Supplementary Materials

Artificial Intelligence-Enabled Fully Automated Detection of Cardiac Amyloidosis Using Electrocardiograms and Echocardiograms

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Supplementary Tables

Supplementary Table 1. Method of diagnosis for patients in ECG cohort

	BWH			MGH		
	Overall	ATTR	AL	Overall	ATTR	AL
Number of patients	144	91	47	52	31	15
Method of Diagnosis						
Myocardial biopsy, n (%)	46 (31.9)	13 (27.7)	32 (35.2)	8 (15.4)	6 (19.4)	2 (13.3)
PYP scan, n (%)	44 (30.6)	44 (30.6)	N/A	16 (30.8)	16 (51.6)	N/A
Fat pad biopsy + TTE, n (%)	2 (1.4)	0 (0.0)	2 (4.3)	2 (3.8)	0 (0.0)	2 (13.3)
Cardiac MRI, n (%)	28 (19.4)	10 (11.0)	16 (34.0)	15 (28.8)	7 (22.6)	7 (46.7)
Genetic test, n (%)	1 (0.7)	1 (1.1)	N/A	1 (1.9)	1 (3.2)	N/A
Biopsy (other) + TTE, n (%)	11 (7.6)	0 (0.0)	11 (23.4)	5 (9.6)	0 (0.0)	4 (26.6)
Unknown, n (%)	12 (8.3)	4 (4.3)	5 (10.6)	5 (9.6)	1 (3.2)	0 (0.0)
Days after diagnosis of first ECG						
≤ -365, n (%)	21 (14.6)	15 (16.5)	6 (12.8)	17 (32.7)	14 (45.2)	2 (13.3)
-364 to - 180, n (%)	3 (2.1)	2 (2.2)	1 (2.1)	2 (3.8)	2 (6.5)	0 (0.0)
-179 to -90, n (%)	3 (2.1)	2 (2.2)	1 (2.1)	3 (5.8)	2 (6.5)	0 (0.0)
-89 to -30, n (%)	8 (5.6)	6 (6.6)	2 (4.3)	4 (7.7)	1 (3.2)	3 (20.0)
-29 to -1	18 (12.5)	10 (11.0)	7 (14.9)	4 (7.7)	2 (6.5)	2 (13.3)
0 to 29, n (%)	27 (18.8)	13 (14.3)	14 (29.8)	5 (9.6)	2 (6.5)	3 (20.0)
30 to 89	17 (11.8)	12 (13.2)	3 (6.4)	0 (0.0)	0 (0.0)	0 (0.0)
90 to 179, n (%)	6 (4.2)	6 (6.6)	0 (0.0)	2 (3.8)	0 (0.0)	2 (13.3)
180 to 364, n (%)	9 (6.2)	6 (6.6)	3 (6.4)	2 (3.8)	1 (3.2)	1 (6.7)
365 ≤ , n (%)	17 (11.8)	13 (14.3)	4 (8.5)	7 (13.5)	5 (16.1)	2 (13.3)
Unknown, n (%)	15 (10.4)	6 (6.6)	6 (12.8)	6 (11.5)	0 (0.0)	2 (6.5)

All the patients diagnosed with cardiac MRI was confirmed with either biopsy or PYP scan. The negative value in "Days after diagnosis of first ECG" indicates the date before diagnosis. N represents the number of patients. PYP scan: Tc-99m pyrophosphate scan, TTE: transthoracic echocardiography, ECG: electrocardiogram, MRI: magnetic resonance imaging, ATTR: amyloid transthyretin, AL: amyloid light-chain, BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital.

Supplementary Table 2. Study date relative to diagnosis in ECG cohort

	BWH			MGH		
	Overall	ATTR	AL	Overall	ATTR	AL
Number of studies	669	411	241	405	270	89
Days after diagnosis						
≤ -365, n (%)	98 (14.6)	70 (17.0)	28 (11.6)	54 (13.3)	51 (18.9)	2 (2.2)
-364 to - 180, n (%)	9 (1.3)	8 (1.9)	1 (0.4)	35 (0.6)	35 (13.0)	0 (0.0)
-179 to -90, n (%)	3 (0.4)	2 (0.5)	1 (0.4)	23 (5.7)	21 (7.8)	0 (0.0)
-89 to -30, n (%)	15 (2.2)	11 (2.7)	4 (1.7)	21 (5.2)	10 (3.7)	9 (10.1)
-29 to -1	38 (5.7)	24 (5.8)	10 (4.1)	29 (7.2)	16 (5.9)	12 (13.5)
0 to 29, n (%)	92 (13.8)	35 (8.5)	56 (23.2)	30 (7.4)	20 (7.4)	8 (9.0)
30 to 89	68 (10.2)	27 (6.6)	35 (14.5)	19 (4.7)	14 (5.2)	5 (5.6)
90 to 179, n (%)	34 (5.1)	20 (4.9)	14 (5.8)	20 (4.9)	9 (3.3)	11 (12.4)
180 to 364, n (%)	67 (10.0)	48 (11.7)	18 (7.5)	35 (8.6)	11 (4.1)	23 (25.8)
365 ≤, n (%)	182 (27.2)	133 (32.4)	48 (19.9)	85 (21.0)	65 (24.1)	19 (21.3)
Unknown, n (%)	63 (9.4)	33 (8.0)	26 (10.8)	54 (13.3)	18 (6.7)	0 (0.0)

The negative value in "Days after diagnosis" indicates the date before diagnosis. N represents the number of studies. ECG: electrocardiogram, ATTR: amyloid transthyretin, AL: amyloid light-chain, BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital.

Supplementary Table 3. Method of diagnosis for patients in echocardiogram cohort

	BWH			MGH			Keio		
	Overall	ATTR	AL	Overall	ATTR	AL	Overall	ATTR	AL
Number of patients	134	96	38	41	21	17	52	45	7
Method of Diagnosis									
Myocardial biopsy, n (%)	34 (25.4)	23 (24.0)	11 (28.9)	6 (14.6)	3 (14.3)	3 (17.6)	36 (69.2)	34 (75.6)	2 (28.6)
PYP scan, n (%)	55 (41.0)	55 (57.3)	N/A	11 (26.8)	11 (52.4)	N/A	11 (21.2)	11 (24.4))	N/A
Fat pad biopsy + TTE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.9)	0 (0.0)	2 (11.8)	3 (5.8)	0 (0.0)	3 (42.9)
Cardiac MRI, n (%)	35 (26.1)	13 (13.5)	35 (26.1)	15 (36.6)	7 (33.3)	7 (41.2)	0 (0.0)	0 (0.0)	0 (0.0)
Genetic test, n (%)	1 (0.7)	1 (1.0)	N/A	0 (0.0)	0 (0.0)	N/A	0 (0.0)	0 (0.0)	0 (0.0)
Biopsy (other) + TTE, n (%)	6 (4.5)	2 (2.1)	3 (7.9)	5 (12.2)	0 (0.0)	5 (29.4)	2 (3.8)	0 (0.0)	2 (28.6)
Unknown, n (%)	3 (2.2)	2 (2.1)	1 (0.7)	2 (4.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Days after diagnosis of first echocardiogram									
≤ -365, n (%)	22 (16.4)	11 (11.5)	11 (28.9)	9 (22.0)	8 (38.1)	0 (0.0)	2 (3.8)	2 (4.4)	0 (0.0)
-364 to - 180, n (%)	5 (3.7)	4 (4.2)	1 (2.6)	2 (4.9)	2 (9.5)	0 (0.0)	2 (3.8)	0 (0.0)	2 (28.6)
-179 to -90, n (%)	2 (1.5)	0 (0.0)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.8)	2 (4.4)	1 (14.3)
-89 to -30, n (%)	3 (2.2)	0 (0.0)	3 (3.1)	4 (9.8)	1 (4.8)	3 (17.6)	10 (19.2)	8 (17.8)	2 (28.6)
-29 to -1	14 (10.4)	2 (5.3)	12 (12.5)	6 (14.6)	2 (9.5)	4 (23.5)	10 (19.2)	8 (17.8)	2 (28.6)
0 to 29, n (%)	24 (17.9)	15 (15.6)	9 (23.7)	1 (2.4)	0 (0.0)	1 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)
30 to 89	12 (9.0)	11 (11.5)	1 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	4 (7.7)	4 (8.9)	0 (0.0)
90 to 179, n (%)	10 (7.5)	8 (8.3)	2 (5.3)	4 (9.8)	0 (0.0)	4 (23.5)	4 (7.7)	4 (8.9)	0 (0.0)
180 to 364, n (%)	14 (10.4)	9 (9.4)	5 (13.2)	4 (9.8)	1 (4.8)	3 (17.6)	11 (21.2)	11 (24.4)	0 (0.0)
365 ≤, n (%)	24 (17.9)	18 (18.8)	6 (15.8)	9 (22.0)	1 (4.8)	2 (11.8)	6 (11.5)	6 (13.3)	0 (0.0)
Unknown, n (%)	4 (3.0)	3 (3.1)	1 (2.6)	2 (4.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

All the patients diagnosed with cardiac MRI was confirmed with either biopsy or PYP scan. The negative value in "Days after diagnosis of first echocardiogram" indicates the date before diagnosis. N represents the number of patients. PYP scan: Tc-99m pyrophosphate scan, TTE: transthoracic echocardiography, MRI: magnetic resonance imaging, ATTR: amyloid transthyretin, AL: amyloid light-chain, BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, Keio: Keio University.

Supplementary Table 4. Study date relative to diagnosis in echocardiogram cohort

	BWH			MGH			Keio		
	Overall	ATTR	AL	Overall	ATTR	AL	Overall	ATTR	AL
Number of studies	513	362	151	110	54	44	118	95	23
Days after diagnosis									
≤ -365, n (%)	39 (7.6)	16 (4.4)	23 (15.2)	18 (16.4)	16 (29.6)	0 (0.0)	4 (3.4)	4 (4.2)	0 (0.0)
-364 to - 180, n (%)	15 (2.9)	5 (1.4)	10 (6.6)	7 (6.4)	7 (13.0)	0 (0.0)	2 (1.7)	0 (0.0)	2 (8.7)
-179 to -90, n (%)	7 (1.4)	5 (1.4)	2 (1.3)	2 (1.8)	1 (1.9)	0 (0.0)	3 (2.5)	2 (2.1)	1 (4.3)
-89 to -30, n (%)	6 (1.2)	5 (1.4)	1 (0.7)	6 (5.5)	3 (5.6)	3 (6.8)	11 (9.3)	8 (8.4)	3 (13.0)
-29 to -1	24 (4.7)	19 (5.2)	5 (3.3)	8 (7.3)	4 (7.4)	4 (9.1)	13 (11.0)	9 (9.5)	4 (17.4)
0 to 29, n (%)	35 (6.8)	19 (5.2)	16 (10.6)	5 (4.5)	2 (3.7)	2 (4.5)	6 (5.1)	5 (5.3)	1 (4.3)
30 to 89	23 (4.5)	18 (5.0)	5 (3.3)	4 (3.6)	0 (0.0)	4 (9.1)	11 (9.3)	6 (6.3)	5 (21.7)
90 to 179, n (%)	23 (4.5)	15 (4.1)	8 (5.3)	7 (6.4)	1 (1.9)	6 (13.6)	8 (6.8)	8 (8.4)	0 (0.0)
180 to 364, n (%)	58 (11.3)	44 (12.2)	14 (9.3)	11 (10.0)	4 (7.4)	7 (15.9)	21 (17.8)	19 (20.0)	2 (8.7)
365 ≤, n (%)	267 (52.0)	204 (56.4)	63 (41.7)	34 (30.9)	16 (29.6)	18 (40.9)	39 (33.1)	34 (35.8)	5 (21.7)
Unknown, n (%)	16 (3.1)	12 (3.3)	4 (2.6)	8 (7.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

The negative value in "Days after diagnosis" indicates the date before diagnosis. N represents the number of studies. ATTR: amyloid transthyretin, AL: amyloid light-chain, BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, Keio: Keio University.

Supplementary Table 5. Study-level demographic information of controls of HCM, HTN and ESRD

	BWH			MGH			UCSF		Keio	
	HCM	ESRD	HTN	HCM	ESRD	HTN	HCM	HTN	HCM	HTN
Number of studies	258	1,180	593	525	939	351	262	1,450	120	235
Age, years ± SD	55.1 ± 13.9	60.1 ± 15.2	65.3 ± 18.4	60.1 ± 15.2	63.6 ± 14.7	70.1 ± 15.1	58.9 ± 14.9	66.7 ± 16.7	59.6 ± 13.5	73.1 ± 13.1
Age Groups										
≤30, n (%)	13 (5.0)	45 (3.8)	43 (7.3)	24 (4.6)	17 (1.8)	6 (1.7)	11 (4.2)	69 (4.8)	3 (2.5)	2 (0.9)
30-50, n (%)	72 (27.9)	234 (19.8)	55 (9.3)	93 (17.7)	157 (16.7)	21 (6.0)	64 (24.4)	138 (9.5)	23 (19.2)	14 (6.0)
50-70, n (%)	137 (53.1)	532 (45.1)	236 (39.8)	264 (50.3)	396 (42.2)	136 (38.7)	126 (48.1)	593 (40.9)	64 (53.3)	67 (28.5)
70-90, n (%)	36 (14.0)	369 (31.3)	236 (39.8)	141 (26.9)	353 (37.6)	165 (47.0)	60 (22.9)	594 (41.0)	30 (25.0)	139 (59.1)
>90, n (%)	0 (0.0)	0 (0.0)	23 (3.9)	3 (0.6)	16 (1.7)	23 (6.6)	1 (0.4)	56 (3.9)	0 (0.0)	13 (5.5)
HR, bpm ± SD	70.6 ± 16.6	77.8 ± 18.7	68.9 ± 14.5	65.8 ± 15.6	75.5 ± 17.9	67.8 ± 16.1	64.8 ± 17.3	72.1 ± 17.7	61.5 ± 13.1	67.3 ± 12.7
Manufacture										
Philips, n (%)	201 (77.9)	867 (73.5)	432 (72.8)	487 (92.8)	910 (96.9)	334 (95.2)	182 (69.5)	1,158 (79.9)	4 (3.3)	64 (27.2)
GE, n (%)	55 (21.3)	296 (25.1)	160 (27.0)	36 (6.9)	29 (3.1)	17 (4.8)	80 (30.5)	290 (20.0)	115 (95.8)	131 (55.7)
Agilent, n (%)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
SonoSite, n (%)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
SIEMENS, n (%)	3 (0.4)	7 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
ACUSON, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
ATL, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TOSHIBA, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	40 (17.0)

N represents the number of studies. HR: heart rate, BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, UCSF: University of California San Francisco, Keio: Keio University. HCM: hypertrophic cardio myopathy. ESRD: end-stage renal disease. HTN: hypertension.

Supplementary Table 6. Patient-level demographic information of controls of HCM, HTN and ESRD

	BWH			MGH			UCSF		Keio	
	HCM	ESRD	HTN	HCM	ESRD	HTN	HCM	HTN	HCM	HTN
Number of patients	114	528	538	243	476	318	159	1,360	54	228
Age, years ± SD	55.8 ± 13.6	60.9 ± 15.1	65.0 ± 18.2	59.6 ± 15.1	64.0 ± 14.3	69.6 ± 15.2	57.3 ± 15.8	66.7 ± 16.7	60.7 ± 13.3	72.9 ± 13.2
Age Groups										
≤30, n (%)	6 (5.3)	21 (4.0)	40 (7.4)	13 (5.3)	10 (2.1)	6 (1.9)	11 (6.9)	68 (5.0)	1 (1.9)	2 (0.9)
30-50, n (%)	30 (26.3)	99 (18.8)	50 (9.3)	44 (18.1)	67 (14.1)	20 (6.3)	41 (25.8)	129 (9.5)	10 (18.5)	14 (6.1)
50-70, n (%)	65 (57.0)	234 (44.3)	219 (40.7)	122 (50.2)	214 (45.0)	124 (39.0)	74 (46.5)	554 (40.7)	28 (51.9)	66 (28.9)
70-90, n (%)	13 (11.4)	174 (33.0)	208 (38.7)	63 (25.9)	179 (37.6)	150 (47.2)	33 (20.8)	554 (40.7)	15 (27.8)	134 (58.8)
>90, n (%)	0 (0.0)	0 (0.0)	21 (3.9)	1 (0.4)	6 (1.3)	18 (5.7)	0 (0.0)	55 (4.0)	0 (0.0)	12 (5.3)
Female, n (%)	35 (30.7)	222 (42.0)	253 (47.0)	84 (34.6)	162 (34.0)	155 (48.7)	68 (42.8)	683 (50.4)	21 (38.9)	119 (52.2)

N represents the number of patients. BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, UCSF: University of California San Francisco, Keio: Keio University Hospital. Age is calculated as mean of all studies for a patient. HCM: hypertrophic cardio myopathy. ESRD: end-stage renal disease. HTN: hypertension.

Supplementary Figures.

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│  480 patients with cardiac amyloidosis , who had ECG │
│   and did not have pacing spikes, were identified    │
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                          │
                          ▼
         ┌─────────────────────────────────────┐
         │  7,934 patients, 10,933 ECG studies  │
         │   (Cases: 480 patients, 2,249 studies) │
         └─────────────────────────────────────┘
                          │
                          ▼
         ┌─────────────────────────────────────┐
         │      Patient level random split      │
         └─────────────────────────────────────┘
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3,985 patients, 5,495 studies were assigned to ECG-derivation cohort (Case: 244 patients, 1,146 studies)	1,639 patients, 2,247 studies were assigned to ECG-validation cohort (Case: 92 patients, 434 studies)	2,310 patients, 3,191 studies were assigned to ECG-test cohort (Case: 144 patients, 669 studies)

Supplementary Figure 1. Cohort selection procedure for the BWH ECG cohort.

ECG: electrocardiogram, BWH: Brigham and Women's Hospital.
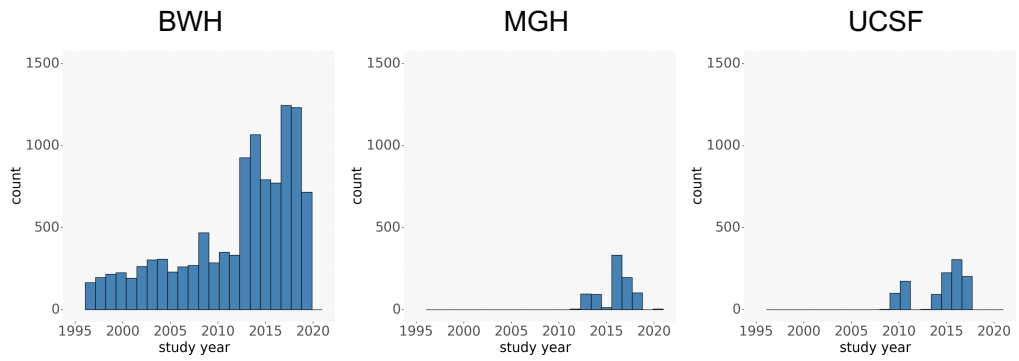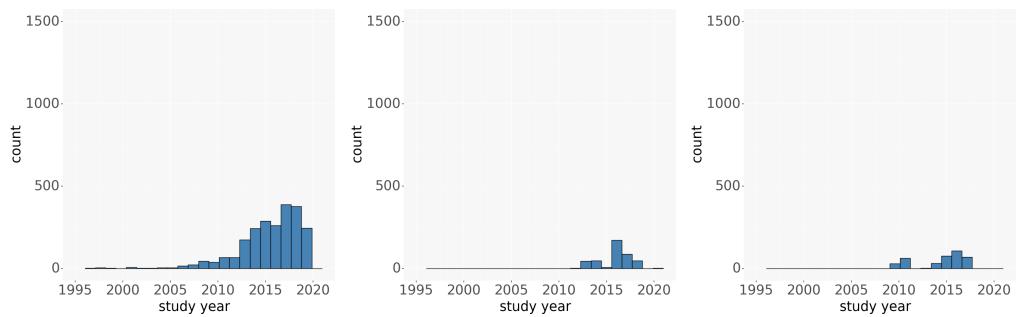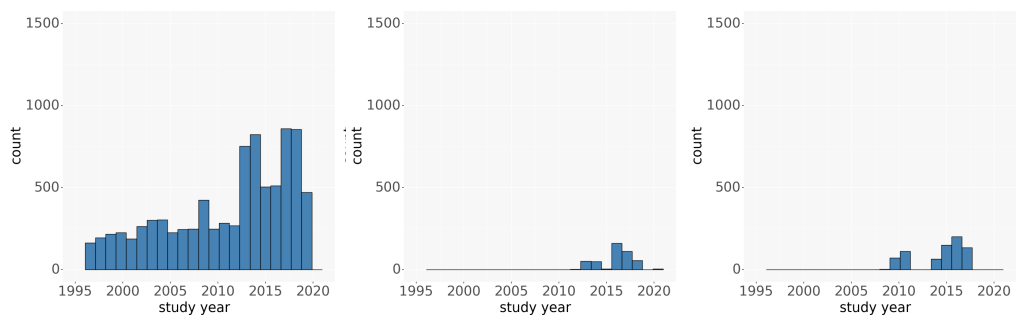
Supplementary Figure 2. Histogram of the dates of ECG studies

Source data are provided as a Source Data file. ECG: electrocardiogram, BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, UCSF: University of California San Francisco.
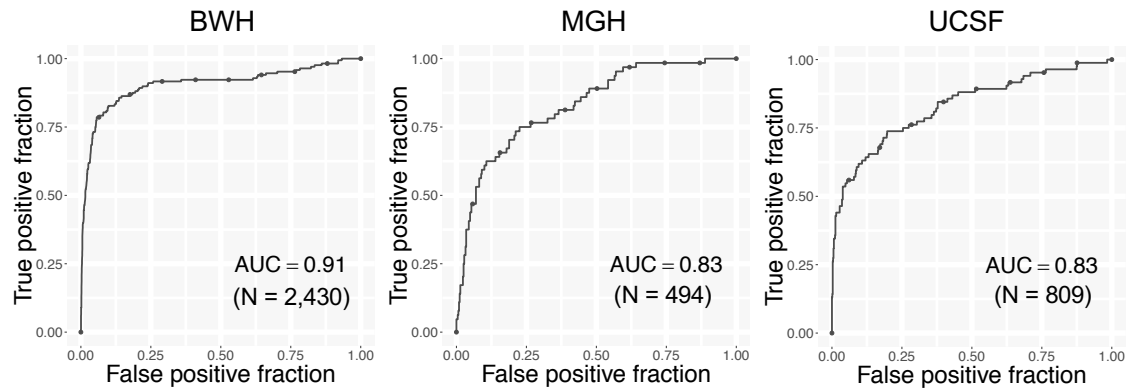
Supplementary Figure 3. Performance of the ECG model on the earliest available study for each patient

ROC plots for detecting cardiac amyloidosis for each institution. The performance on the test dataset is shown for BWH. Source data are provided as a Source Data file. ECG: electrocardiogram, BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, UCSF: University of California San Francisco. AUC: area under the curve.
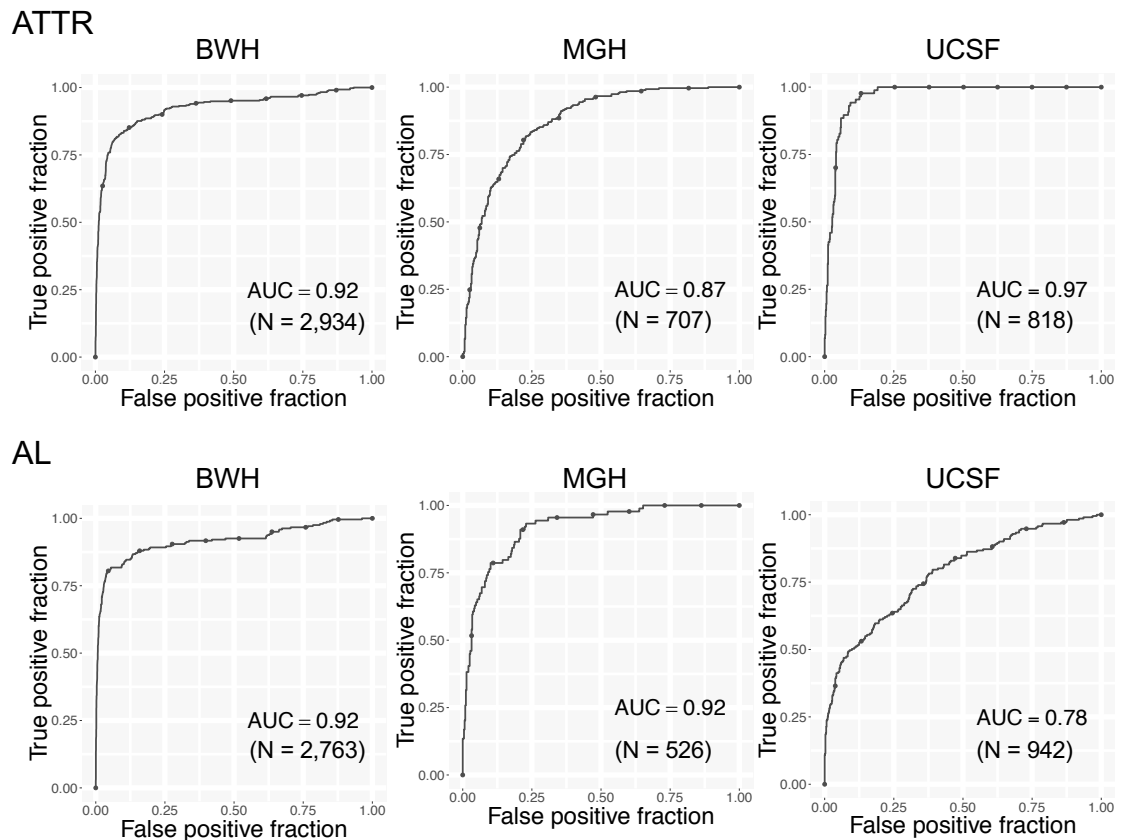
Supplementary Figure 4. Performance of ECG model by amyloid subtype

ROC plots for detecting cardiac amyloidosis on amyloid subtype for each institution. The performance on a test dataset is shown for BWH. N is the numbers of studies. Source data are provided as a Source Data file. ECG: electrocardiogram, ATTR: amyloid transthyretin, AL: amyloid light-chain, BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, UCSF: University of California San Francisco. AUC: area under the curve.
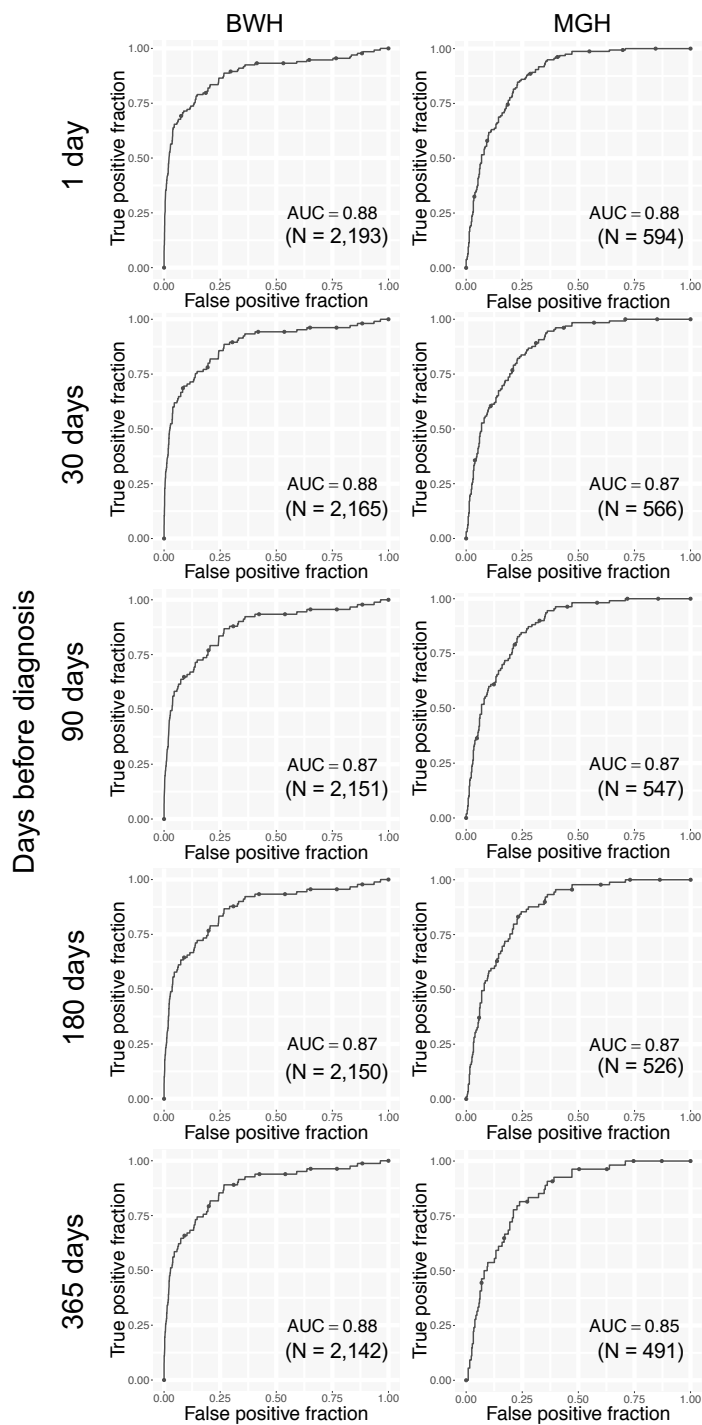
Supplementary Figure 5. Performance of the ECG model using studies collected up to various time points prior to the diagnosis.

ROC plots for detecting cardiac amyloidosis on datasets for each institution. The performance on a test dataset is shown for BWH. Source data are provided as a Source Data file. ECG: electrocardiogram, BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, AUC: area under the curve.

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┌─────────────────────────┐
│ 418 patients with cardiac│
│      amyloidosis , who had│
│ echocardiography, were    │
│        identified         │
└─────────────────────────┘
            │
            ▼
┌─────────────────────────┐   ┌─────────────────────────┐   ┌─────────────────────────┐
│ Matched to randomly      │   │ 253 patients who had     │   │ 383 patients who had     │
│ selected control studies │   │ pacemaker or ICD lead,   │   │ HCM were identified      │
│ based on age and gender  │   │ without amyloidosis,     │   │                          │
│                          │   │ were identified          │   │                          │
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            │                           │                           │
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┌───────────────────────────────────────────────────────────────────┐
│              3,354 patients 5,780 studies                           │
│              (Case: 418 patients,1,869 studies)                     │
└───────────────────────────────────────────────────────────────────┘
                                        │
                                        │──────────────►┌─────────────────────────┐
                                        │               │ 137 studies for 97      │
                                        │               │ patients failed video   │
                                        │               │ conversion              │
                                        │               └─────────────────────────┘
                                        ▼
┌───────────────────────────────────────────────────────────────────┐
│         3,257 patients, 5,643 studies, 290,680 videos               │
│         (Case: 418 patients, 1861 studies, 96,969 videos)           │
└───────────────────────────────────────────────────────────────────┘
                                        │
                                        │──────────────►┌─────────────────────────┐
                                        │               │ 521 studies for 230     │
                                        │               │ patients did not have   │
                                        │               │ A4C videos              │
                                        │               └─────────────────────────┘
                                        ▼
┌───────────────────────────────────────────────────────────────────┐
│        3,027 patients, 5,122 studies had A4C videos                 │
│                   (15,274 videos)                                   │
│        (Case: 418 patients, 1,744 studies, 6,046 videos)            │
└───────────────────────────────────────────────────────────────────┘
                                        │
                                        ▼
┌───────────────────────────────────────┐
│        Patient level random split      │
└───────────────────────────────────────┘
            │                           │                           │
            ▼                           ▼                           ▼
┌─────────────────────────┐   ┌─────────────────────────┐   ┌─────────────────────────┐
│ 1,483 patients, 2,472   │   │ 619 patients, 1,030      │   │ 925 patients, 1,620      │
│ studies were assigned to│   │ studies were assigned to │   │ studies were assigned to │
│ echocardiography-       │   │ echocardiography-        │   │ echocardiography-test    │
│ derivation cohort       │   │ validation cohort        │   │ cohort (4,901 videos)    │
│ ( 7,343 videos)         │   │ (3,030 videos)           │   │ (Case: 137 patients,     │
│ (Case: 208 patients,    │   │ (Case: 73 patients,      │   │ 611 studies, 2147 videos)│
│ 832 studies, 2904       │   │ 301 studies, 995 videos) │   │                          │
│ videos)                 │   │                          │   │                          │
└─────────────────────────┘   └─────────────────────────┘   └─────────────────────────┘
            │                           │                           │
            ▼                           ▼                           ▼
┌─────────────────────────┐   ┌─────────────────────────┐   ┌─────────────────────────┐
│ 6,376 videos            │   │ 2,684 videos             │   │ 4,117 videos             │
│ (1,391 patients, 2,210  │   │ (580 patients, 933       │   │ (857 patients, 1,422     │
│ studies) had frames ≥ 40│   │ studies) had frames ≥ 40 │   │ studies) had frames ≥ 40 │
│ with FPS ≥ 30           │   │ with FPS ≥ 30            │   │ with FPS ≥ 30            │
│ (Case: 203 patients,    │   │ (Case: 73 patients,      │   │ (Case: 134 patients,     │
│ 832 studies, 2904       │   │ 265 studies, 862 videos) │   │ 513 studies, 1,676       │
│ videos)                 │   │                          │   │ videos)                  │
└─────────────────────────┘   └─────────────────────────┘   └─────────────────────────┘
```

Supplementary Figure 6. Cohort selection procedure for the BWH echocardiography cohort.

BWH: Brigham and Women's Hospital, HCM: hypertrophic cardiomyopathy, ICD: implantable cardioverter defibrillator, FPS: frames per second, A4C: apical 4 chamber view.
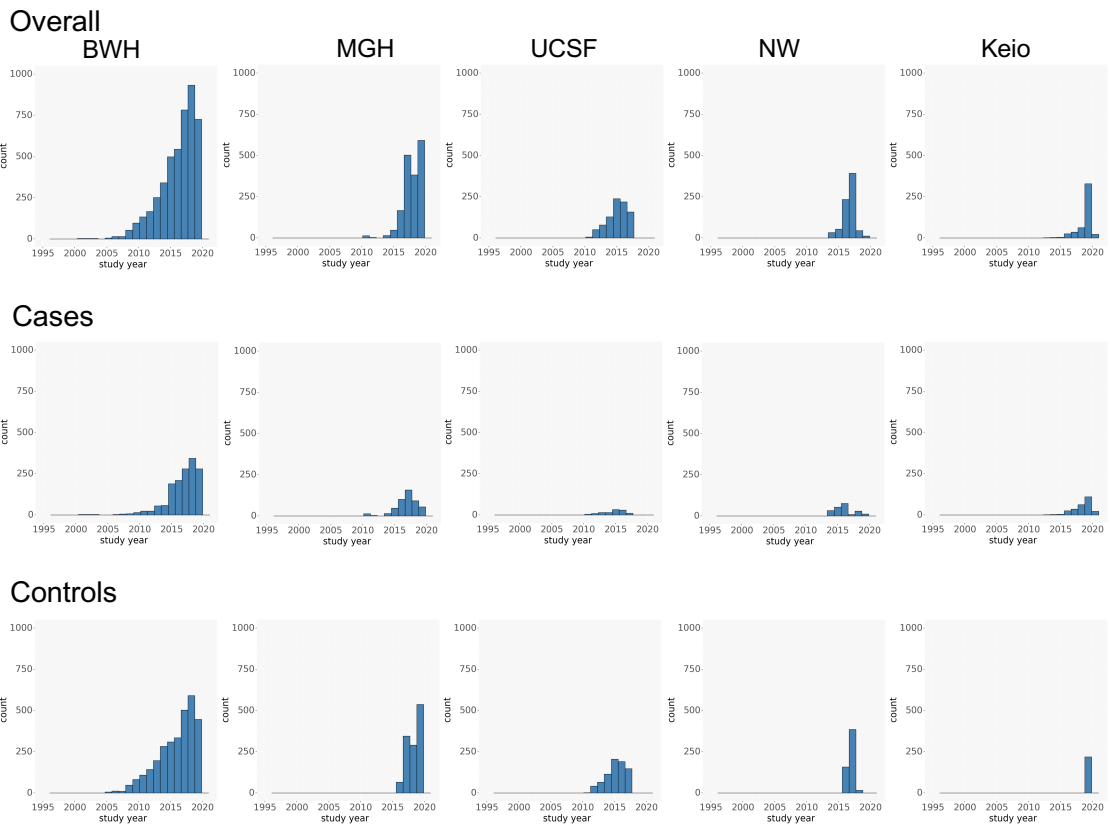
Supplementary Figure 7. Histogram of the dates of echocardiology studies

Source data are provided as a Source Data file. BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, UCSF: University of California San Francisco, NW: Northwestern University, Keio: Keio University.
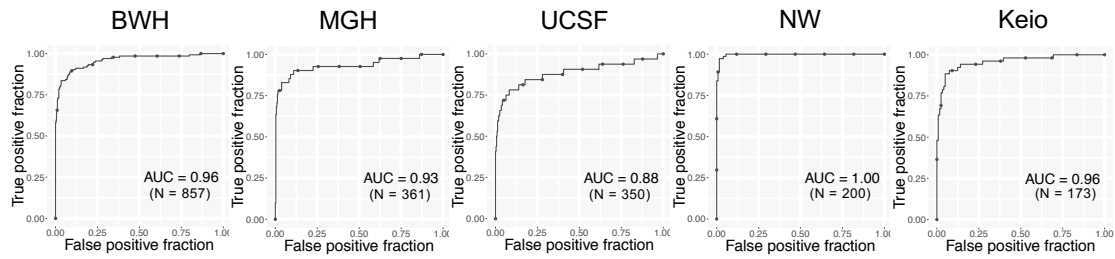
Supplementary Figure 8. Performance of the echocardiography model using the earliest available study for each patient

ROC plots for detecting cardiac amyloidosis for each institution. The performance on the test dataset is shown for BWH. N is the numbers of studies. Source data are provided as a Source Data file. BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, UCSF: University of California San Francisco, NW: Northwestern University, Keio: Keio University. AUC: area under the curve.

ATTR

AL
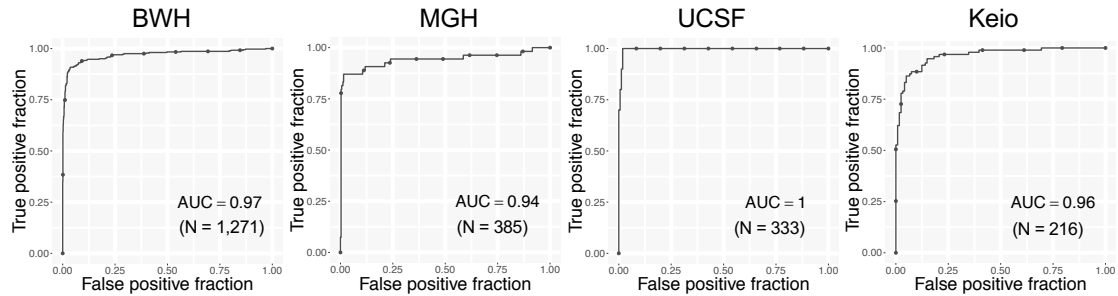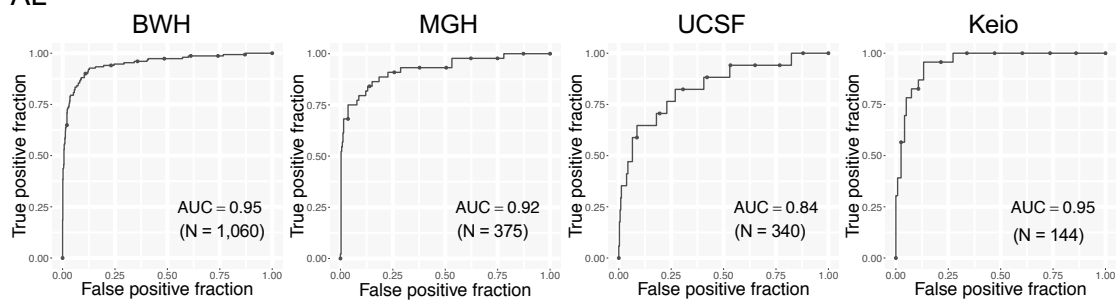
Supplementary Figure 9. Performance of echocardiography model by amyloid subtype

ROC plots for detecting cardiac amyloidosis by subtype for each institution. The performance on a test dataset is shown for BWH. N is the numbers of studies. Source data are provided as a Source Data file. ATTR: amyloid transthyretin, AL: amyloid light-chain, BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, UCSF: University of California San Francisco, Keio: Keio University, AUC: area under the curve.
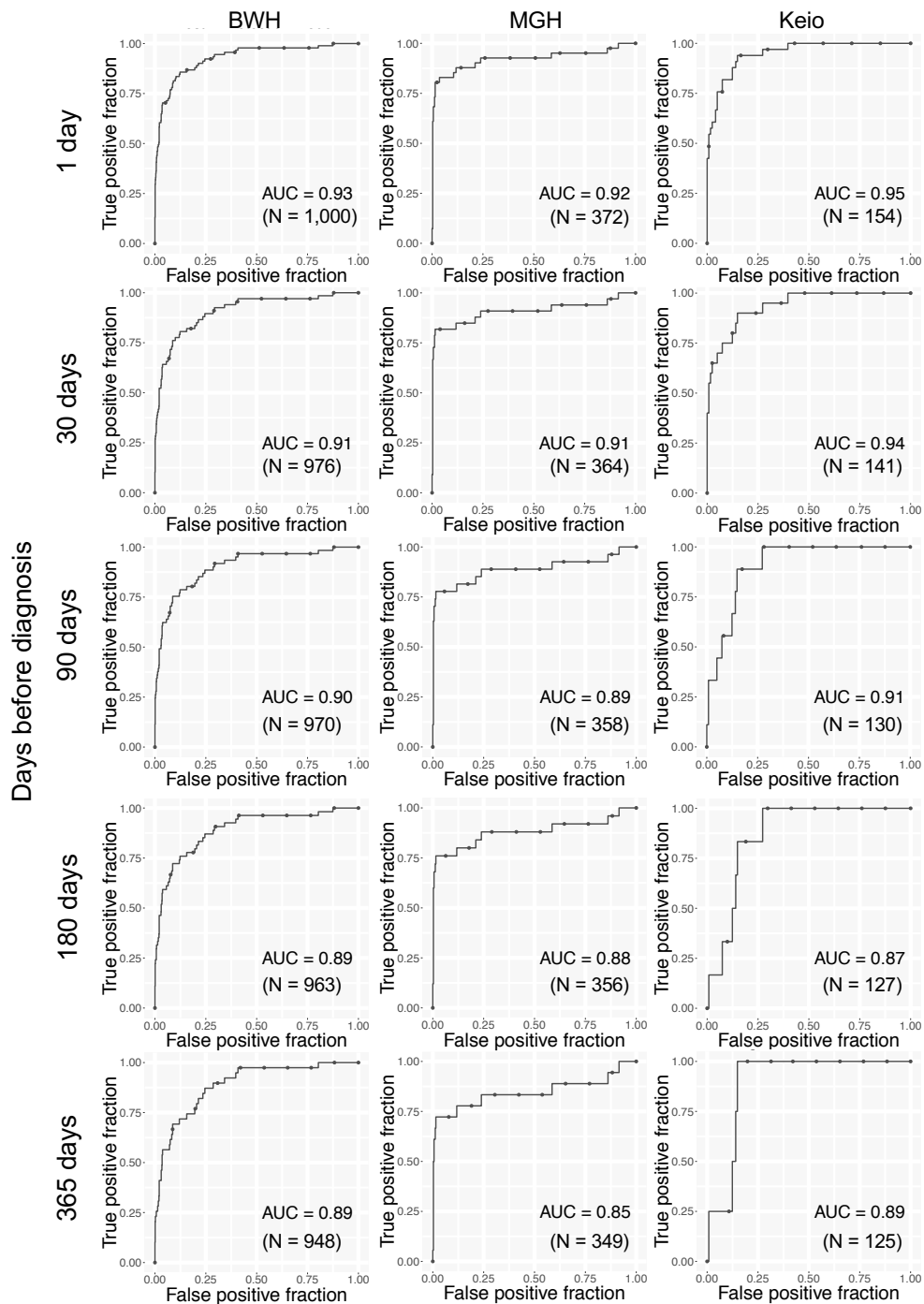
Supplementary Figure 10. Performance of the echocardiography model on the studies from various time points before diagnosis

ROC plots for detecting cardiac amyloidosis for each institution. The performance on the test dataset is shown for BWH. Source data are provided as a Source Data file. BWH: Brigham and Women's Hospital, MGH: Massachusetts General Hospital, Keio: Keio University. AUC: area under the curve.
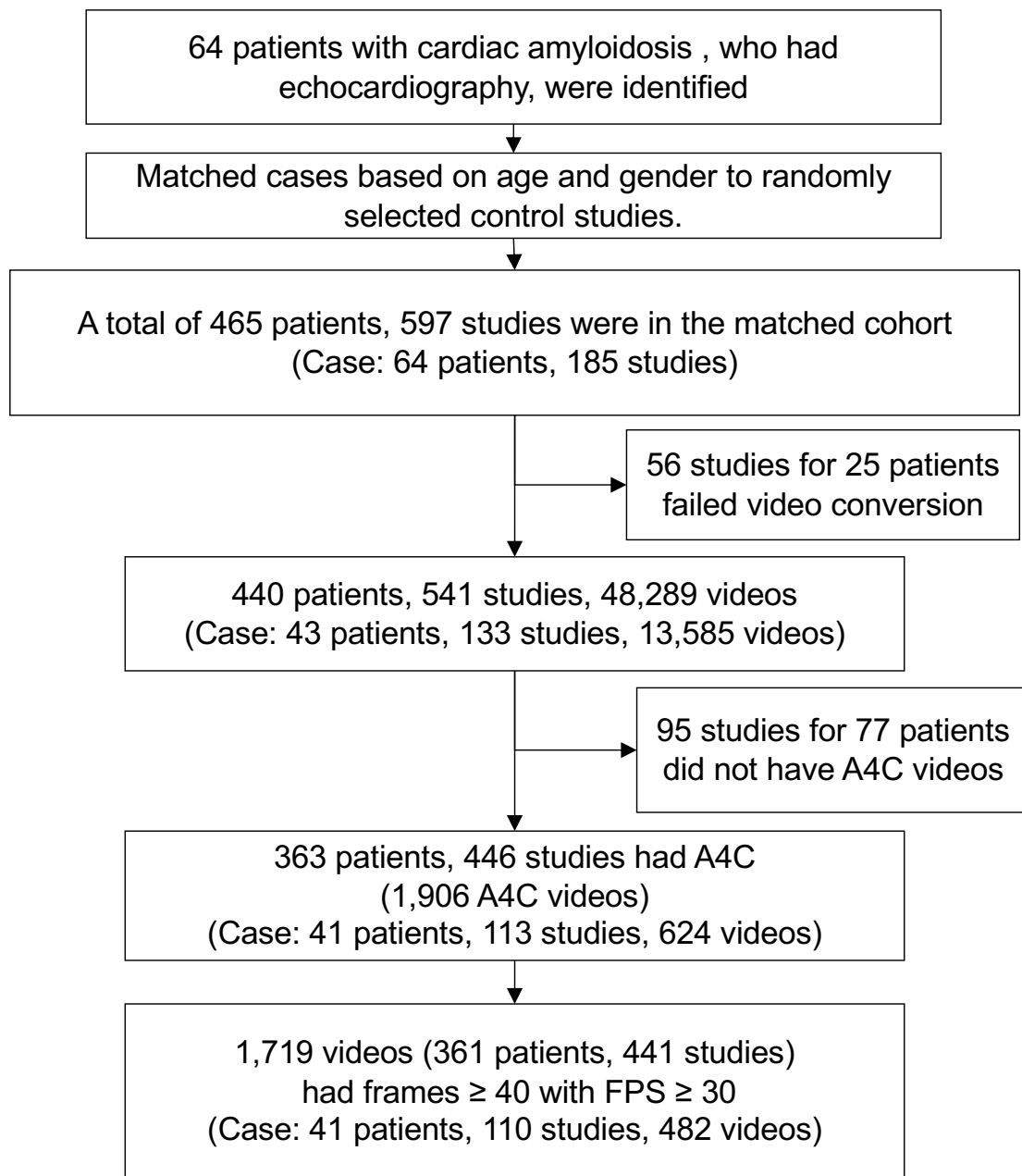
Supplementary Figure 11. Cohort selection procedure for the MGH echocardiography cohort.

MGH: Massachusetts General Hospital, FPS: frames per second, A4C: apical 4 chamber view.

```
┌─────────────────────────────────────────────────┐
│    56 patients with cardiac amyloidosis , who had │
│       echocardiography, were identified           │
└─────────────────────────────────────────────────┘
                        │
                        ▼
┌─────────────────────────────────────────────────┐
│    Matched to randomly selected control studies   │
│          based on age and gender                  │
└─────────────────────────────────────────────────┘
                        │
                        ▼
┌─────────────────────────────────────────────────┐
│  A total of 824 patients, 930 studies were in the │
│              matched cohort                       │
│         (Case: 56 patients, 128 studies)          │
└─────────────────────────────────────────────────┘
                        │          ┌──────────────────────┐
                        ├─────────▶│  23 studies for 29    │
                        │          │  patients failed      │
                        │          │  video conversion     │
                        ▼          └──────────────────────┘
┌─────────────────────────────────────────────────┐
│       804 patients, 907 studies, 24311 videos     │
│     (Case: 56 patients, 125 studies, 3,382 videos)│
└─────────────────────────────────────────────────┘
                        │          ┌──────────────────────┐
                        ├─────────▶│  338 studies for 284  │
                        │          │  patients did not have│
                        │          │  A4C videos           │
                        ▼          └──────────────────────┘
┌─────────────────────────────────────────────────┐
│        520 patients, 569 studies had A4C          │
│               (1,341 A4C videos)                  │
│      (Case: 42 patients, 79 studies, 199 videos)  │
└─────────────────────────────────────────────────┘
                        │
                        ▼
┌─────────────────────────────────────────────────┐
│  876 videos (350 patients, 369 studies) had       │
│              Frames ≥ 40                           │
│                with FPS ≥ 30                       │
│      (Case: 32 patients, 46 studies, 122 videos)  │
└─────────────────────────────────────────────────┘
```

Supplementary Figure 12. Cohort selection procedure for the UCSF echocardiography cohort.

UCSF: University of California San Francisco, FPS: frames per second, A4C: apical 4 chamber view.
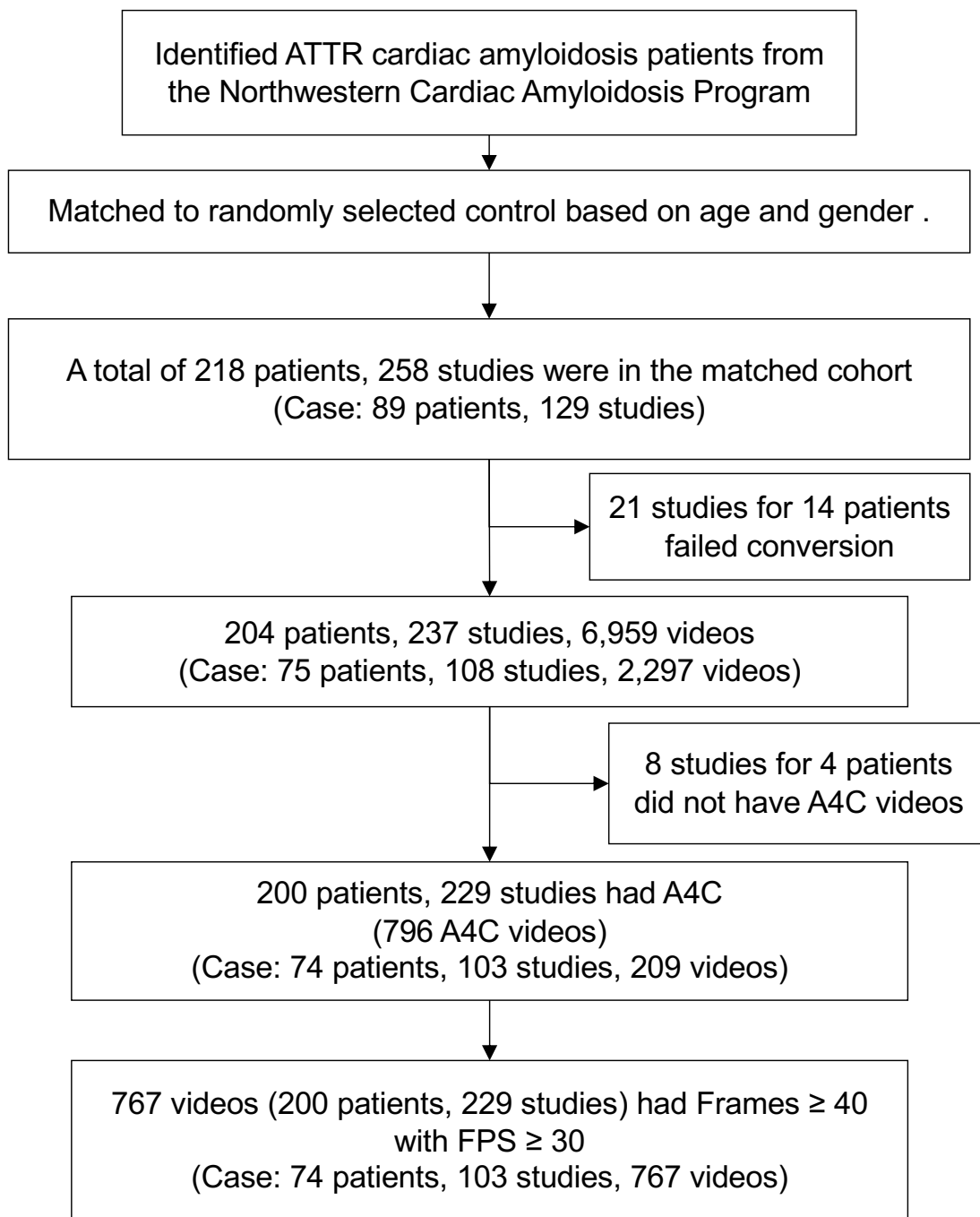
Supplementary Figure 13. Cohort selection procedure for the NW echocardiography cohort.

NW: Northwestern University, ATTR: amyloid transthyretin, FPS: frames per second, A4C: apical 4 chamber view.

Identified all the patients who were diagnosed as cardiac amyloidosis in Keio University Hospital (54 patients 138 studies).

Matched, based on age and gender, with patients randomly selected from all the patients who had echocardiography within 2019/7/1-2019/7/31 and had no known cardiac amyloidosis (890 patients, 909 studies)

A total of 192 patients, 276 studies were in the matched cohort

No studies failed video conversion

192 patients, 276 studies, 11,472 videos
(Case: 54 patients, 138 studies, 5,637 videos)

1 study did not have A4C videos

192 patients, 275 studies had A4C
(548 A4C videos)
(Case: 54 patients, 137 studies, 308 videos)

480 videos (173 patients, 239 studies) had Frames ≥ 40
with FPS ≥ 30
(Case: 52 patients, 118 studies, 480 videos)

Supplementary Figure 14. Cohort selection procedure for the Keio echocardiography cohort.

Keio: Keio University, FPS: frames per second, A4C: apical 4 chamber view.

```
┌─────────────────────────────────────────────────────────────┐
│   A total of 247 patients, 600 studies with HCM were identified │
└─────────────────────────────────────────────────────────────┘
                    │
                    │────────────────►┌────────────────────────┐
                    │                 │  30 studies for 1 patient │
                    │                 │  failed video conversion  │
                    ▼                 └────────────────────────┘
┌─────────────────────────────────────────────────────────┐
│      246 patients, 570 studies, 50,124 videos            │
└─────────────────────────────────────────────────────────┘
                    │
                    │────────────────►┌────────────────────────┐
                    │                 │  34 studies for 2 patients │
                    │                 │  did not have A4C videos   │
                    ▼                 └────────────────────────┘
┌─────────────────────────────────────────────────────────┐
│          244 patients, 536 studies had A4C               │
│                 (2,254 A4C videos)                       │
└─────────────────────────────────────────────────────────┘
                    │
                    ▼
┌─────────────────────────────────────────────────────────┐
│      2,181 videos (243 patients, 525 studies)            │
│          had frames ≥ 40 with FPS ≥ 30                   │
└─────────────────────────────────────────────────────────┘
```
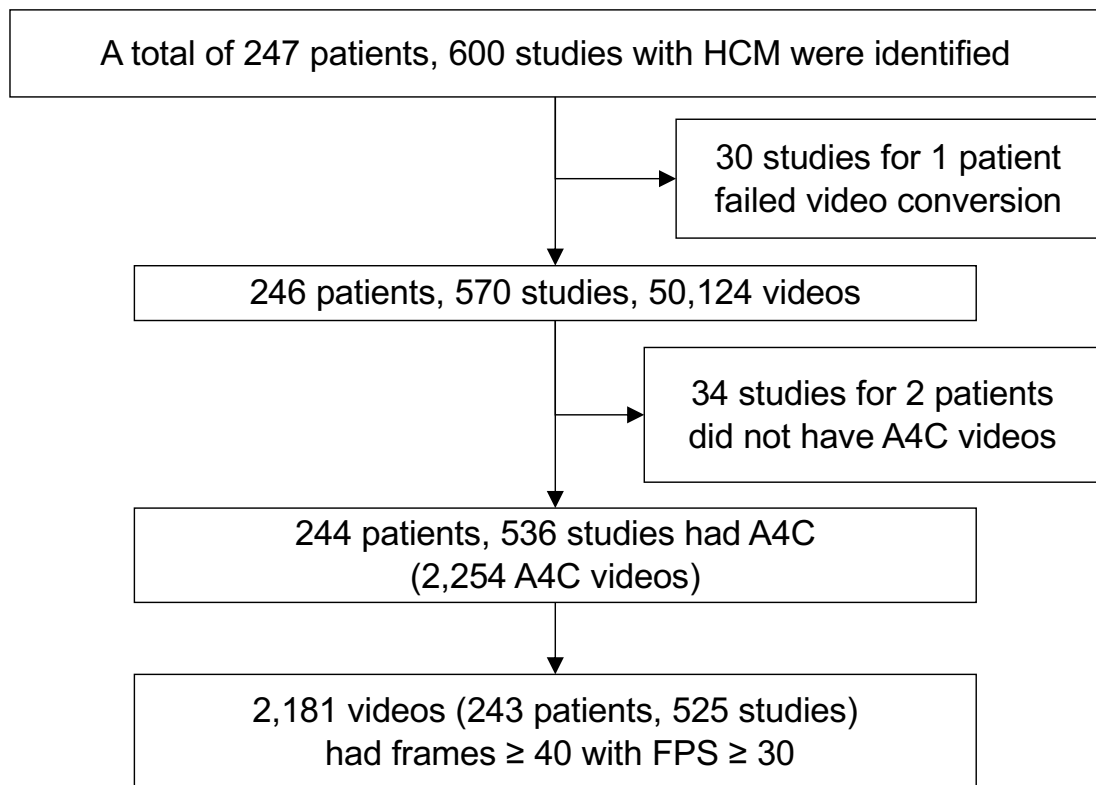
Supplementary Figure 15. Cohort selection procedure for the MGH echocardiography HCM comparison group.

MGH: Massachusetts General Hospital, HCM: hypertrophic cardiomyopathy, FPS: frames per second, A4C: apical 4 chamber view.

```
┌─────────────────────────────────────────────────────────┐
│   A total of 206 patients, 389 studies with HCM were identified   │
└─────────────────────────────────────────────────────────┘
                │
                │          ┌──────────────────────────┐
                ├─────────▶│   No studies failed video    │
                │          │        conversion            │
                │          └──────────────────────────┘
                ▼
┌─────────────────────────────────────────────────────────┐
│        206 patients, 389 studies, 20,922 videos              │
└─────────────────────────────────────────────────────────┘
                │
                │          ┌──────────────────────────┐
                ├─────────▶│  9 studies for 4 patients did  │
                │          │     not have A4C videos        │
                │          └──────────────────────────┘
                ▼
┌─────────────────────────────────────────────────────────┐
│          202 patients, 380 studies had A4C                  │
│                (1,335 A4C videos)                            │
└─────────────────────────────────────────────────────────┘
                │
                ▼
┌─────────────────────────────────────────────────────────┐
│         961 videos (159 patients, 262 studies)              │
│              had frames ≥ 40 with FPS ≥ 30                   │
└─────────────────────────────────────────────────────────┘
```
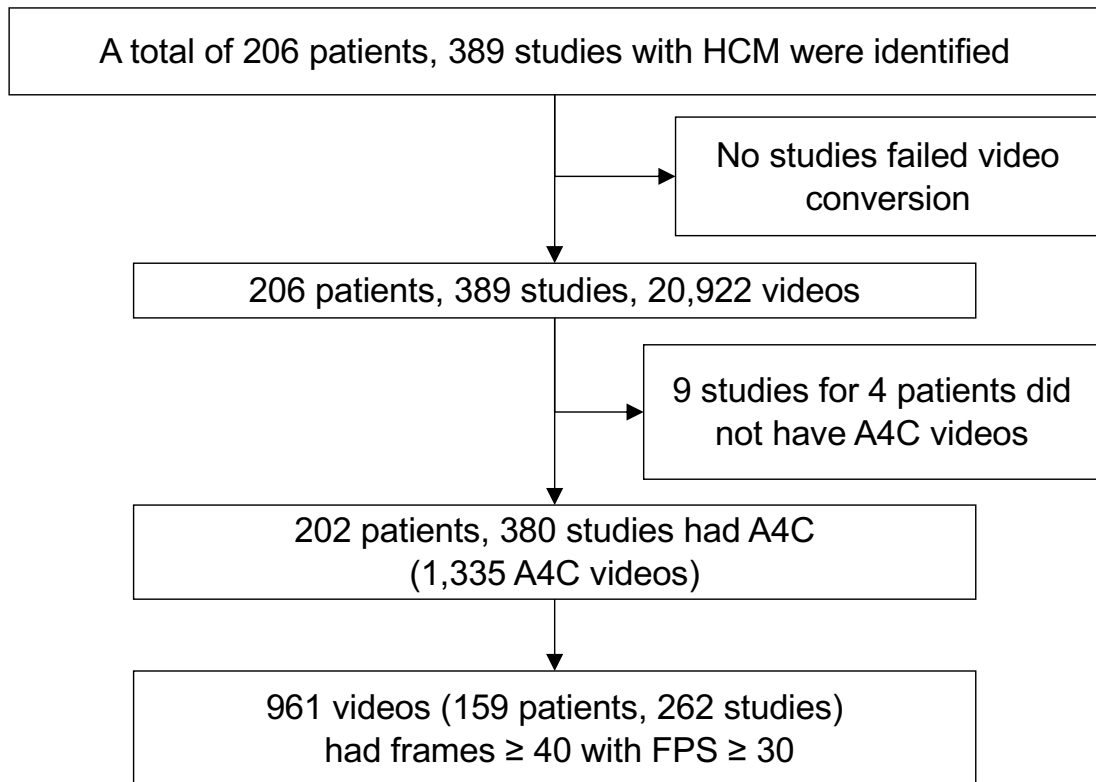
Supplementary Figure 16. Cohort selection procedure for the UCSF echocardiography HCM comparison group.

UCSF: University of California San Francisco, HCM: hypertrophic cardiomyopathy, FPS: frames per second, A4C: apical 4 chamber view.

```
┌─────────────────────────────────────────────────────────────────┐
│        A total of 54 patients, 122 studies with HCM were identified │
└─────────────────────────────────────────────────────────────────┘
                              │
                              │         ┌──────────────────────────┐
                              ├────────▶│   No studies failed video │
                              │         │        conversion         │
                              ▼         └──────────────────────────┘
┌─────────────────────────────────────────────────────────────────┐
│            54 patients, 122 studies, 5,149 videos                 │
└─────────────────────────────────────────────────────────────────┘
                              │
                              │         ┌──────────────────────────┐
                              ├────────▶│  2 studies did not have A4C │
                              │         │          videos            │
                              ▼         └──────────────────────────┘
┌─────────────────────────────────────────────────────────────────┐
│               54 patients, 120 studies had A4C                    │
│                    (209 A4C videos)                               │
└─────────────────────────────────────────────────────────────────┘
                              │
                              ▼
┌─────────────────────────────────────────────────────────────────┐
│          205 videos (54 patients, 120 studies)                    │
│            had frames ≥ 40 with FPS ≥ 30                           │
└─────────────────────────────────────────────────────────────────┘
```

Supplementary Figure 17. Cohort selection procedure for the Keio echocardiography HCM comparison group.

Keio: Keio University, HCM: hypertrophic cardiomyopathy, FPS: frames per second, A4C: apical 4 chamber view.

```
┌─────────────────────────────────────────────────────────────────┐
│     A total of 605 patients, 677 studies with HTN were identified │
└─────────────────────────────────────────────────────────────────┘
                            │
                            │──────────────►┌──────────────────────┐
                            │               │ 11 studies for 8 patients │
                            │               │ failed video conversion │
                            ▼               └──────────────────────┘
┌─────────────────────────────────────────────────┐
│     597 patients, 666 studies, 34,016 videos     │
└─────────────────────────────────────────────────┘
                            │
                            │──────────────►┌──────────────────────┐
                            │               │ 55 studies for 44 patients │
                            │               │ did not have A4C videos │
                            ▼               └──────────────────────┘
┌─────────────────────────────────────────────────┐
│     553 patients, 611 studies had A4C            │
│              (1,725 A4C videos)                  │
└─────────────────────────────────────────────────┘
                            │
                            ▼
┌─────────────────────────────────────────────────┐
│   1,651 videos (538 patients, 593 studies)       │
│       had frames ≥ 40 with FPS ≥ 30              │
└─────────────────────────────────────────────────┘
```

Supplementary Figure 18. Cohort selection procedure for the BWH echocardiography hypertension comparison group.

BWH: Brigham and Women's Hospital, HTN: hypertension, FPS: frames per second, A4C: apical 4 chamber view.

```
┌─────────────────────────────────────────────────────────────────┐
│     A total of 332 patients, 367 studies with HTN were identified │
└─────────────────────────────────────────────────────────────────┘
                            │
                            │────────────→ ┌──────────────────────┐
                            │              │  No studies failed video │
                            │              │      conversion          │
                            ↓              └──────────────────────┘
┌─────────────────────────────────────────────────┐
│     332 patients, 367 studies, 32,092 videos      │
└─────────────────────────────────────────────────┘
                            │
                            │────────────→ ┌──────────────────────┐
                            │              │  11 studies for 10 patients │
                            │              │  did not have A4C videos    │
                            ↓              └──────────────────────┘
┌─────────────────────────────────────────────────┐
│     322 patients, 356 studies had A4C             │
│            (1,500 A4C videos)                      │
└─────────────────────────────────────────────────┘
                            │
                            ↓
┌─────────────────────────────────────────────────┐
│     1,473 videos (318 patients, 351 studies)      │
│        had frames ≥ 40 with FPS ≥ 30              │
└─────────────────────────────────────────────────┘
```
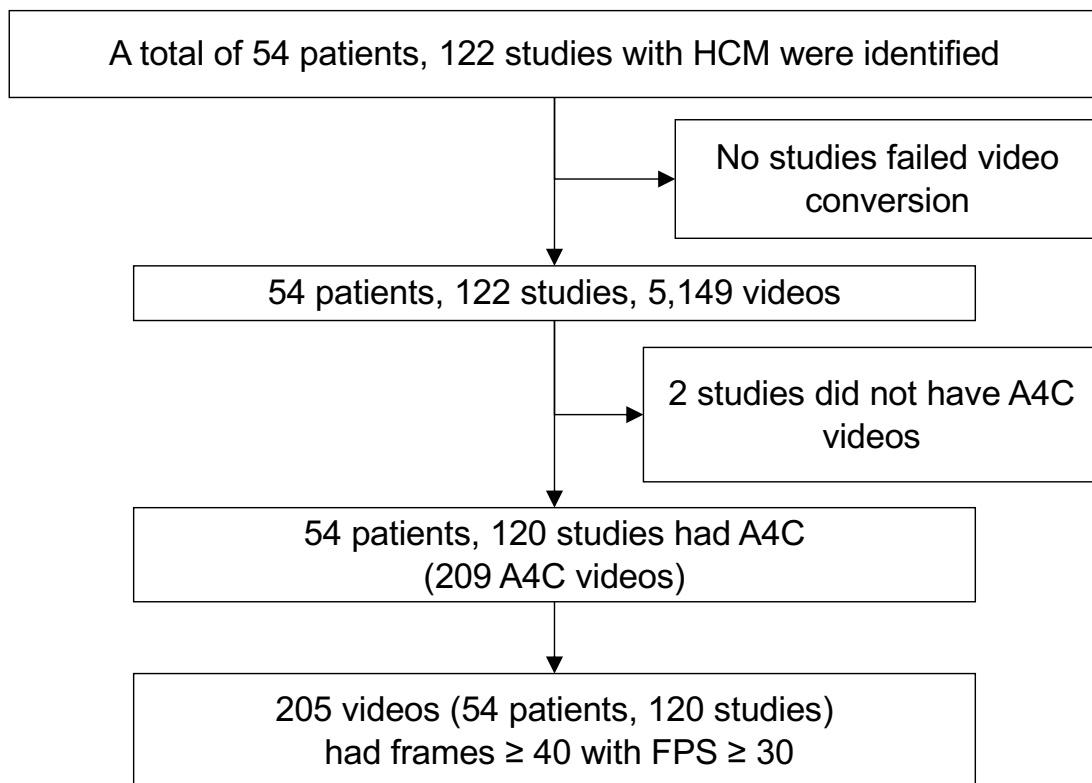
Supplementary Figure 19. Cohort selection procedure for the MGH echocardiography hypertension comparison group.

MGH: Massachusetts General Hospital, HTN: hypertension, FPS: frames per second, A4C: apical 4 chamber view.

A total of 1,824 patients, 1,991 studies with HTN were identified

75 studies for 65 patients failed video conversion

1,759 patients, 1,916 studies, 104,211 videos

141 studies for 111 patients did not have A4C videos

1,648 patients, 1,775 studies had A4C (6,213 A4C videos)

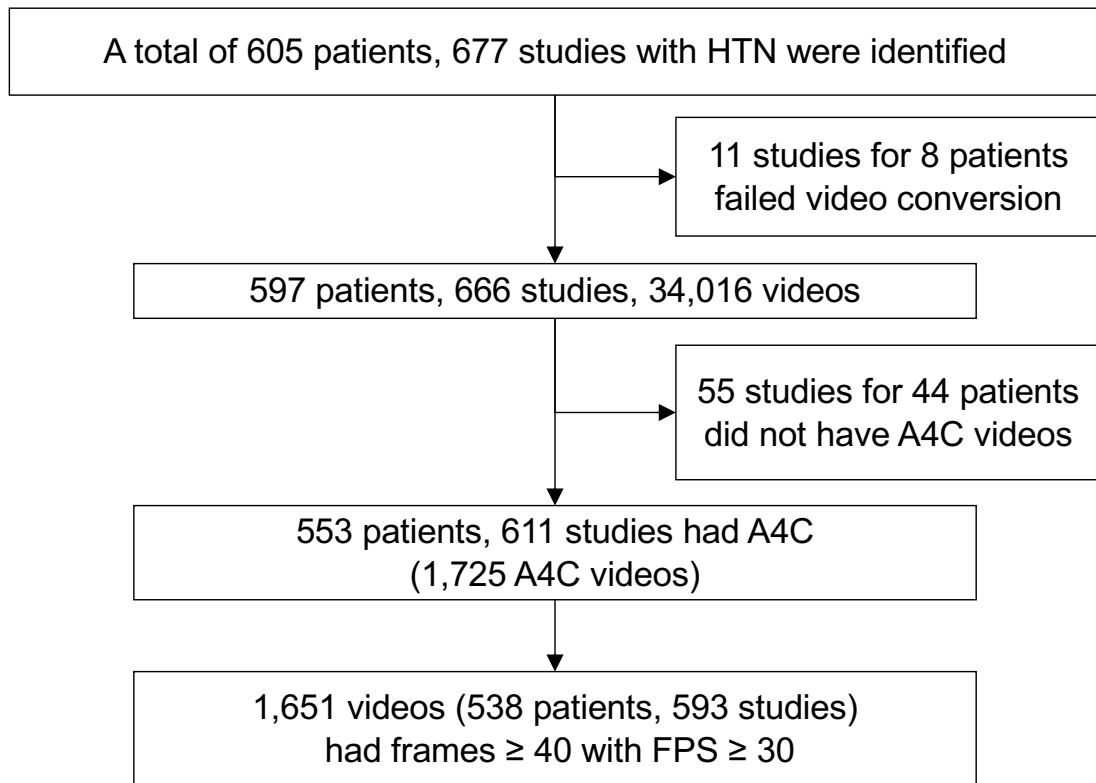5,103 videos (1,360 patients, 1,450 studies) had frames ≥ 40 with FPS ≥ 30

Supplementary Figure 20. Cohort selection procedure for the UCSF echocardiography hypertension comparison group.

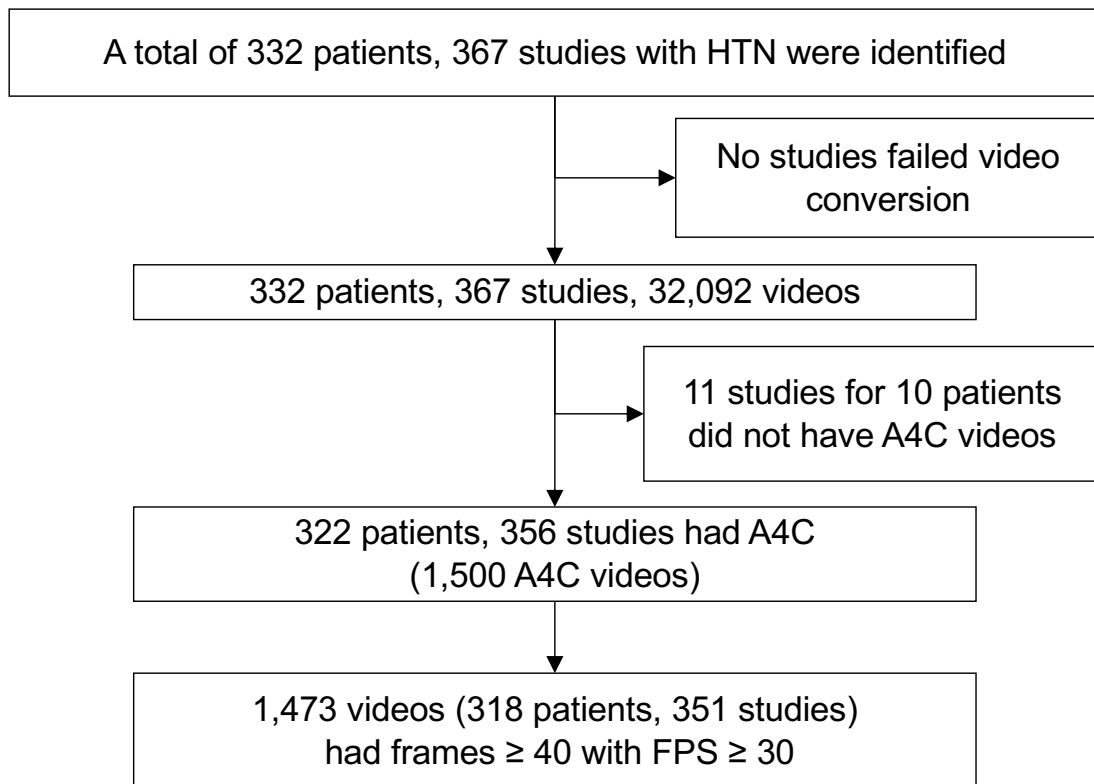UCSF: University of California San Francisco, HTN: hypertension, FPS: frames per second, A4C: apical 4 chamber view.

```
┌─────────────────────────────────────────────────────────────┐
│   A total of 232 patients, 239 studies with HTN were identified │
└─────────────────────────────────────────────────────────────┘
                              │
                              │──────────→ ┌──────────────────────┐
                              │            │  1 study for 1 patient │
                              │            │  failed video conversion│
                              ↓            └──────────────────────┘
┌─────────────────────────────────────────────────┐
│   231 patients, 238 studies, 9,502 videos          │
└─────────────────────────────────────────────────┘
                              │
                              │──────────→ ┌──────────────────────┐
                              │            │ 3 studies for 3 patients did│
                              │            │   not have A4C videos  │
                              ↓            └──────────────────────┘
┌─────────────────────────────────────────────────┐
│   228 patients, 235 studies had A4C                │
│   (399 A4C videos)                                 │
└─────────────────────────────────────────────────┘
                              │
                              ↓
┌─────────────────────────────────────────────────┐
│   399 videos (228 patients, 235 studies)           │
│   had frames ≥ 40 with FPS ≥ 30                     │
└─────────────────────────────────────────────────┘
```

Supplementary Figure 21. Cohort selection procedure for the Keio echocardiography hypertension comparison group.

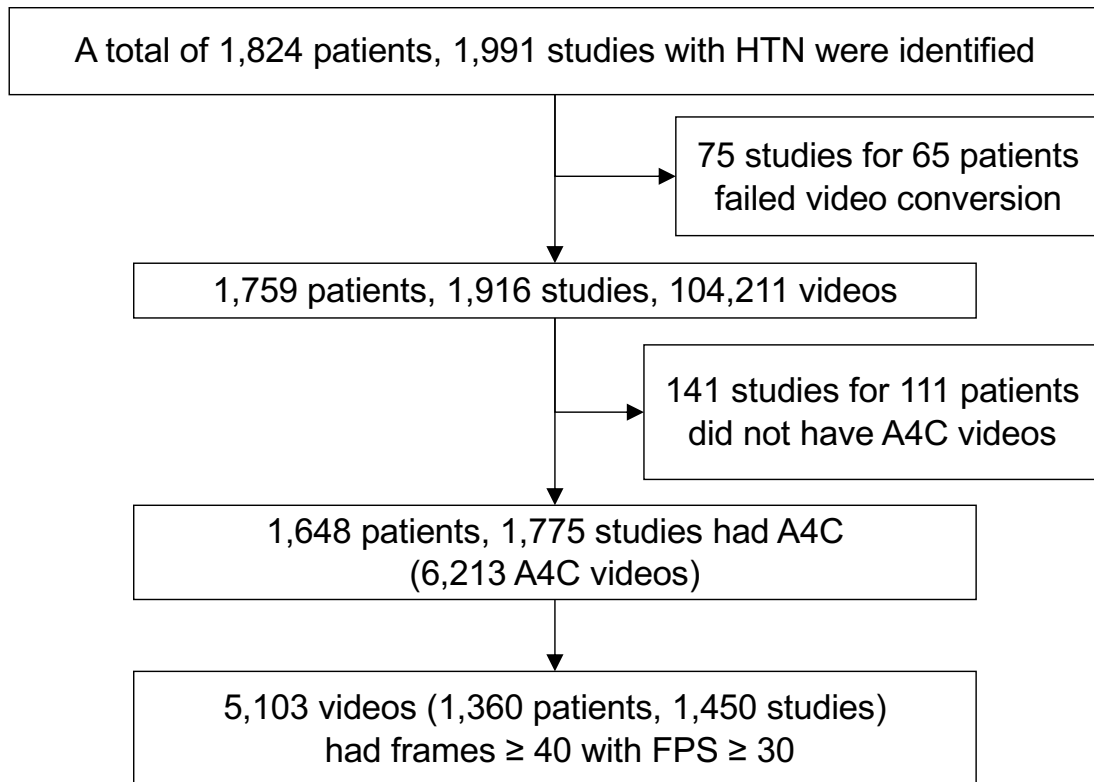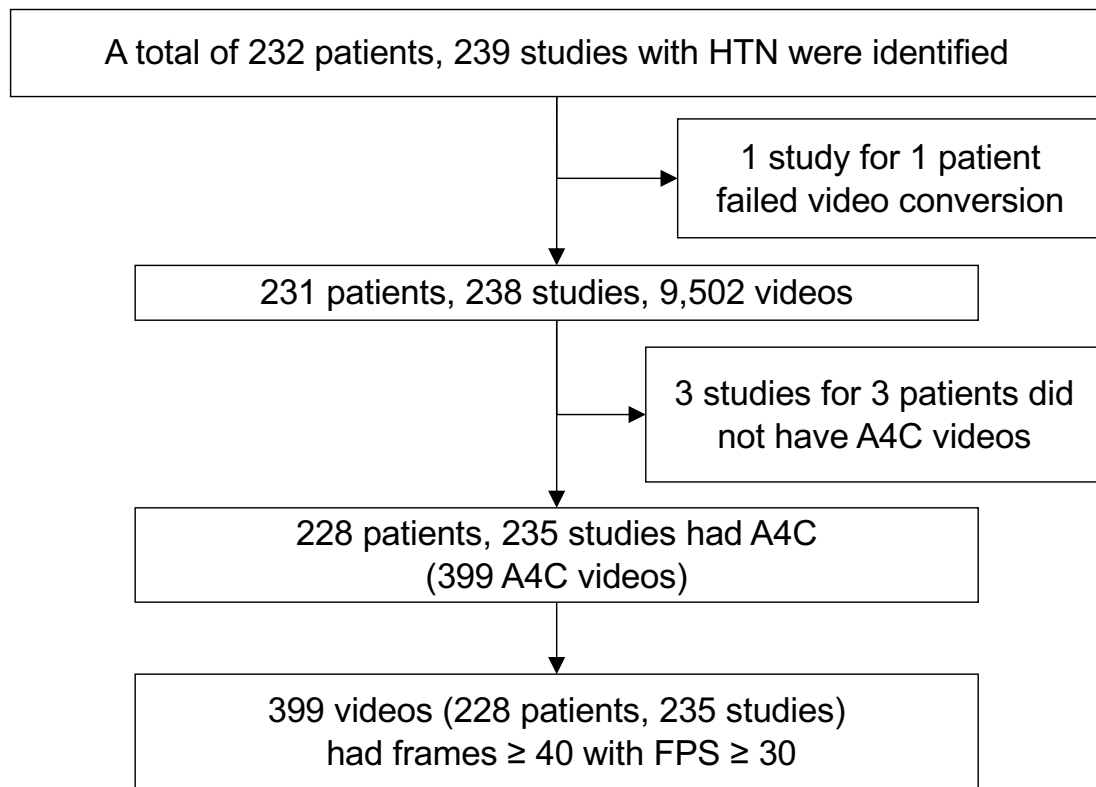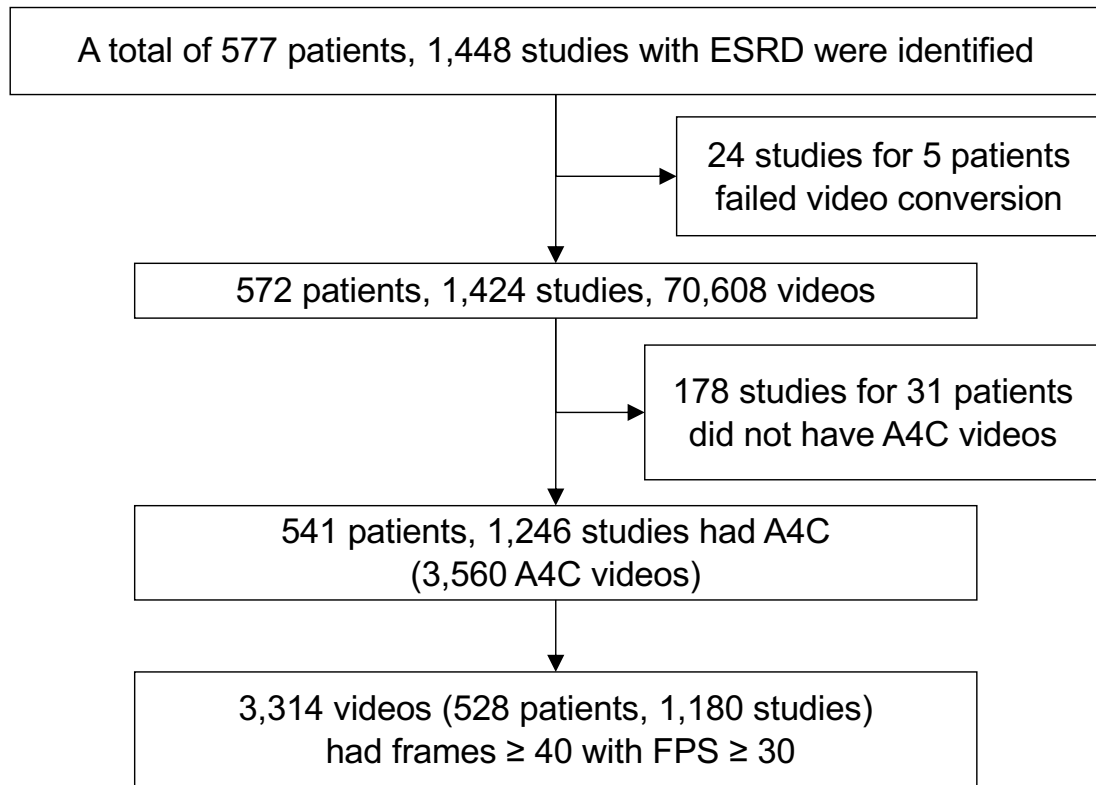Keio: Keio University, HTN: hypertension, FPS: frames per second, A4C: apical 4 chamber view.

```
┌─────────────────────────────────────────────────────────┐
│  A total of 577 patients, 1,448 studies with ESRD were   │
│                     identified                            │
└─────────────────────────────────────────────────────────┘
                          │
                          │        ┌──────────────────────────┐
                          ├───────▶│  24 studies for 5 patients│
                          │        │  failed video conversion  │
                          │        └──────────────────────────┘
                          ▼
┌─────────────────────────────────────────────────────────┐
│      572 patients, 1,424 studies, 70,608 videos           │
└─────────────────────────────────────────────────────────┘
                          │
                          │        ┌──────────────────────────┐
                          ├───────▶│  178 studies for 31 patients│
                          │        │   did not have A4C videos  │
                          │        └──────────────────────────┘
                          ▼
┌─────────────────────────────────────────────────────────┐
│           541 patients, 1,246 studies had A4C             │
│                   (3,560 A4C videos)                      │
└─────────────────────────────────────────────────────────┘
                          │
                          ▼
┌─────────────────────────────────────────────────────────┐
│      3,314 videos (528 patients, 1,180 studies)           │
│           had frames ≥ 40 with FPS ≥ 30                   │
└─────────────────────────────────────────────────────────┘
```

Supplementary Figure 22. Cohort selection procedure for the BWH echocardiography end-stage renal disease controls.

BWH: Brigham and Women's Hospital, ERSD: end-stage renal disease, FPS: frames per second, A4C: apical 4 chamber view.
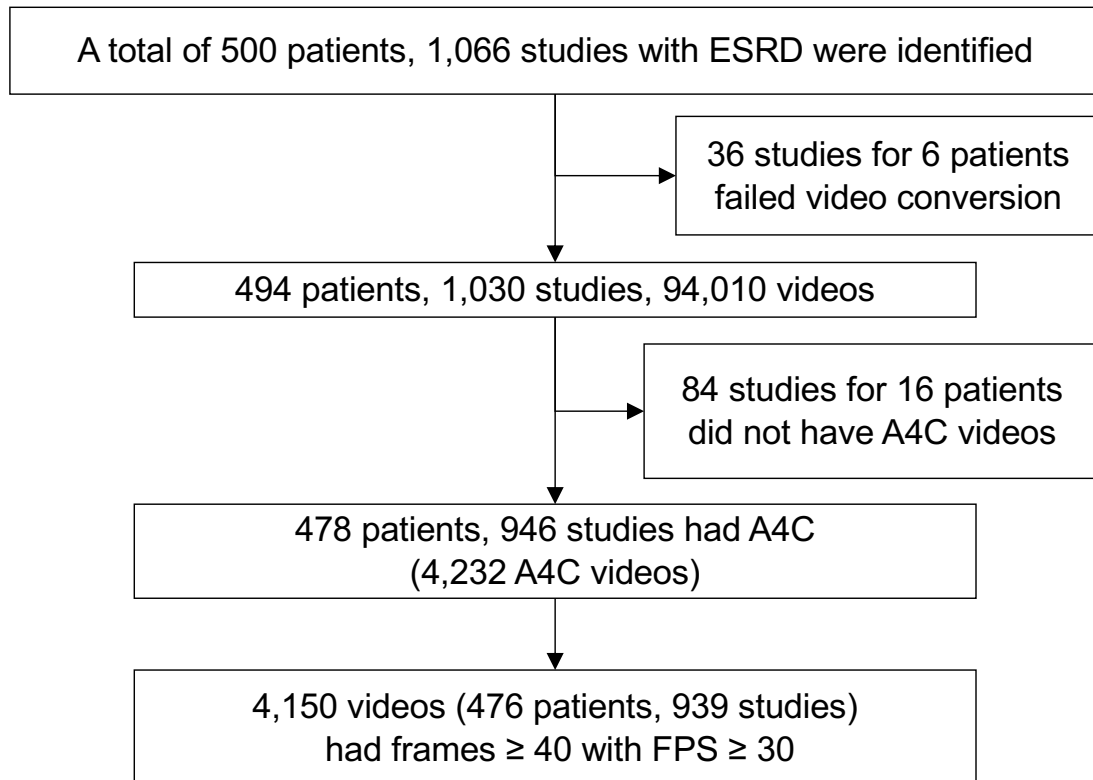
Supplementary Figure 23. Cohort selection procedure for the MGH echocardiography end-stage renal disease controls.

MGH: Massachusetts General Hospital, ERSD: end-stage renal disease, FPS: frames per second, A4C: apical 4 chamber view.

a

b
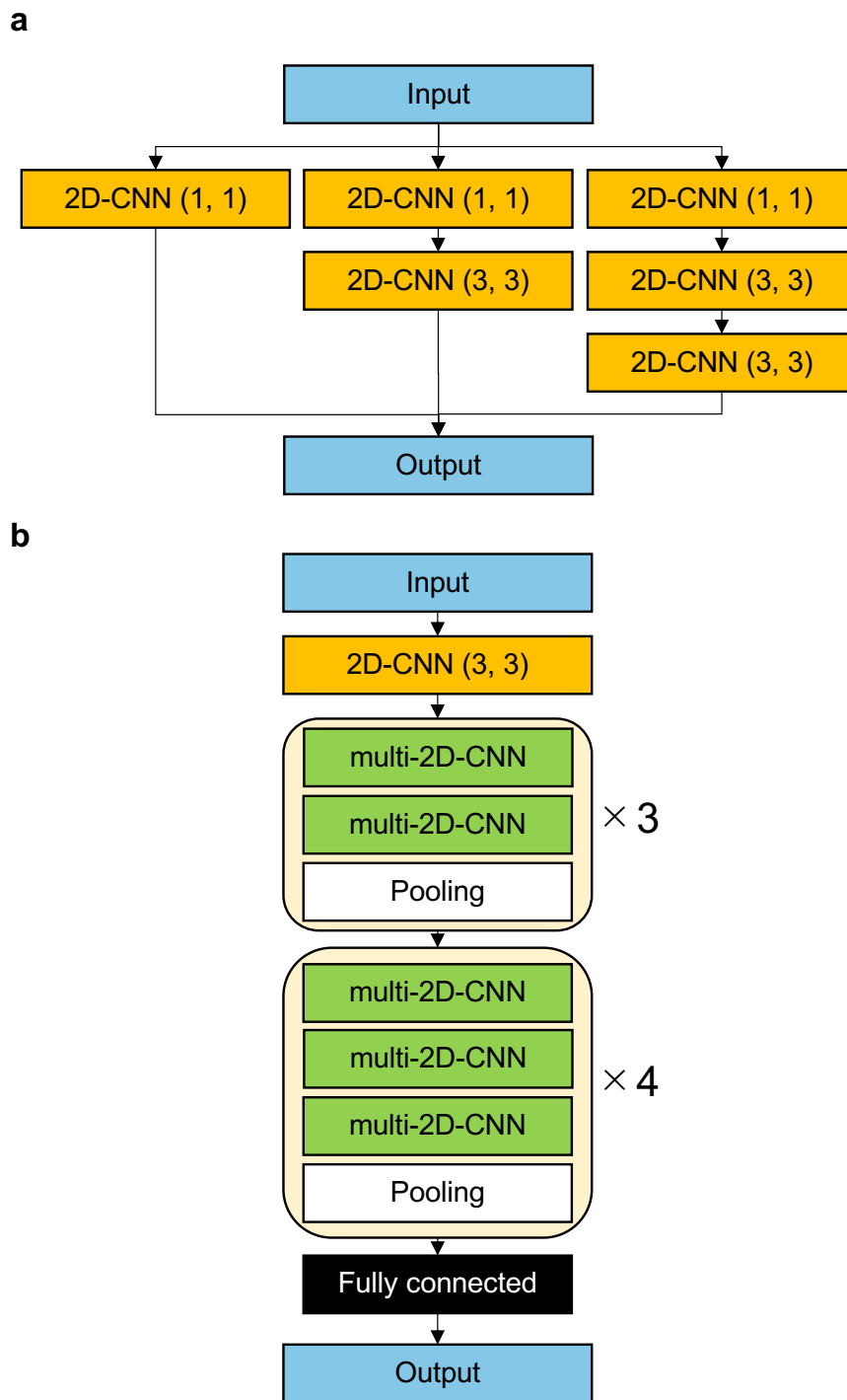
Supplementary Figure 24. Schematic drawing of the network structure of ECG model.

(A) Structure of the multi-2D-CNN module and (B) the full network structure of ECG model. ECG: electrocardiogram, CNN: convolutional neural network.
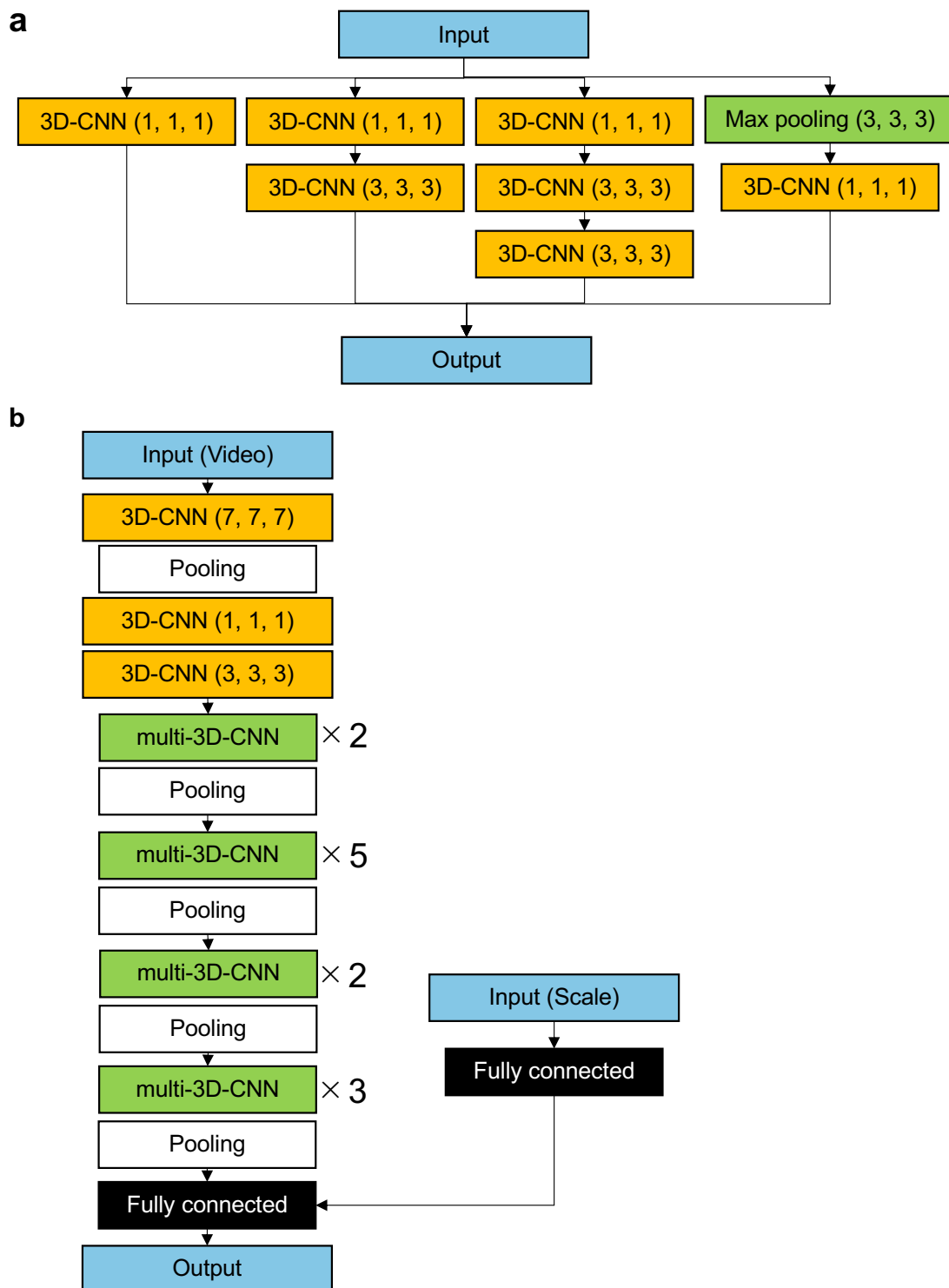
Supplementary Figure 25. Schematic drawing of the network structure of echocardiography model.

(A) Structure of the multi-3D-CNN module and (B) the full network structure of echocardiography model. CNN: convolutional neural network.

```
┌─────────────────────────────────────────────────────┐
│      Identified 12,970 patients who underwent ECG before an   │
│           echocardiography study within 180 days             │
└─────────────────────────────────────────────────────┘
                              │
                              ▼
┌─────────────────────────────────────────────────────┐
│        Selected a pair of ECG and echocardiography study     │
│              closest to each other for each patient          │
└─────────────────────────────────────────────────────┘
                              │            ┌──────────────────────────┐
                              ├───────────▶│  Echo studies for 167 patients │
                              │            │    failed video conversion     │
                              ▼            └──────────────────────────┘
┌─────────────────────────────────────────┐
│        12,803 patients with echo videos         │
│             (1,118,219 videos)                  │
└─────────────────────────────────────────┘
                              │            ┌──────────────────────────┐
                              ├───────────▶│   1,101 patients did not       │
                              │            │      have A4C videos           │
                              ▼            └──────────────────────────┘
┌─────────────────────────────────────────┐
│           11,702 patients had A4C               │
│              (49,372 A4C videos)                │
└─────────────────────────────────────────┘
                              │
                              ▼
┌─────────────────────────────────────────┐
│       47,214 videos (11,541 patients) had       │
│          Frames ≥ 40 with FPS ≥ 30              │
└─────────────────────────────────────────┘
```

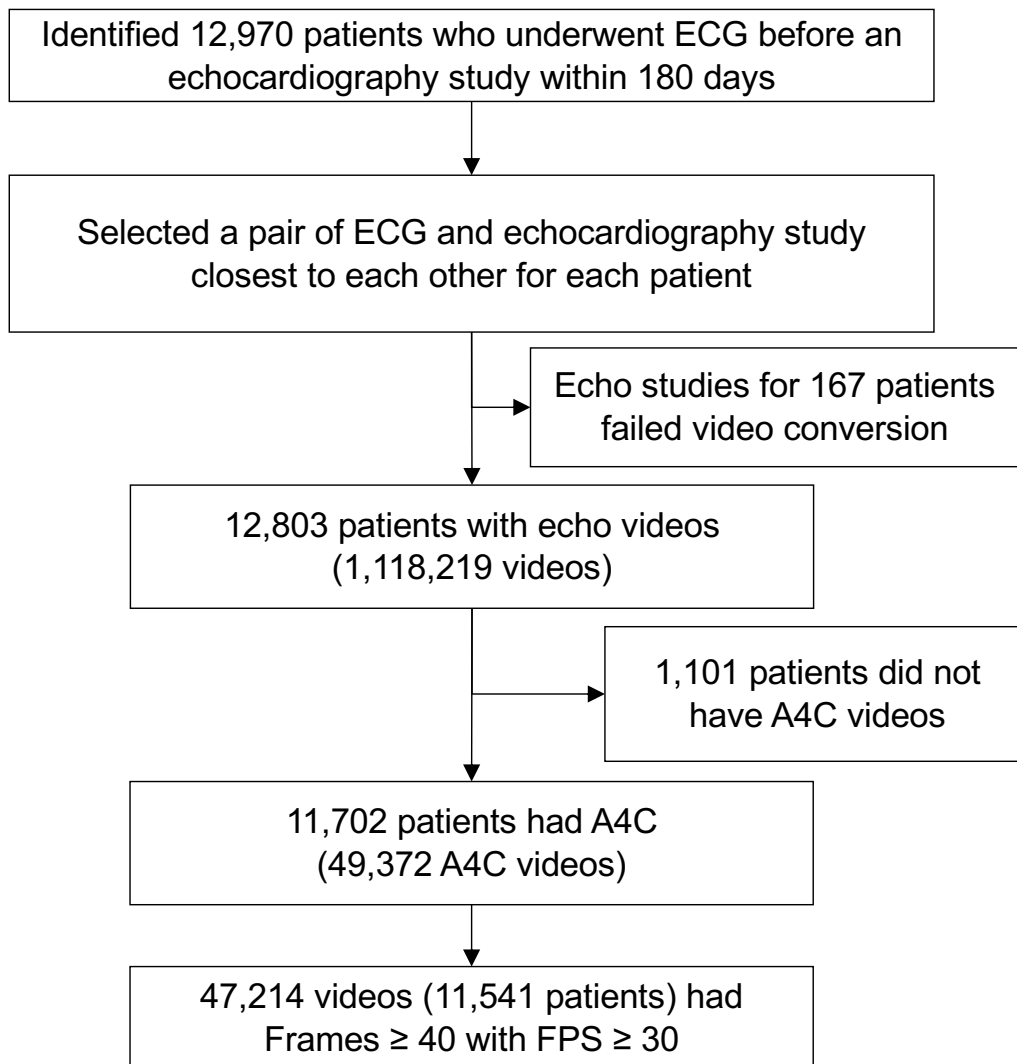**Supplementary Figure 26. Cohort selection procedure for the MGH surveillance cohort.**

MGH: Massachusetts General Hospital, ECG: electrocardiogram, FPS: frames per second, A4C: apical 4 chamber view.

```
┌─────────────────────────────────────────────────────────┐
│   Identified 9,777 patients who underwent ECG before an   │
│        echocardiography study within 180 days             │
└─────────────────────────────────────────────────────────┘
                           │
                           ▼
┌─────────────────────────────────────────────────────────┐
│     Selected a pair of ECG and echocardiography study     │
│            closest to each other for each patient          │
└─────────────────────────────────────────────────────────┘
                           │          ┌──────────────────────────┐
                           │─────────▶│  Echo studies for 65 patients │
                           │          │    failed video conversion    │
                           ▼          └──────────────────────────┘
┌─────────────────────────────────────────────────────────┐
│           9,712 patients with echo videos                 │
│                 (530,142 videos)                          │
└─────────────────────────────────────────────────────────┘
                           │          ┌──────────────────────────┐
                           │─────────▶│  1,794 patients did not have  │
                           │          │          A4C videos           │
                           ▼          └──────────────────────────┘
┌─────────────────────────────────────────────────────────┐
│              7,918 patients had A4C                        │
│                 (27,160 A4C videos)                        │
└─────────────────────────────────────────────────────────┘
                           │
                           ▼
┌─────────────────────────────────────────────────────────┐
│        22,281 videos (6,792 patients) had                 │
│            Frames ≥ 40 with FPS ≥ 30                       │
└─────────────────────────────────────────────────────────┘
```
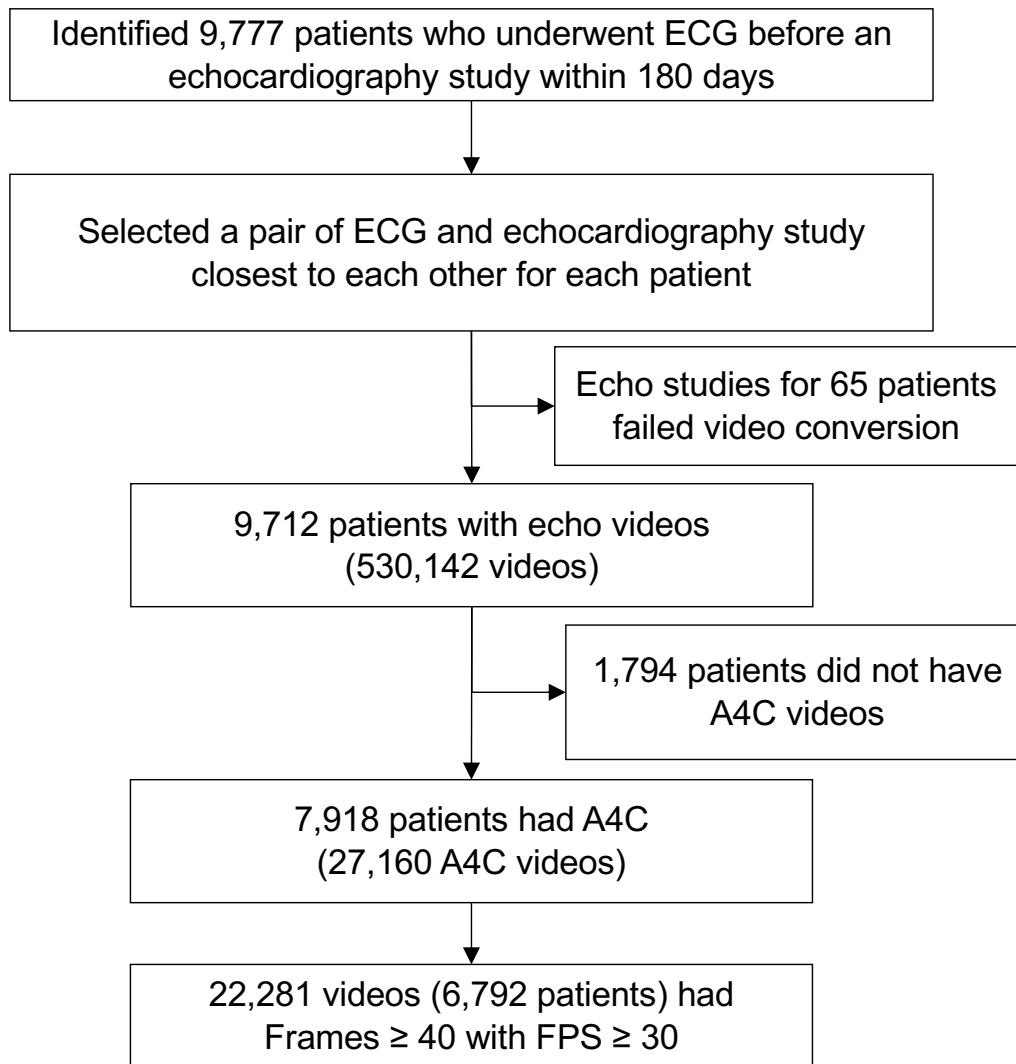
Supplementary Figure 27. Cohort selection procedure for the UCSF surveillance cohort.

UCSF: University of California San Francisco, ECG: electrocardiogram, FPS: frames per second, A4C: apical 4 chamber view.