline clinical characteristics

Table 1 Baseline clinical characteristics

Variable	Patients without ATTR-CM (n = 320)	Patients with ATTR-CM (n = 54)	P value
Demographics			
Age, y	75 (67, 82)	82 (76, 86)	<0.0001
Male	192 (60)	42 (78)	0.01
Body mass index, kg/m^2	26.7 ± 4.9	26.0 ± 4.4	0.29
Body surface area, m^2	1.9 ± 0.2	1.9 ± 0.2	0.55
Comorbidities			
Diabetes	94 (29)	13 (24)	0.52
Hypertension	217 (68)	35 (65)	0.64
Heart failure	204 (64)	49 (91)	<0.0001
Atrial fibrillation	161 (50)	37 (69)	0.02
Device therapy	43 (13)	13 (24)	0.06
Prior cerebrovascular event	43 (13)	6 (11)	0.83
Chronic kidney disease	110 (34)	18 (33)	1.00
Coronary artery disease	126 (39)	20 (37)	0.77
Aortic stenosis	72 (23)	7 (13)	0.15
High-grade AV block	27 (8)	6 (11)	0.60

Data expressed as mean ± standard deviation for normally distributed continuous variables, median (interquartile range) for non-normal continuous variables, and number (percentage) for categorical variables.

ATTR-CM, transthyretin amyloid cardiomyopathy; *AV*, atrioventricular.

Patients with ATTR-CM were more likely to be:

- Older
- Male

Patients with ATTR-CM tended to have a history of:

- Heart failure
- Atrial fibrillation

Results: Baseline echo characteristics

Table 2 Baseline conventional echocardiographic characteristics

Variable	Patients without ATTR-CM (n = 320)	Patients with ATTR-CM (n = 54)	P value
Left ventricular ejection fraction (%)	52.8 ± 12.5	51.6 ± 11.0	0.47
Interventricular septal dimension (mm)	11.0 ± 2.8	15.4 ± 2.6	<0.0001
Posterior wall dimension (mm)	10.3 ± 2.0	14.5 ± 2.6	<0.0001
Indexed LV end-diastolic dimension (mm/m^2)	26.7 ± 4.7	22.8 ± 3.2	<0.0001
LV mass index (g/m^2)	106.4 ± 35.1	139.9 ± 41.2	<0.0001
Relative wall thickness	0.43 ± 0.14	0.70 ± 0.19	<0.0001
Tricuspid annular plane systolic excursion (mm)	19.8 ± 4.8	16.5 ± 4.1	<0.0001
Right ventricular basal diameter (mm)	38.6 ± 6.2	38.7 ± 5.9	0.89
Early mitral inflow (E wave) velocity (cm/s)	87.1 ± 31.9	86.2 ± 24.3	0.40
Late mitral inflow (A wave) velocity (cm/s)[†]	73.6 ± 30.7	47.2 ± 29.5	0.0002
Early septal mitral annular (e') velocity (cm/s)	5.7 ± 2.0	4.2 ± 1.1	<0.0001
Early lateral mitral annular (e') velocity (cm/s)	8.0 ± 2.9	5.9 ± 2.1	<0.0001
Average E/e' ratio	13.7 ± 6.1	18.3 ± 7.1	<0.0001
Peak tricuspid regurgitation velocity (m/s)	2.8 ± 0.6	2.8 ± 0.4	0.63
Pulmonary artery systolic pressure (mmHg)	37.6 ± 13.2	39.7 ± 10.9	0.26
Left atrial volume index (mL/m^2)	51.9 ± 21.6	52.7 ± 13.0	0.71
Right atrial volume index (mL/m^2)	37.8 ± 22.2	47.8 ± 15.8	<0.0001
Pericardial effusion	56 (18)	17 (31)	0.02

[†] Late mitral inflow (A wave) velocity could not be measured in 133 patients due to atrial fibrillation/flutter.

ATTR-CM, transthyretin amyloid cardiomyopathy; *IVSd,* interventricular septal dimension; *LV*, left ventricular.

Patients with ATTR-CM tended to demonstrate:

- Thicker LV walls
- Smaller LV cavities

- Reduced longitudinal motion of the right ventricle

- More LV diastolic dysfunction

- Larger right atrial volumes
- More pericardial effusions

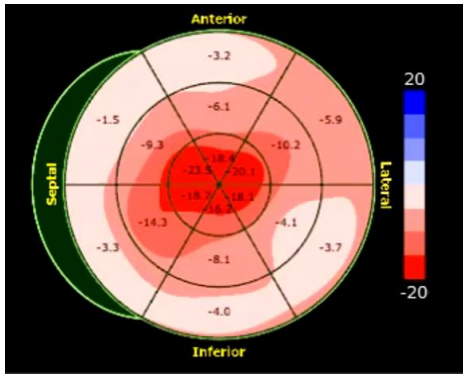
Results: Strain measurements

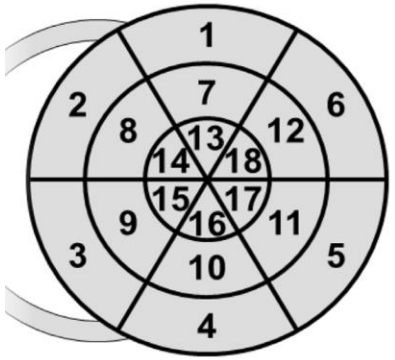
Table 3 Left ventricular longitudinal strain measurements

Variable	Patients without ATTR-CM (n = 320)	Patients with ATTR-CM (n = 54)	P value
Global longitudinal strain (%)	-18.8 ± 4.6	-15.3 ± 4.4	<0.0001
Relative apical longitudinal strain ratio	0.7 ± 0.2	1.2 ± 0.4	<0.0001
Septal apical to basal longitudinal strain ratio	1.8 (1.3, 2.7)	3.4 (2.0, 6.4)	<0.0001
Ejection fraction to strain ratio	2.8 (2.5, 3.2)	3.3 (2.8, 3.9)	<0.0001

Patients with ATTR-CM tended to demonstrate:

- More abnormal LV GLS
- Higher RALS, SAB, EFSR





all models

1. basal anterior
2. basal anteroseptal
3. basal inferoseptal
4. basal inferior
5. basal inferolateral
6. basal anterolateral
7. mid anterior
8. mid anteroseptal
9. mid inferoseptal
10. mid inferior
11. mid inferolateral
12. mid anterolateral

18 segment model only

13. apical anterior
14. apical anteroseptal
15. apical inferoseptal
16. apical inferior
17. apical inferolateral
18. apical anterolateral

$$RALS = \frac{average\ apical\ LS}{average\ basal\ LS + average\ mid\ LS}$$

$$SAB = \frac{apical\ inferoseptal\ LS}{basal\ inferoseptal\ LS}$$

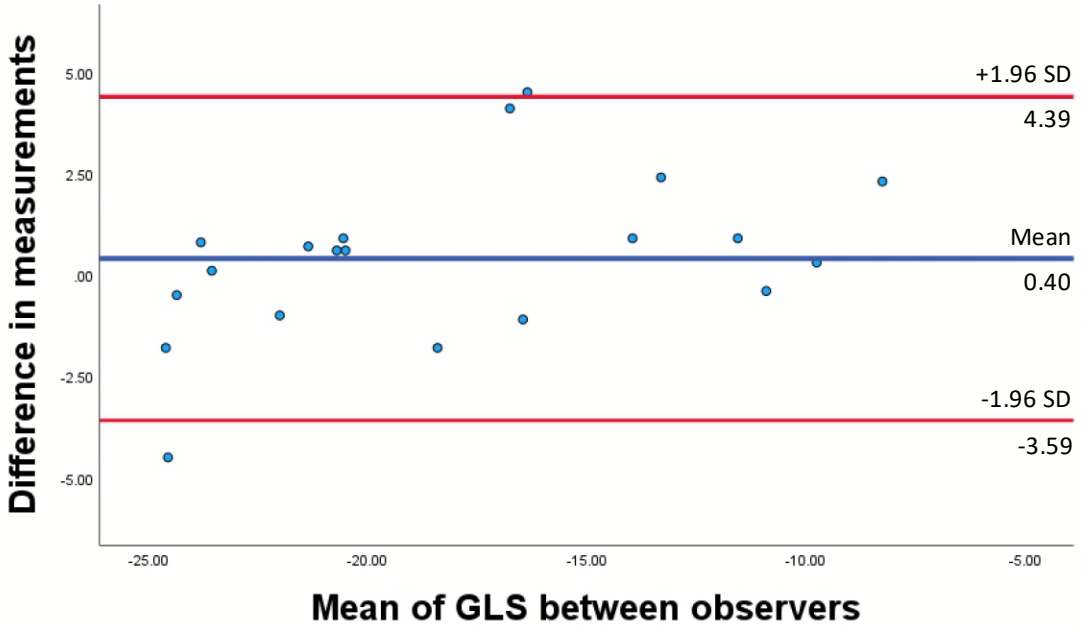
$$EFSR = \left| \frac{LV\ ejection\ fraction}{LV\ global\ longitudinal\ strain} \right|$$

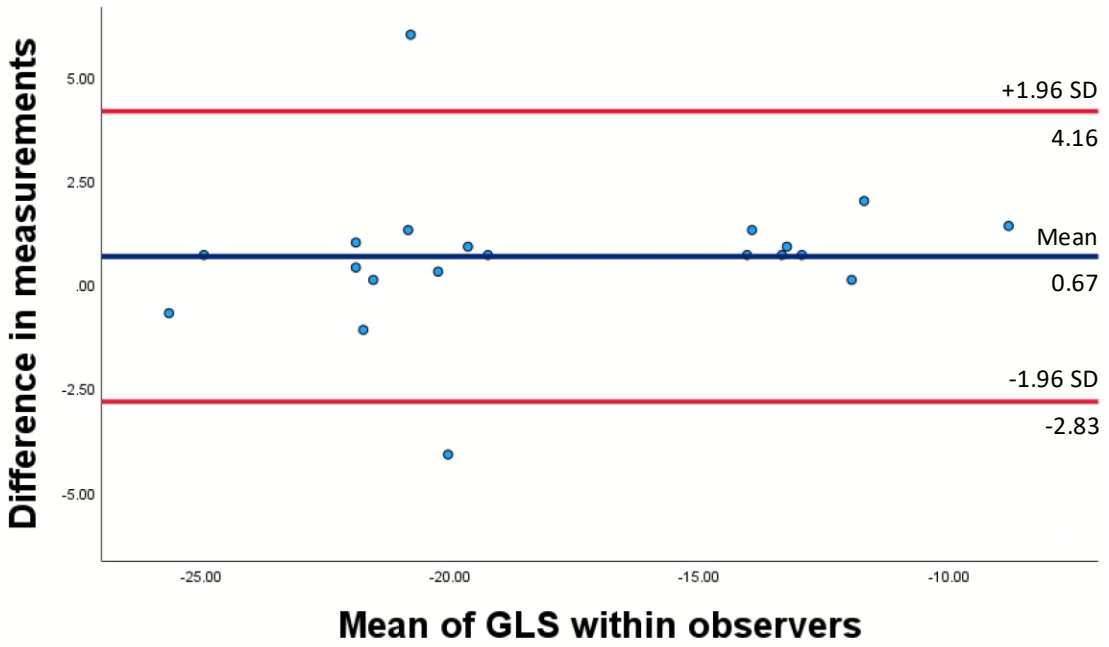
Phelan D et al (*Heart*, 2012); Liu et al (*Circ Cardiovasc Imaging*, 2013); Pagourelias et al (*JACC Cardiovasc Imaging*, 2016)

Results: Reproducibility of strain analysis

Supplementary Table 1 Intraclass correlation coefficients for strain measurements

Variable	Inter-observer variability	Intra-observer variability
LV global longitudinal strain	0.964 (0.908, 0.986)	0.967 (0.916, 0.987)





Results: ROC curves for highest performing measures

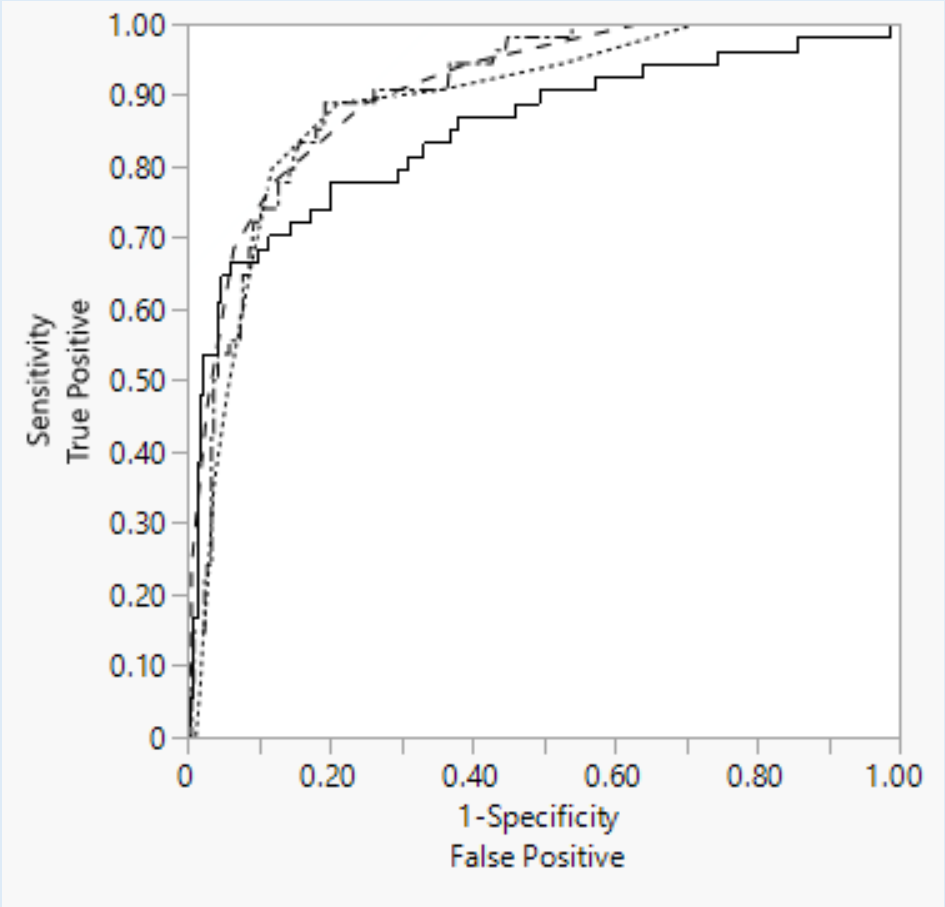


Figure 3 Receiver operating characteristic curves for select echocardiographic parameters.

Interventricular septal dimension AUC 0.89 (0.86, 0.94)

Posterior wall dimension AUC 0.91 (0.86, 0.94)

Relative wall thickness AUC 0.90 (0.86, 0.93)

Relative apical longitudinal strain AUC 0.85 (0.78, 0.91)

$$Relative\ wall\ thickness\ = \frac{Posterior\ wall\ dimension\ \times\ 2}{LV\ end\ diastolic\ dimension}$$

$$RALS = \frac{average\ apical\ LS}{average\ basal\ LS + average\ mid\ LS}$$

Optimal cut-off values that maximized the combination of sensitivity and specificity were chosen for each variable.

Results: Univariate analysis

Table 4 Univariate analysis based on demographic, clinical, and echocardiographic parameters

Variable	Odds ratio (95% CI)	Beta estimate	P value
Age ≥80 years	3.2 (1.8, 5.8)	1.16	0.0001
Male	2.3 (1.2,4.6)	0.85	0.01
Heart failure	5.6 (2.2, 14.4)	1.72	<0.0001
Atrial fibrillation	2.1 (1.2, 4.0)	0.77	0.02
IVSd ≥14 mm	29.0 (13.8, 61.0)	3.37	<0.0001
PWd ≥13 mm	25.2 (12.2, 52.0)	3.23	<0.0001
LVEDDi <26 mm/m^2	7.4 (3.1, 17.8)	2.00	<0.0001
LVMI >115 g/m^2	4.8 (2.5, 9.0)	1.57	<0.0001
RWT >0.50	30.8 (12.6, 75.0)	3.43	<0.0001
TAPSE ≤17 mm	6.1 (3.2, 11.8)	1.81	<0.0001
Medial e' <5 cm/s	3.4 (1.8, 6.5)	1.22	<0.0001
Lateral e' <7 cm/s	6.0 (3.0, 12.2)	1.79	<0.0001
Average E/e' >15	3.8 (2.0, 7.2)	1.34	<0.0001
RAVI >32 mL/m^2	5.4 (2.5, 11.9)	1.69	<0.0001
Pericardial effusion	2.2 (1.1, 4.1)	0.79	0.02
Average LV GLS >16%	4.3 (2.3, 7.8)	1.46	<0.0001
RALS > 1.0	30.0 (14.5, 61.9)	3.40	<0.0001
SAB > 2.8	11.4 (5.9, 21.9)	2.43	<0.0001
EFSR >3.5	8.7 (4.5, 16.9)	2.16	<0.0001

EFSR, left ventricular ejection fraction to global longitudinal strain ratio; *IVSd,* interventricular septal dimension; *LV GLS,* left ventricular global longitudinal strain; *PWd,* posterior wall dimension; *LVEDDi,* indexed left ventricular end-diastolic dimension; *LVMI*, left ventricular mass index; *RALS,* relative apical longitudinal strain ratio; *RAVI*, right atrial volume index; *RWT*, relative wall thickness; *SAB*, septal apical-to-basal longitudinal strain ratio; *TAPSE*, tricuspid annular plane systolic excursion.

Published cut-offs from initial studies:

- RALS > 1.0
- SAB > 2.1
- EFSR > 4.1

Slight difference in optimal cutoff determined in this cohort

Results: Multivariate analysis

Table 5 Multivariate analysis based on demographic, clinical, and echocardiographic parameters

Variable	Odds ratio (95% CI)	Beta estimate	P value
RALS >1.0	15.7 (5.5, 44.9)	2.75	<0.0001
RWT >0.51	9.8 (3.1, 30.8)	2.28	0.0001
RAVI >32 mL/m^2	9.5 (3.0, 30.1)	2.25	0.0001
Lateral e' <7 cm/s	7.2 (2.5, 20.4)	1.97	0.0002
LVEDDi ≤26 mm/m^2	5.2 (1.2, 22.0)	1.65	0.03

LVEDDi, indexed left ventricular end-diastolic dimension; *RALS,* relative apical longitudinal strain ratio; RAVI, right atrial volume index; *RWT*, relative wall thickness.

Simplified UBC amyloid score:

2 points RALS >1.0
1 point RWT >0.51
1 point RAVI >32 mL/m^2
1 point Lateral e' <7 cm/s
1 point LVEDDi ≤26 mm/m^2

Score ≥4 maximizes sensitivity and specificity

Results: Test characteristics of echo parameters

Table 6 Test characteristics of the best performing echo parameters using internally derived cut-offs

Variable	TP	TN	FP	FN	Total	Sensitivity	Specificity	PPV	NPV	Accuracy
IVSd ≥14	43	282	38	11	374	0.80	0.88	0.53	0.96	0.87
PWd ≥13	42	281	39	12	374	0.78	0.88	0.52	0.96	0.86
RWT >0.51	48	258	62	6	374	0.89	0.81	0.44	0.98	0.82
RALS > 1.0	36	301	19	18	374	0.67	0.94	0.65	0.94	0.90
UBC Score ≥4	43	301	19	11	374	0.80	0.94	0.69	0.96	0.92

IVSd ≥14 mm, PWd ≥13 mm, RWT >1.0, and RALS >1.0 were the best single measures to suggest ATTR-CM.

UBC Score ≥4 modestly outperformed these single measures but requires external validation.

Discussion: Summary of results

Patients with ATTR-CM tended to be older and male, and were more likely to have a history of heart failure and atrial fibrillation.

As expected, patients with ATTR-CM tended to demonstrate thicker LV walls, smaller LV cavities, reduced basal longitudinal LV and RV function, more abnormal LV diastolic function, larger right atrial volumes, and more pericardial effusions.

Right atrial enlargement has been considered a non-specific finding but could be an under-utilized parameter to differentiate ATTR-CM from other causes of LV hypertrophy.

This study provided external validation for RALS >1.0 as an optimal cut-off point that maximized test characteristics with a sensitivity of 67% and specificity of 94% in this diverse real world cohort of patients with suspected ATTR-CM.

Discussion: Summary of results (continued)

Other previously published longitudinal strain metrics (SAB and EFSR) did demonstrate some ability to predict ATTR-CM but different optimal cutoffs were identified in this cohort and they did not outperform RALS.

IVSd ≥14 mm, PWd ≥13 mm, RWT >1.0, and RALS >1.0 were the best single measures to suggest ATTR-CM. The UBC Score ≥4 modestly outperformed these single measures but requires external validation.

Since starting this study, other groups have published scores with similar components:

- IWT score: RWT >0.6, E/e' >11, TAPSE ≤19 mm, LV GLS ≥-13%, SAB >2.9
- Mayo score: age ≥80, male, RWT >0.57, PWd ≥12, LVEF <60%, Hx HTN

Which score to use may largely depend on the cohort being examined.

Discussion: Limitations

This is a retrospective study subject to the usual limitations (e.g., missing data).

- This was somewhat mitigated by the collection of routinely acquired data, and raw echo images were re-reviewed to obtain measurements if possible for missing data.

There was a large number of studies excluded due to a lack of echo studies performed within the academic affiliated health authorities within 1 year of the PYP scan.

- However, it is unlikely for this to have significantly influenced the overall trends in the study although it could have provided more useful data points for the ATTR-CM group.

This study was initiated in 2021 but since then, there have been at least 2 large studies published with similar study design, which reduces the novelty of the current study.

- Nevertheless, our study cohort is unique in that it represents a diverse population with a lower threshold for referral for PYP scan.

Future directions

Our internally derived score will require external validation. We plan to obtain a validation cohort either from the echo studies performed in other health authorities (which would largely represent the rural population) or from a different time period (e.g., 2021 to present).

Similarly, we will also aim to conduct a prospective study that compares and possibly consolidates the various published scoring systems to date.

Finally, our group has an interest in the development of artificial intelligence models to better identify patients with cardiomyopathy at risk for heart failure. The data collected from this study that comprehensively characterized patients with suspected ATTR-CM would provide important input data for development of those models.

Questions/comments?

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