令和1年6月19日
函館循環器病懇談会

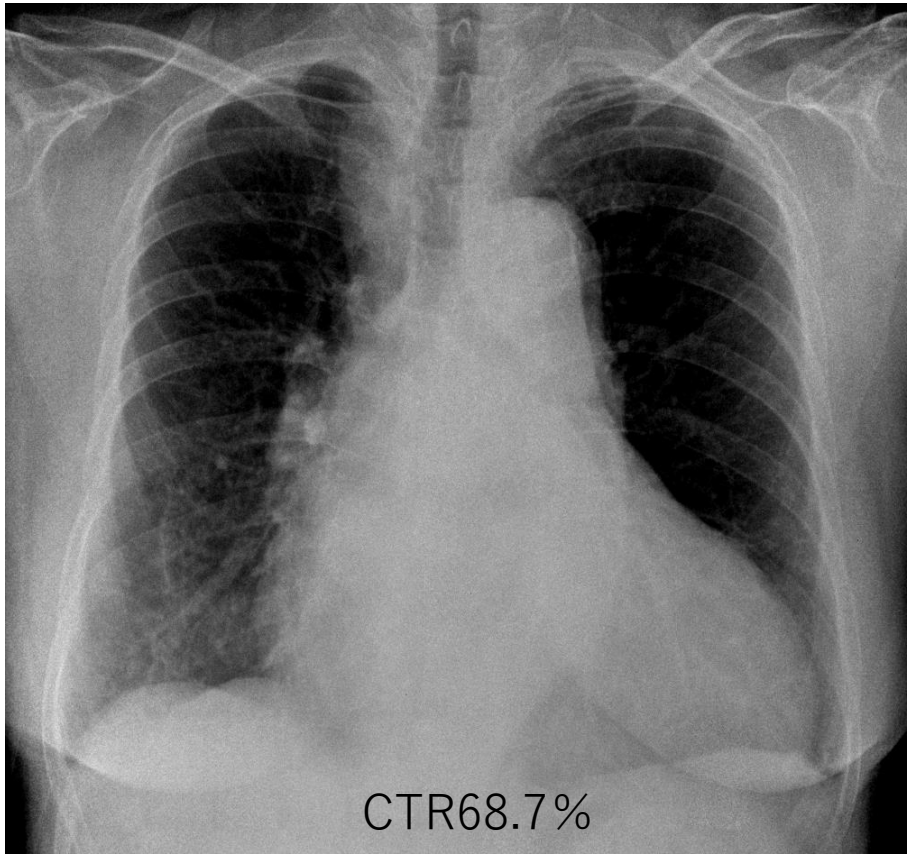
心アミロイドーシスが疑われた２例

中島内科循環器科メンタルクリニック
中島　滋夫

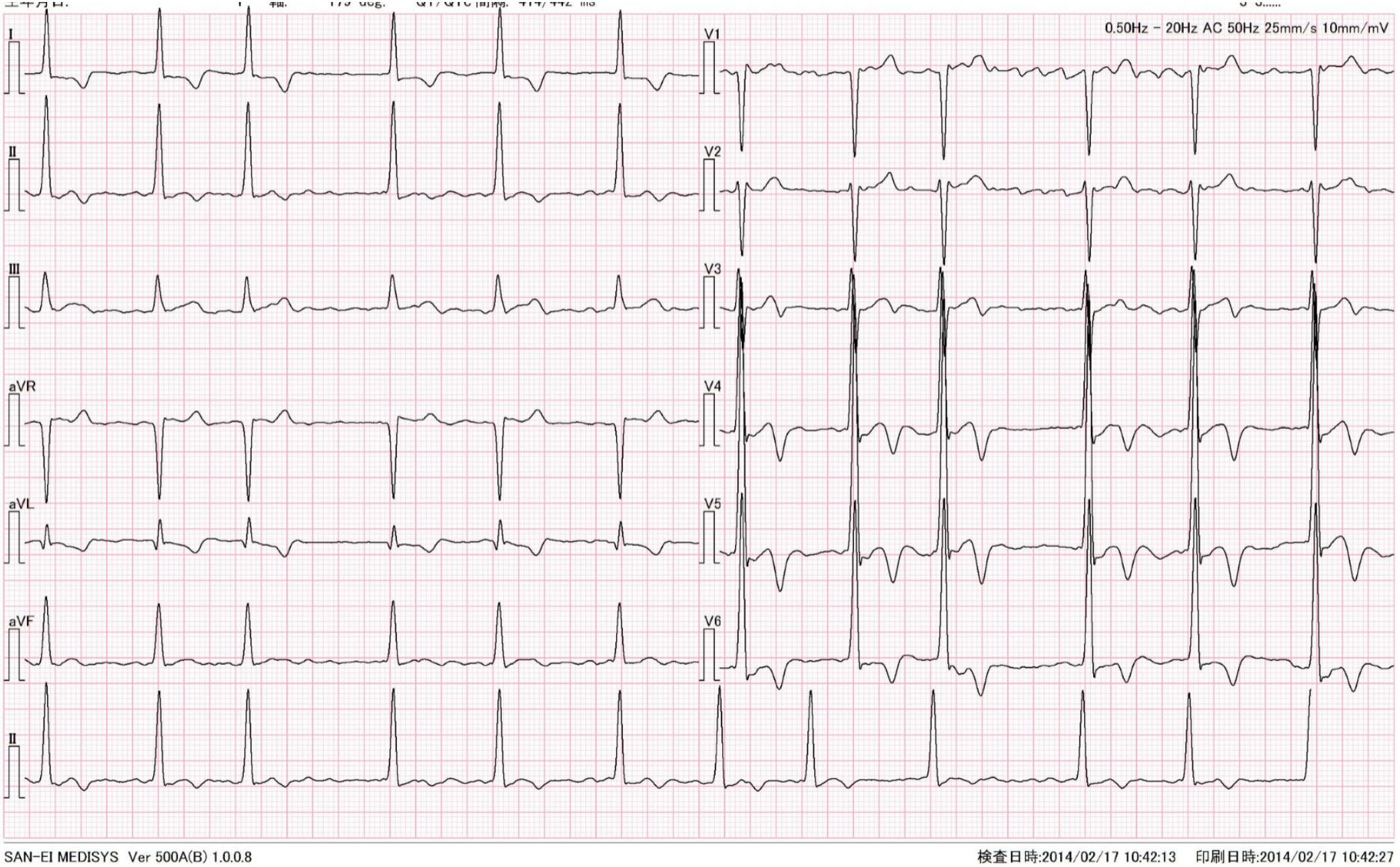
Case1 8372 84歳　♀

- 平成25年3月頃より労作時の息切れあり。9月30日に当院初診

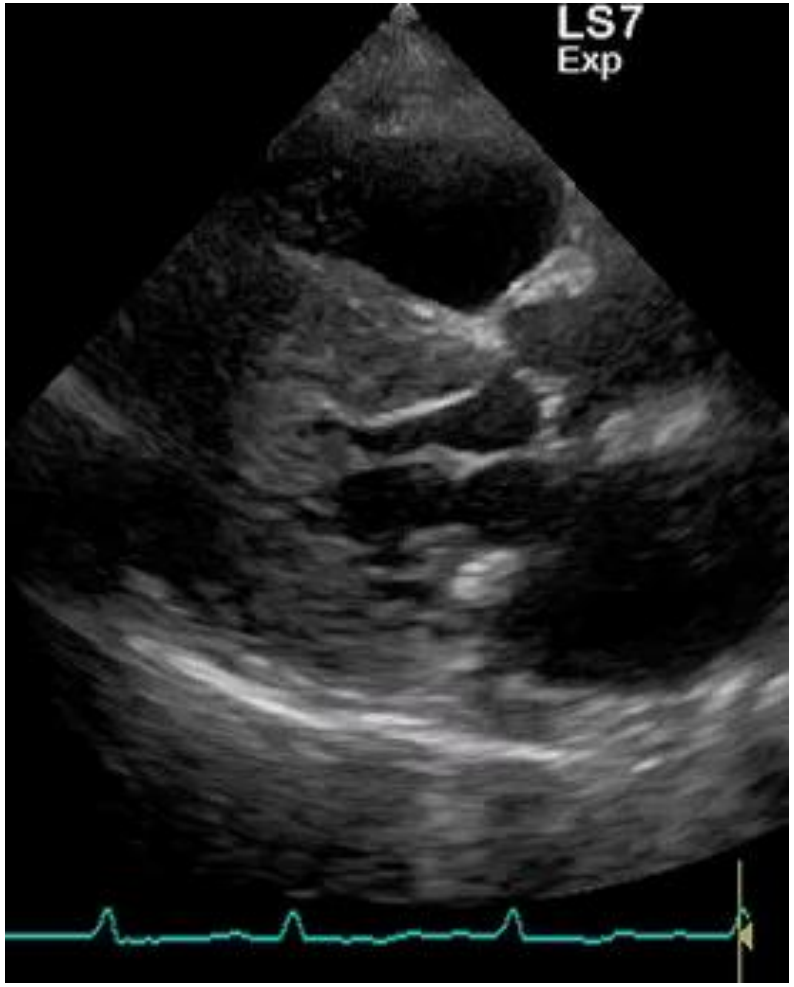
胸部XP　11/19/2013

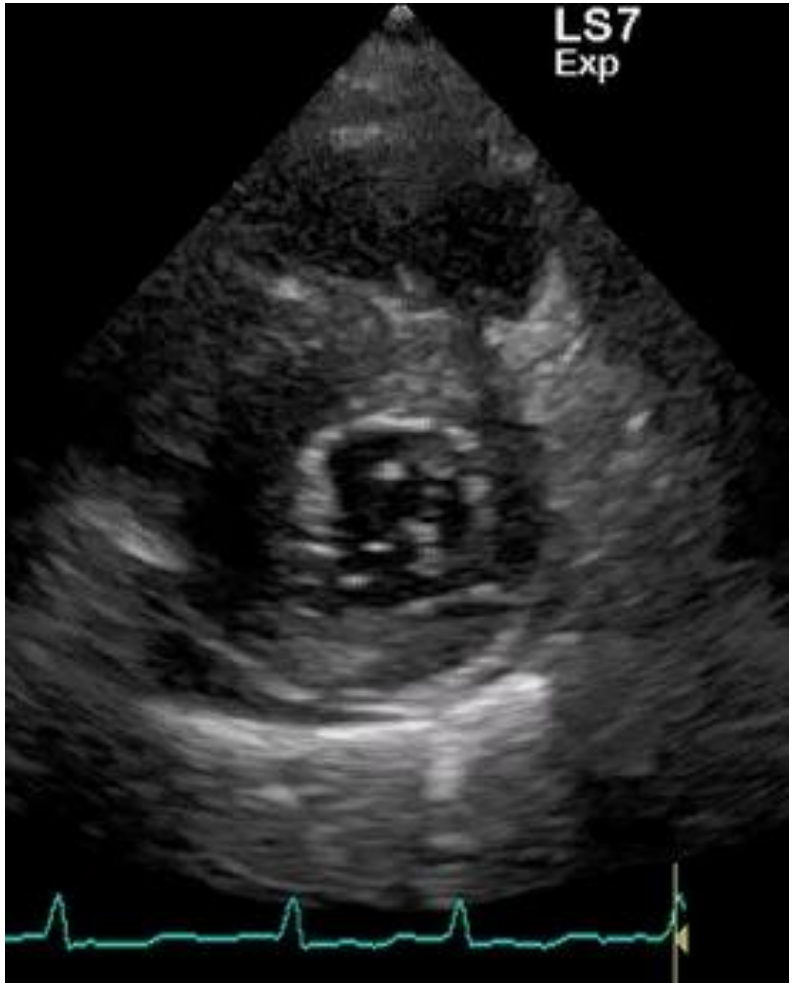


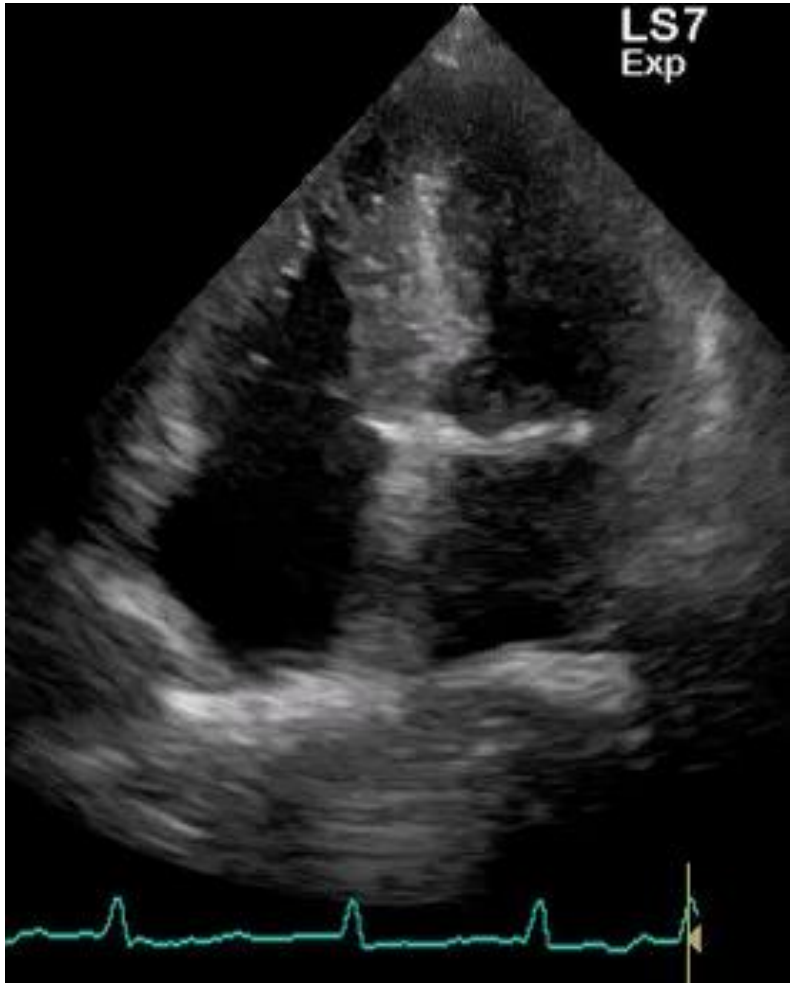
Case1 8372 84歳　♀



Case1 8372 84歳　♀



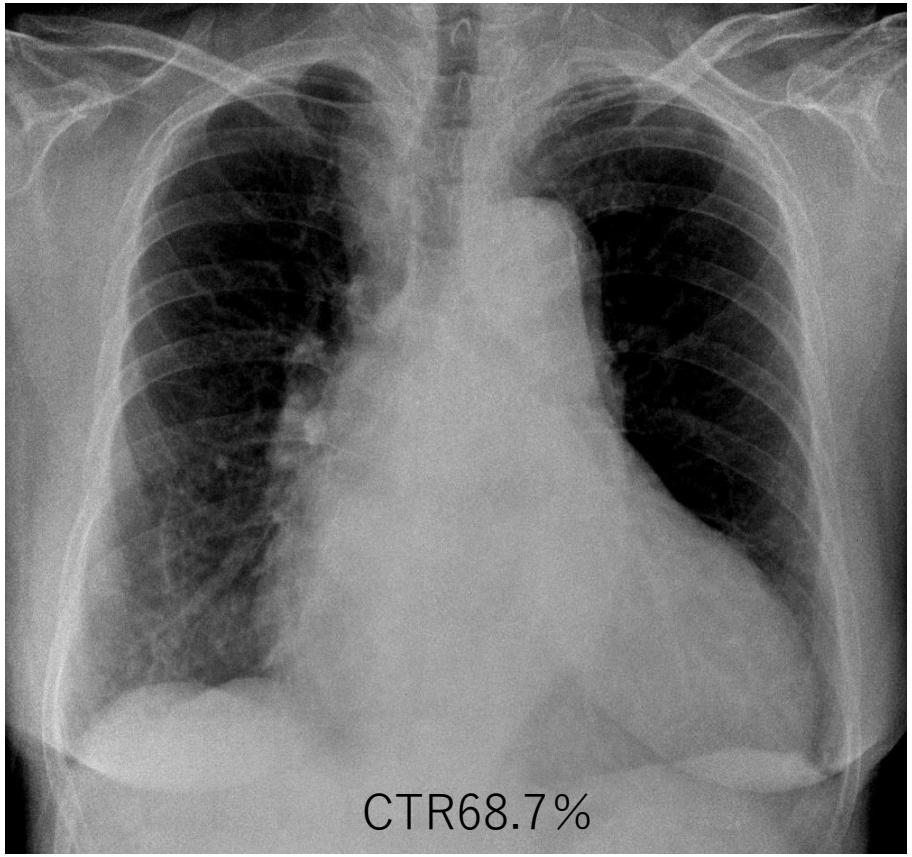




Case1 8372 84歳　♀

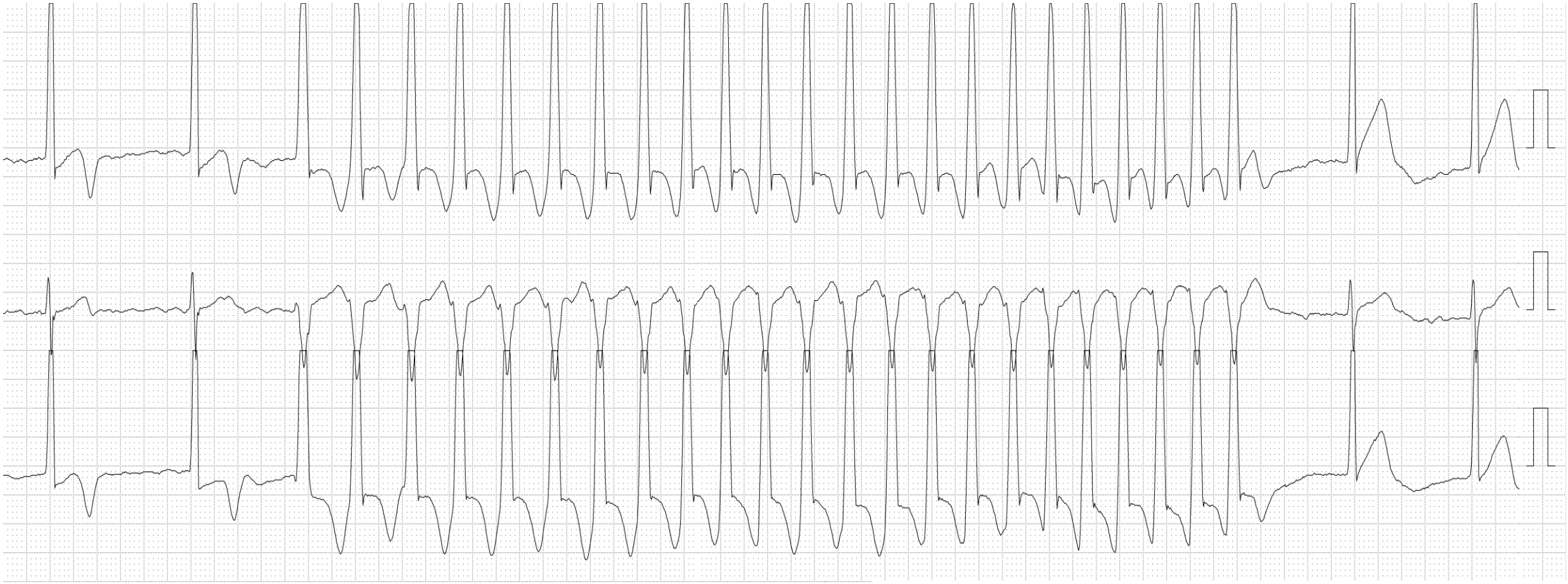
- 平成25年3月頃より労作時の息切れあり9月30日に当院初診
- 平成27年2月2日意識消失し心室細動、AEDで蘇生し○病院救急搬送ICD植え込み術施行。

胸部XP　11/19/2013

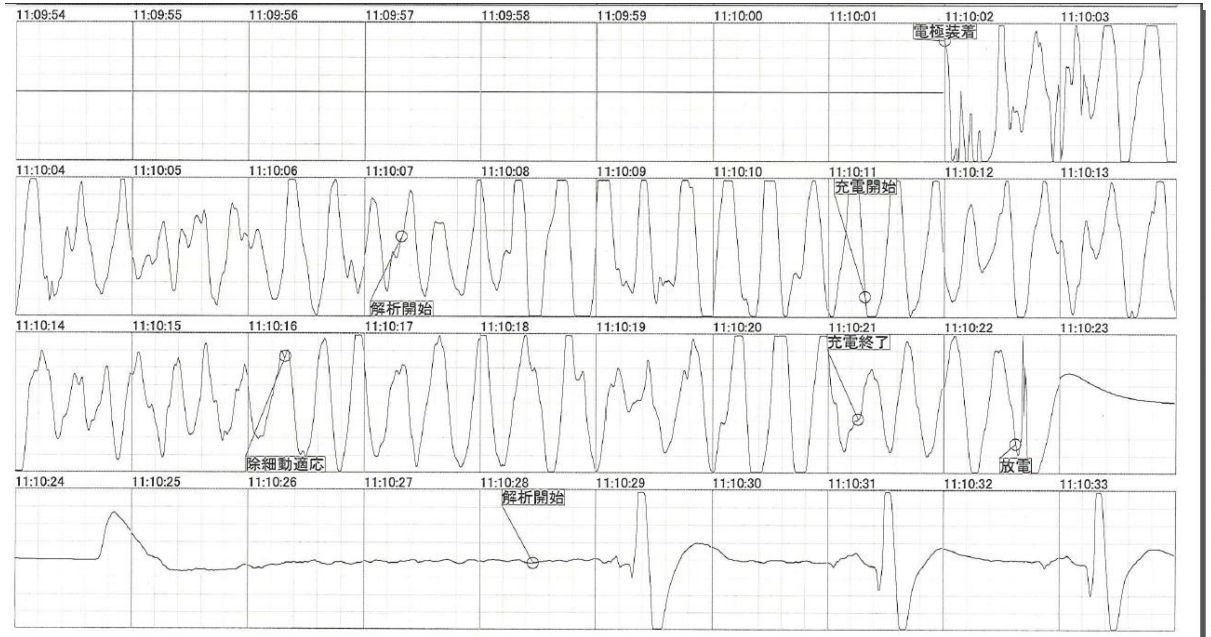


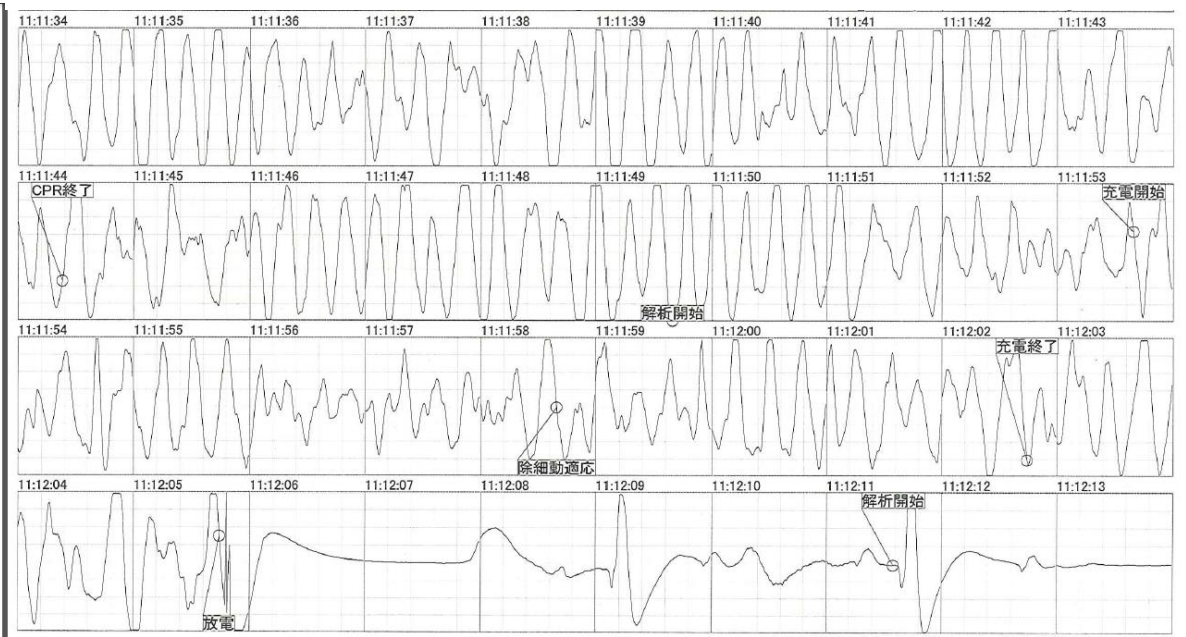
Case1 8372 84歳　♀

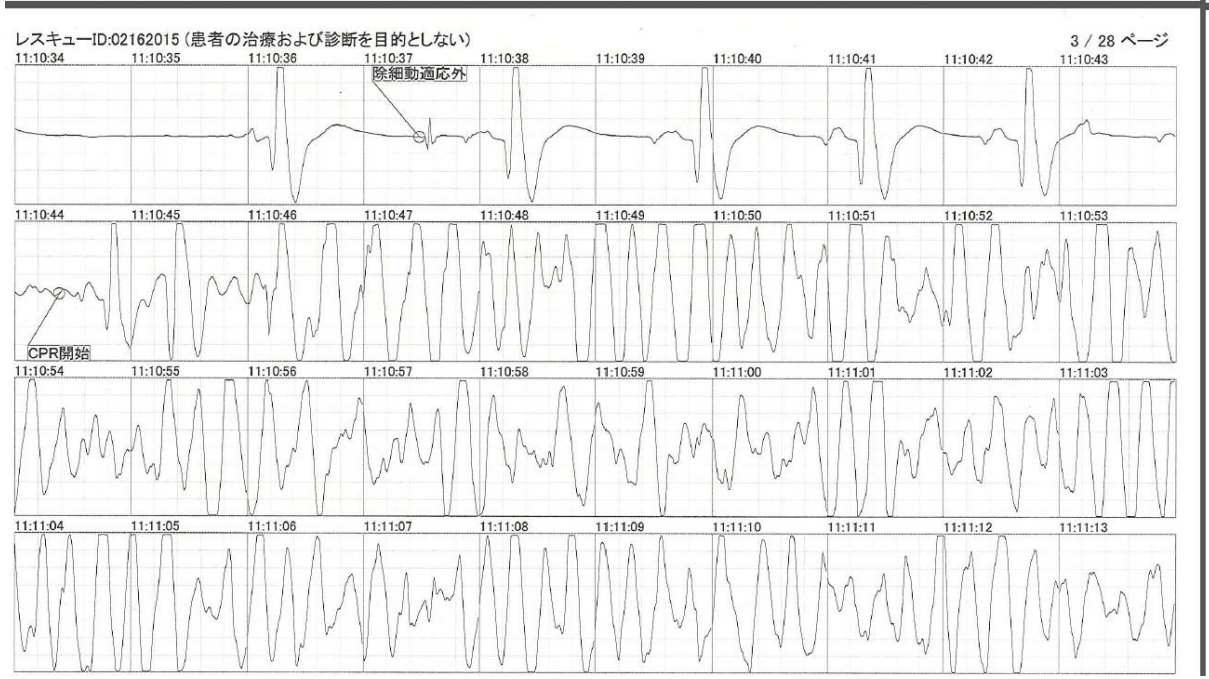
02/09/2015　17：57　ホルターECG

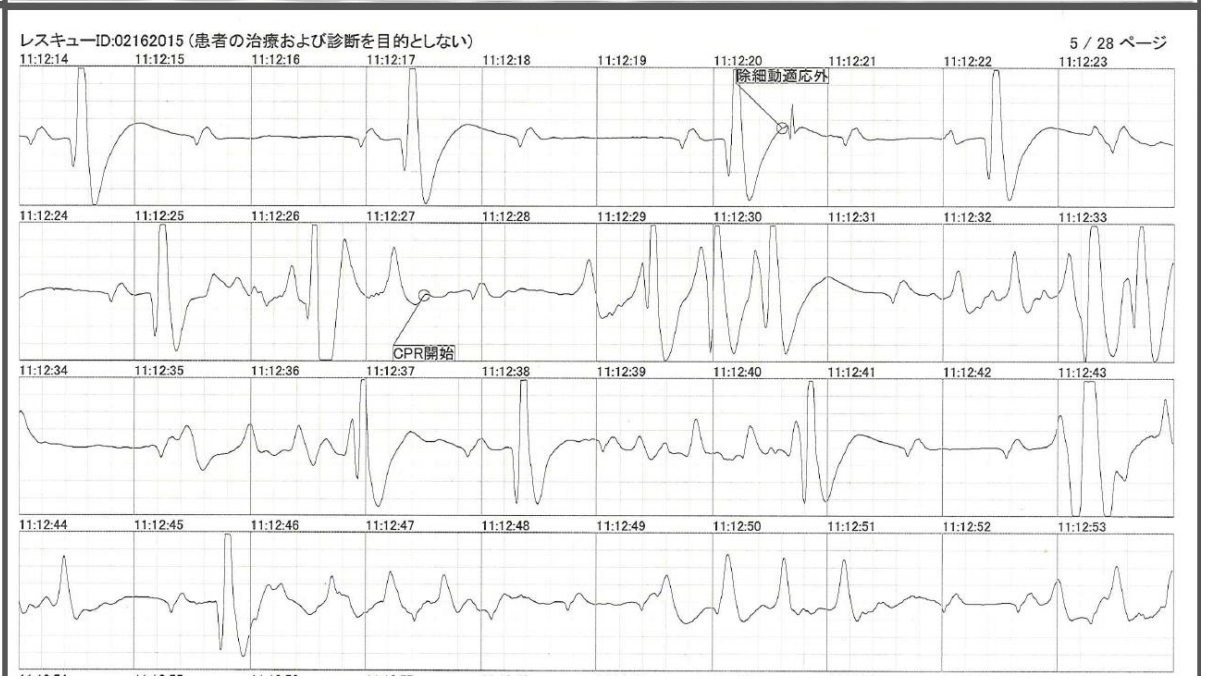


Case1 8372 84歳　♀2/16/2015AED





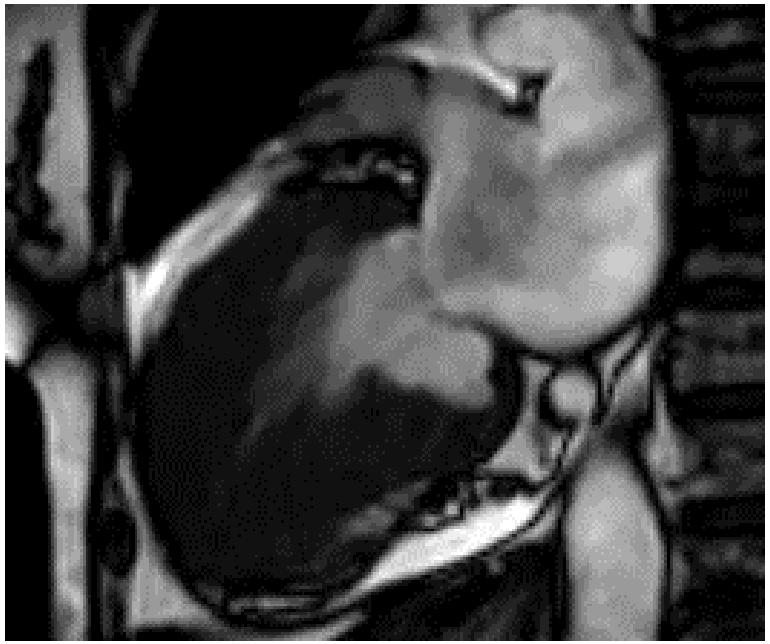
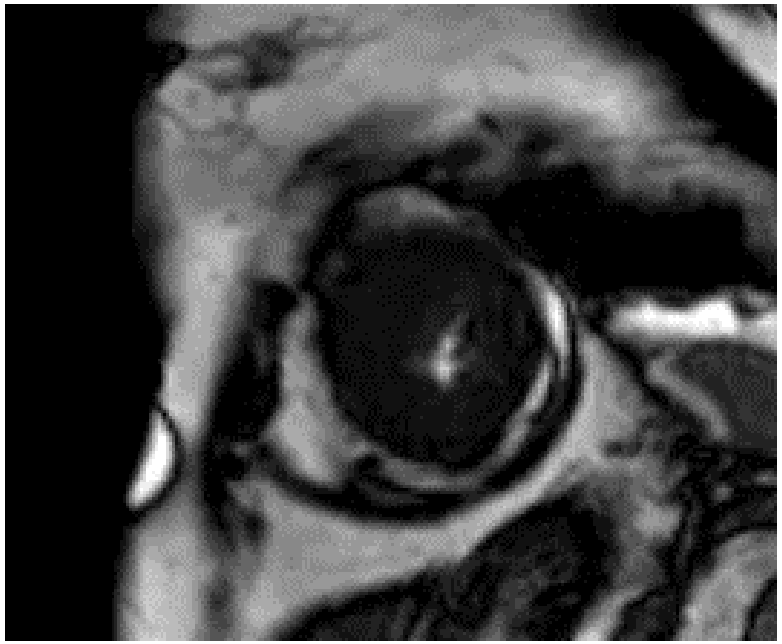
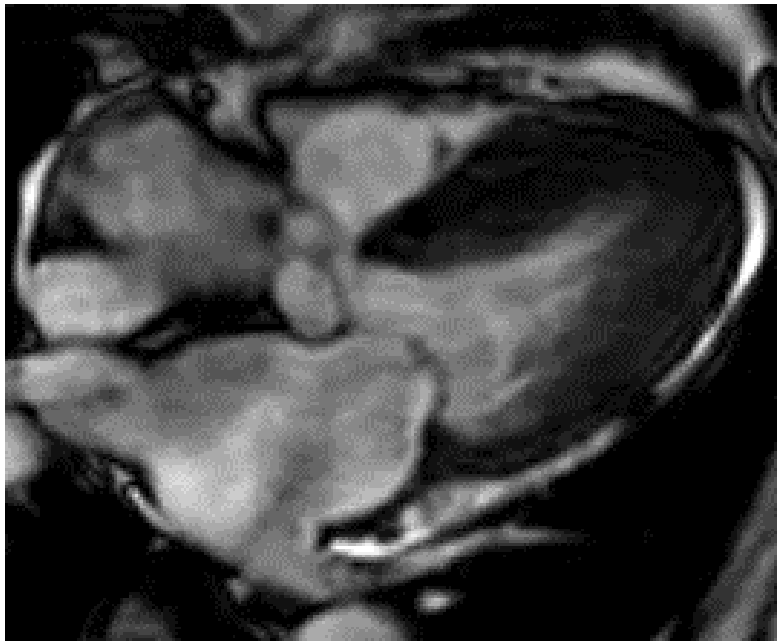




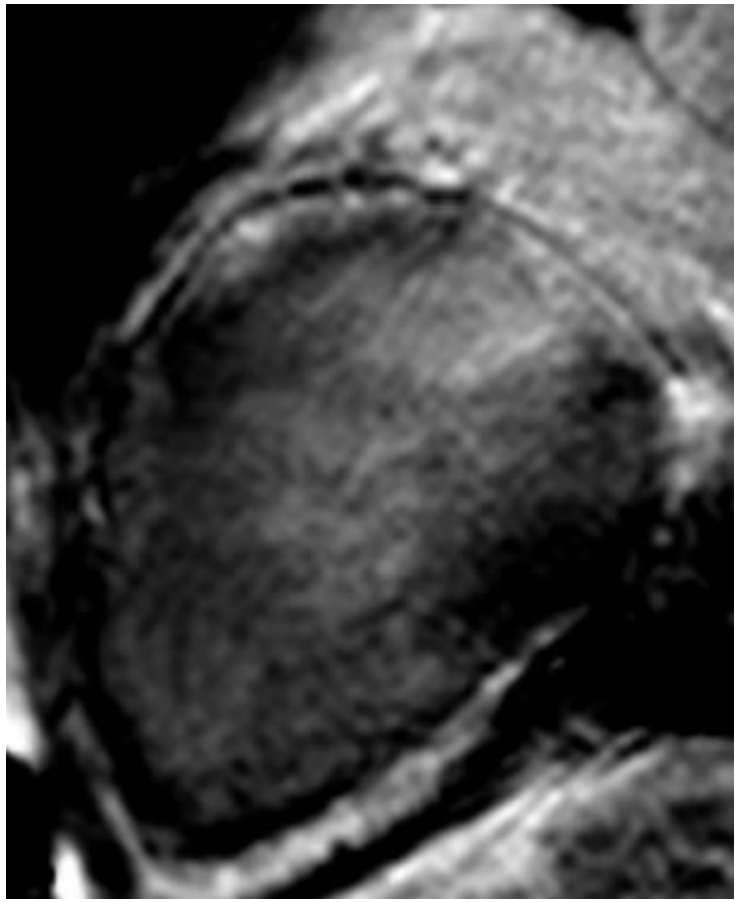
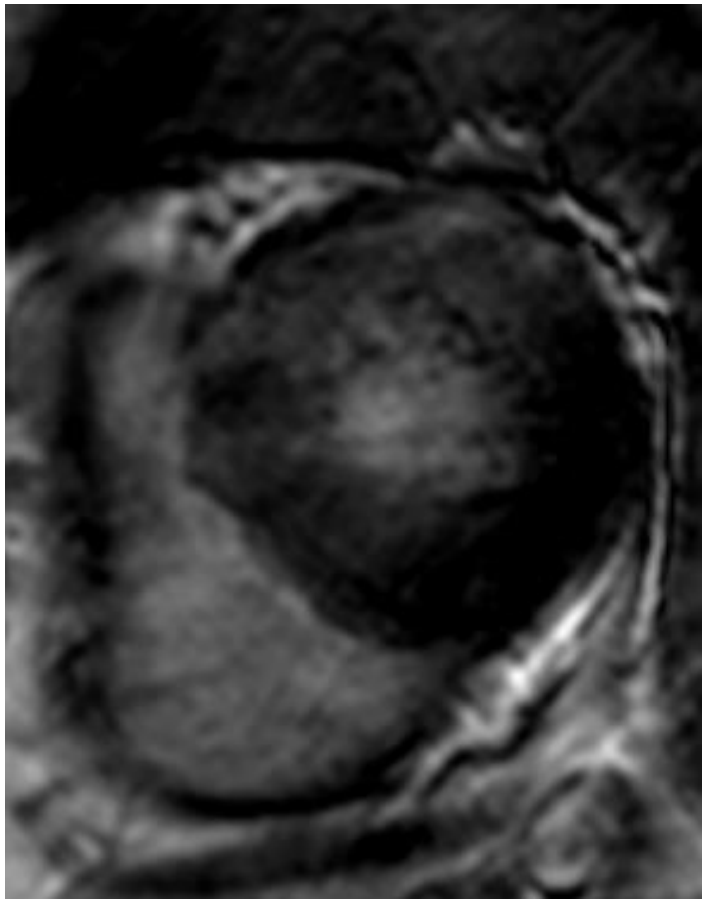
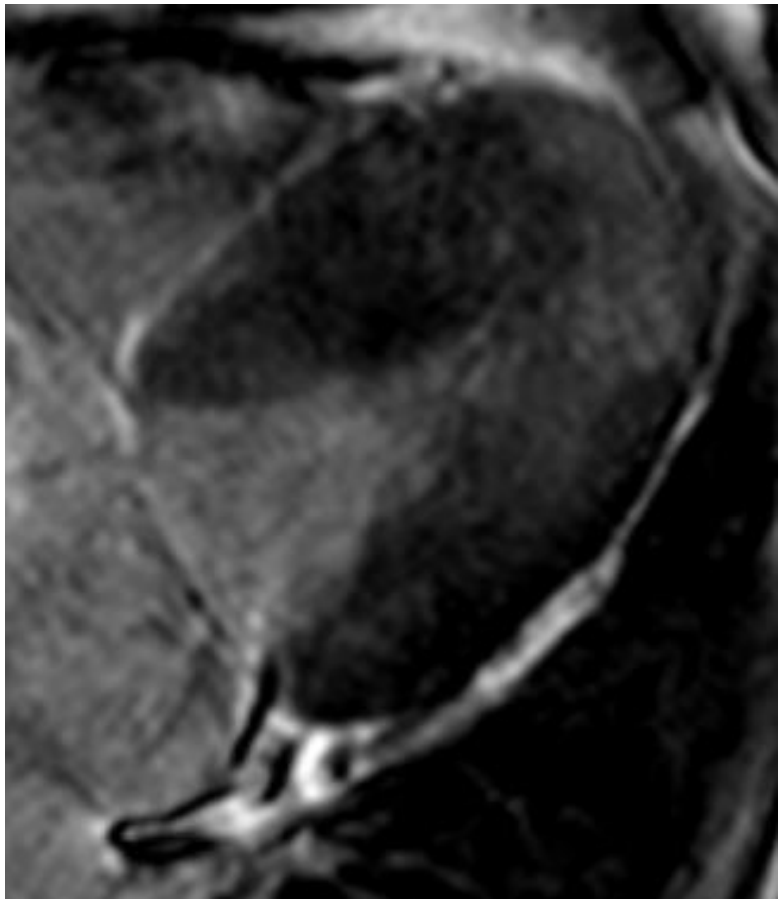
Case1 8372 84歳　♀

検査項目名	HL	検査結果	ｺﾒﾝﾄ	低	正常	高	単位	基準値
白血球数		5.9					10**3	4.0～8.0
赤血球数	▲	557					10**4	380～500
ﾍﾓｸﾞﾛﾋﾞﾝ		13.5					G/DL	12.0～16.0
ﾍﾏﾄｸﾘｯﾄ		44.8					%	36.0～48.0
MCV	▽	80					FL	84～93
MCH	▽	24.2					PG	27.0～32.0
MCHC	▽	30.1					%	32.0～36.0
血液像 好中球		58					%	45～74
血液像 ﾘﾝﾊﾟ球		34					%	20～45
血液像 単 球		7					%	2～8
血液像 好酸球		1					%	0～6
血液像 好塩基球		0					%	0～3
血小板数		26.6					10**4	12.0～40.0
尿pH		7.5						5.0～7.5
尿蛋白		(+-)						(-)
尿糖(定性)		(+++)						(-)
ｳﾛﾋﾞﾘﾉｰｹﾞﾝ		(+-)						(+-)
尿 沈 渣 赤血球		<1/HPF						
尿 沈 渣 白血球		1-4/HPF						
尿 沈 渣 扁平上皮		5-9/HPF						
尿 沈 渣 細 菌		(-)						
尿蛋白定量 濃 度	▲	22.9					MG/DL	100以下
尿ｹﾄﾝ体		(-)						(-)
梅毒TP抗体定性(LA)		(-)						(-)
梅毒脂質抗体定性(RPR)		(-)						(-)
HBs抗原		(-)						(-)
総蛋白		8.3					G/DL	6.7～8.3
尿素窒素	▲	40.6	[W]				MG/DL	8.0～20.0
尿 酸		4.0					MG/DL	2.0～7.0
ｸﾚｱﾁﾆﾝ	▲	1.36					MG/DL	0.50～0.86
総ｺﾚｽﾃﾛｰﾙ		175					MG/DL	130～220
中性脂肪	▲	163					MG/DL	30～149
HDLｺﾚｽﾃﾛｰﾙ		53					MG/DL	40～100
Na		139					MEQ/L	137～147
K	▲	5.1					MEQ/L	3.5～5.0
Cl		102					MEQ/L	98～108
血清鉄	▽	38					MIC/DL	50～160
UIBC	▲	517	[W]				MIC/DL	180～270
ALP		303					U/L	105～330
AST(GOT)		38					U/L	8～38
ALT(GPT)		27					U/L	4～44
LD(LDH)	▲	291					U/L	120～245
ｶﾞﾝ-GT	▲	145					U/L	30以下
LAP	▲	83					U/L	30～70
CK(CPK)		106					U/L	40～170
総ﾋﾞﾘﾙﾋﾞﾝ		0.9					MG/DL	0.2～1.2
血清ｱﾐﾗｰｾﾞ1本	▲	126					U/L	37～125
血 糖1本		91					MG/DL	70～109
尿 糖1本	▲	804					MG/DL	20以下
ｱﾙﾌﾞﾐﾝ		4.3					G/DL	3.8～5.3
ﾌﾟﾚｱﾙﾌﾞﾐﾝ		22.6					MG/DL	22.0～40.0
CK-MB	▲	5.4					NG/ML	5.0以下
HCV抗体(3rd) 判 定		(+)						(-)
HCV抗体(3rd) ｶｯﾄｵﾌ ｲﾝﾃﾞｯｸｽ	▲	1.3					C.O.I.	1.0未満
ﾄﾛﾎﾟﾆﾝ-T	▲	0.216					NG/ML	0.014以下
BNP	▲	1051.5					PG/ML	184以下

Case1 8372 84歳　♀ 10/23/2014 CMR Cine

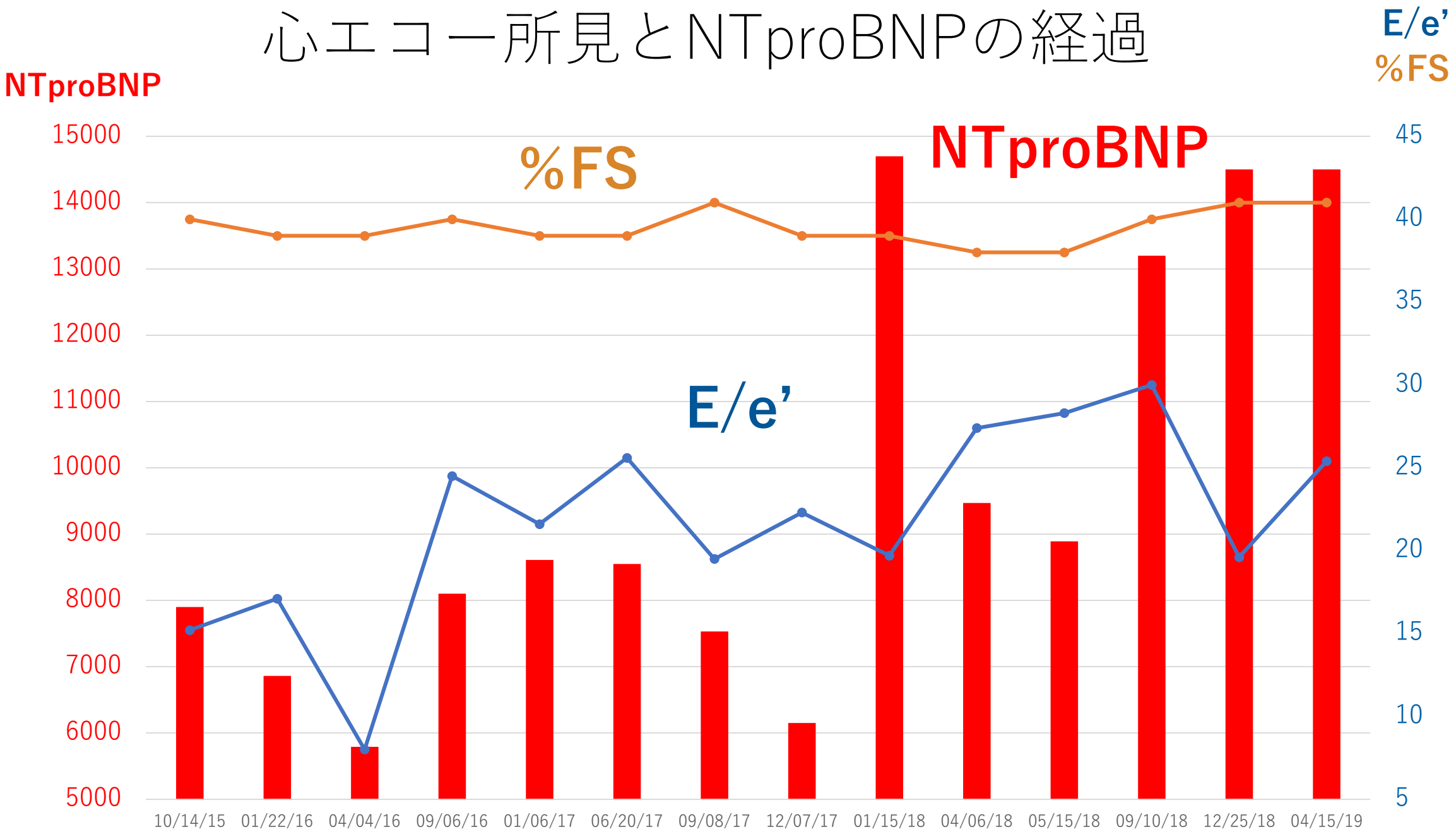
Case1 8372 84歳　♀　10/23/2014 CMR LGE

Case1 8372 84歳　♀ 心エコー、NTproBNP経過

DATE	LVDd	LVds	IVS	PW	LAD	E/e'	IVC	TRFV	EF	FS	NTproBNP
10/14/15	37.8	22.5	20.3	12.7	42.6	15.2	10.2	2.52	0.72	40	7900
01/22/16	38.9	23.6	20.6	13.1	43.1	17.1	9.5	2.43	0.70	39	6860
04/04/16	39.6	24.1	20.4	12.4	43.6	8.0	9.2	2.41	0.70	39	5790
09/06/16	38.4	22.7	18.8	11.6	43.1	24.5	9.7	2.41	0.72	40	8100
01/06/17	38.8	23.3	17.6	12.2	44.5	21.6	9.6	2.44	0.71	39	8610
06/20/17	39.0	23.6	17.4	11.1	44.5	25.6	9.9	2.43	0.70	39	8550
09/08/17	40.9	23.9	16.6	11.4	44.6	19.5	7.6	2.41	0.72	41	7530
12/07/17	38.2	23.1	17.8	10.1	43.1	22.3	9.4	2.41	0.70	39	6150
01/15/18	40.9	24.6	17.7	11.1	43.1	19.7	7.4	2.48	0.70	39	14700
04/06/18	40.2	24.7	17.5	10.2	45.9	27.4	8.1	2.49	0.69	38	9470
05/15/18	41.0	25.4	17.1	10.6	45.0	28.3	10.5	2.52	0.68	38	8890
09/10/18	40.3	24.1	17.2	9.8	47.6	30.0	8.4	2.43	0.71	40	13200
12/25/18	40.8	23.9	17.3	9.6	46.7	19.6	10.1	2.38	0.72	41	14500
04/15/19	40.1	23.5	17.8	9.0	46.3	25.4	13.5	2.44	0.72	41	14500

心エコー所見とNTproBNPの経過



Case1 8372 84歳　♀

測定結果報告書

3/19/2015

中島内科循環器科メンタルクリニック様

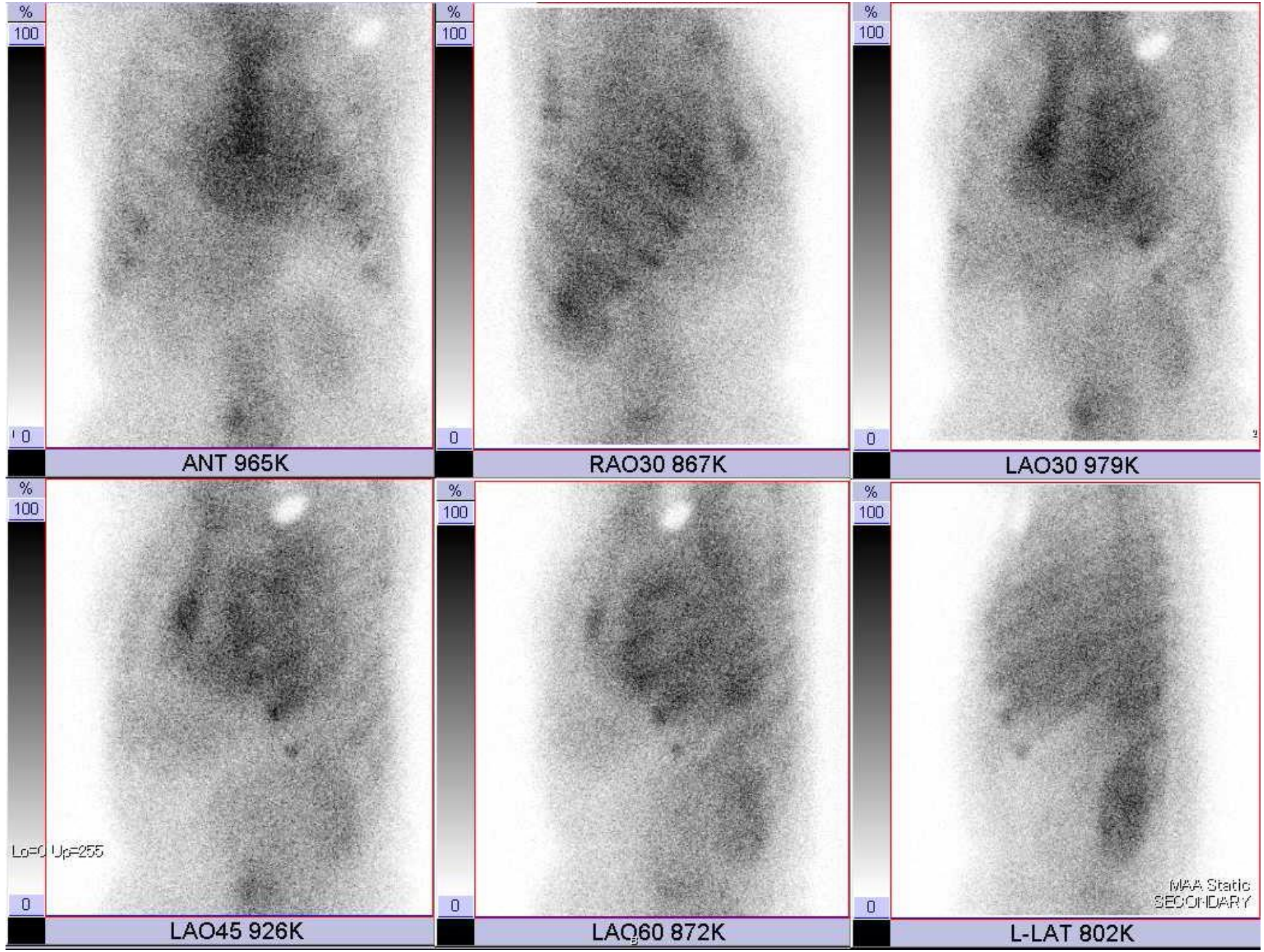
サンプル名	LysoGb3 濃度 (ng/ml)	α-Gal A 活性 (nmol/h/ml)
NJCCH (8372)	0.9	9.5

＊お預かりしました血漿サンプルの LysoGb3 濃度及びα-Gal A 活性を上記のようにご報告いたします。

なお、健常者についての LysoGb3 濃度測定が不十分であり、現時点では正確な正常値は申し上げられませんが、男性女性ともおそらく 2 ng/mL 以下であれば正常範囲内であると考えています。

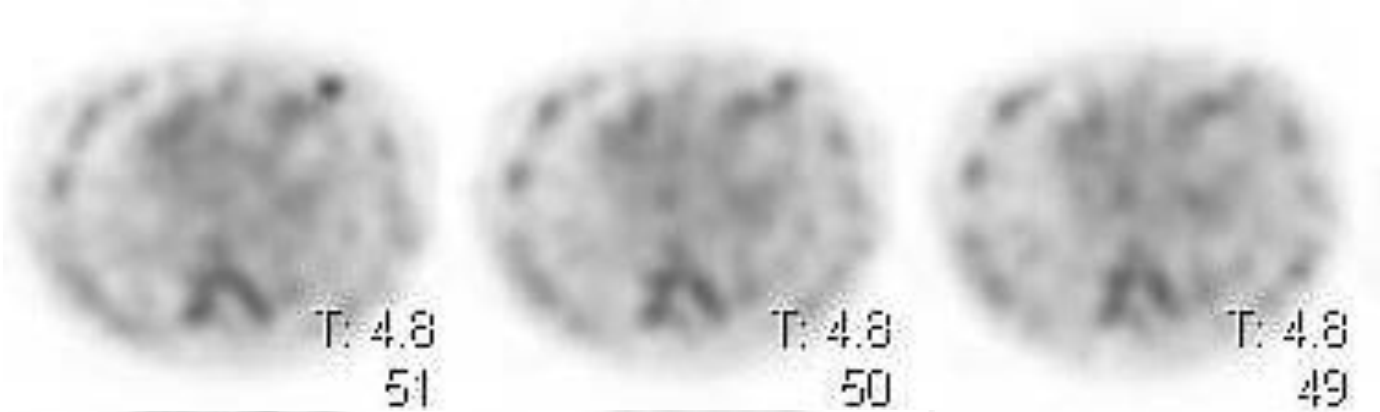
また、男性血漿のα-Gal A 活性は 4.0 nmol/h/mL 以上が正常値です。

Case1 8372 84歳　♀
3/29/2019 ^{99m}Tc-PYP

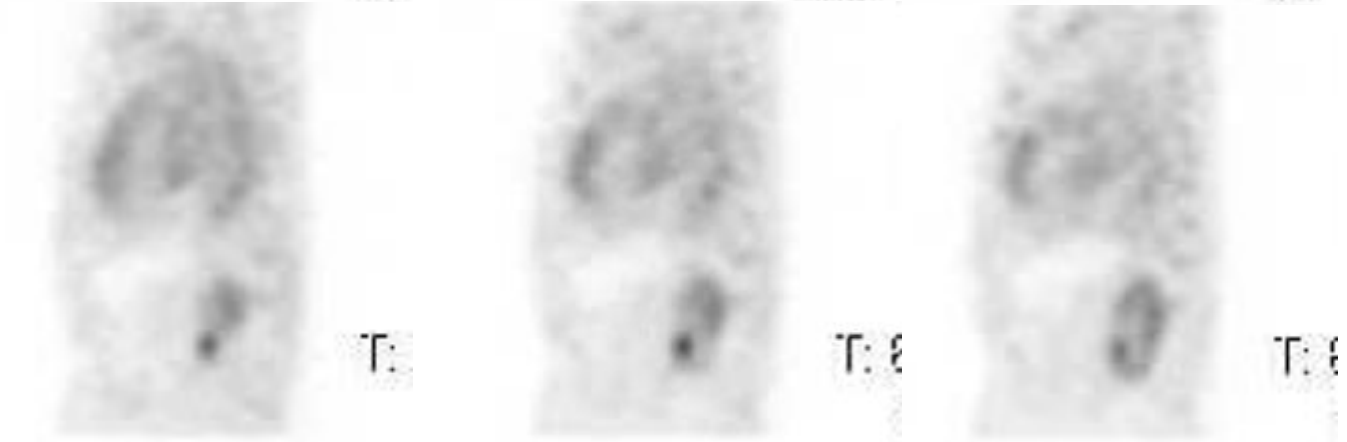


Case1 8372 84歳　♀
3/29/2019 ^{99m}Tc-PYP

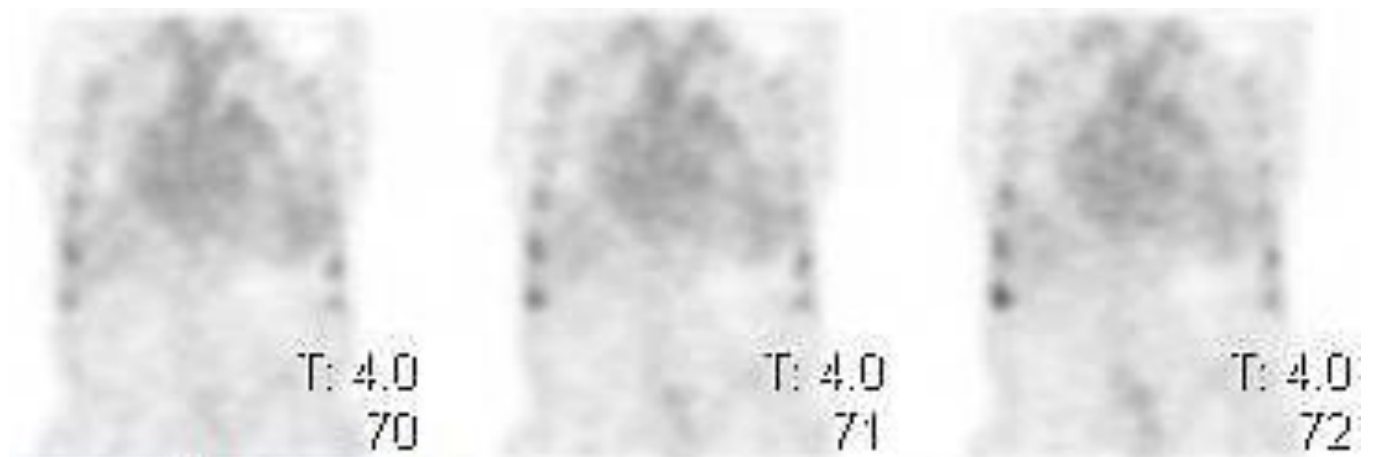
Axial



Sagital



Coronal



Case1 8372 84歳　♀

病理診断

No deposit of amyloid: See comments please: Skin and subcutaneous tissue

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所見

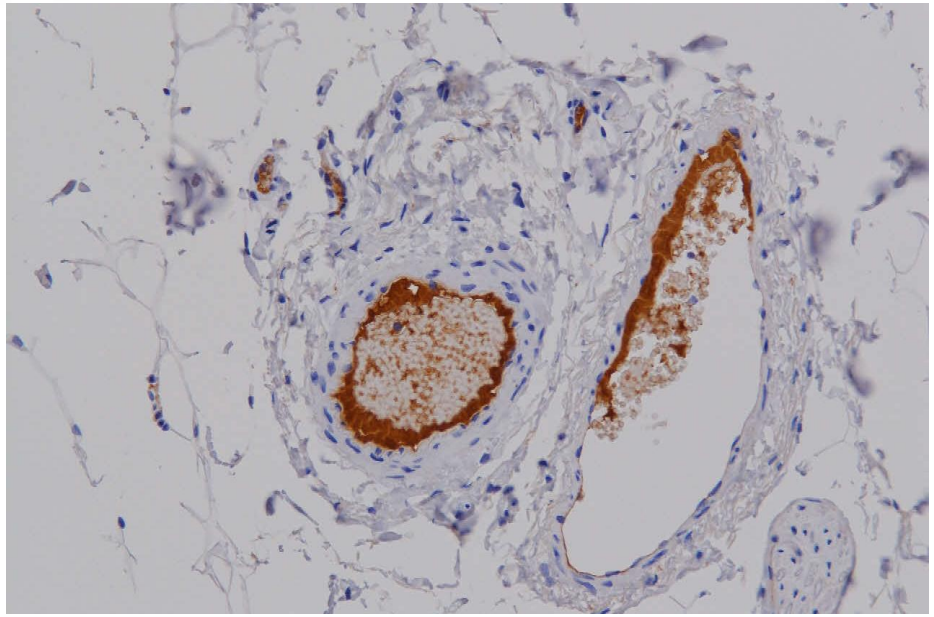
病院で生検された組織の未染色標本を当院で染色いたしました。

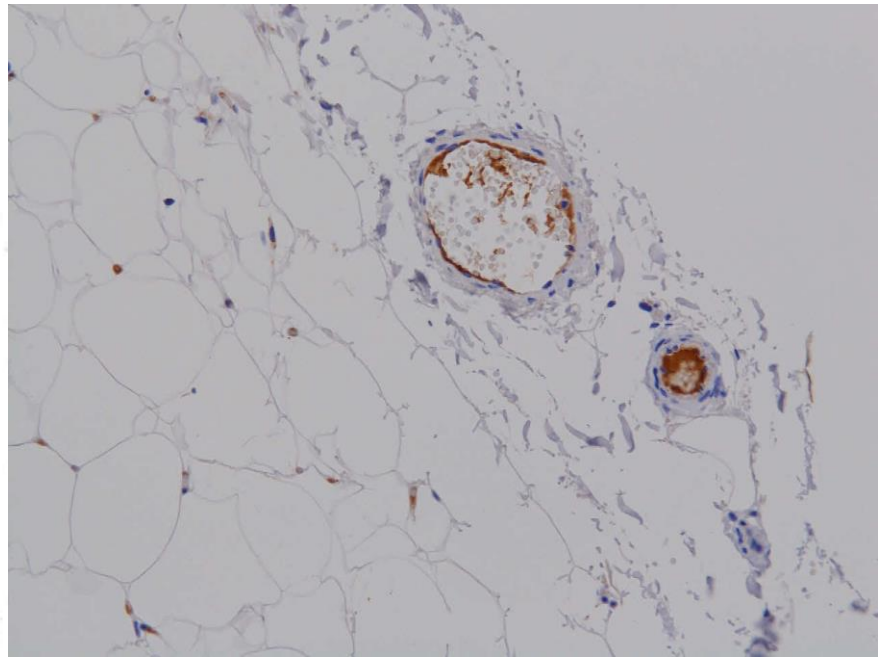
腹壁の生検 1 個です。

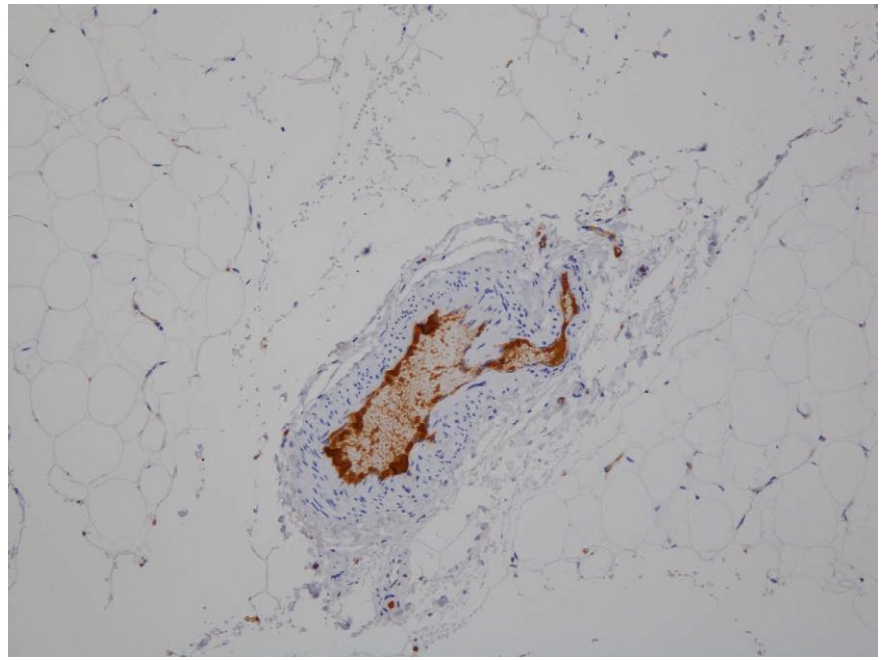
アミロイドーシスの有無を調べるために、アミロイド染色(DFS)とアミロイドの一種の transthyretin (TTR)の免疫染色を施行しました。

この組織にはアミロイドの沈着は認められませんが、血管内皮および血管内に TTR 陽性所見が認められます。血中を流れている高濃度の TTR が沈着している可能性も考えられます。これをアミロイドーシスの診断の根拠にはできませんが、興味深い所見です。

もし組織にアミロイドが沈着している部位を採取できれば、TTR 陽性の可能性も否定できません。画像を添付します。







遺伝子解析検査報告書

(A02)
施設名　　様
匿名符号
科名
病棟
カルテ No.

報告日　2019 年 05 月 20 日
受付日　2019 年 04 月 23 日

検査項目　TTR遺伝子変異解析

TTR-a

＜検査結果＞
バリアントを認めない

＜判定医からのコメント＞

TTR遺伝子にバリアントを認めません

判定医　信州大学第三内科　関島良樹

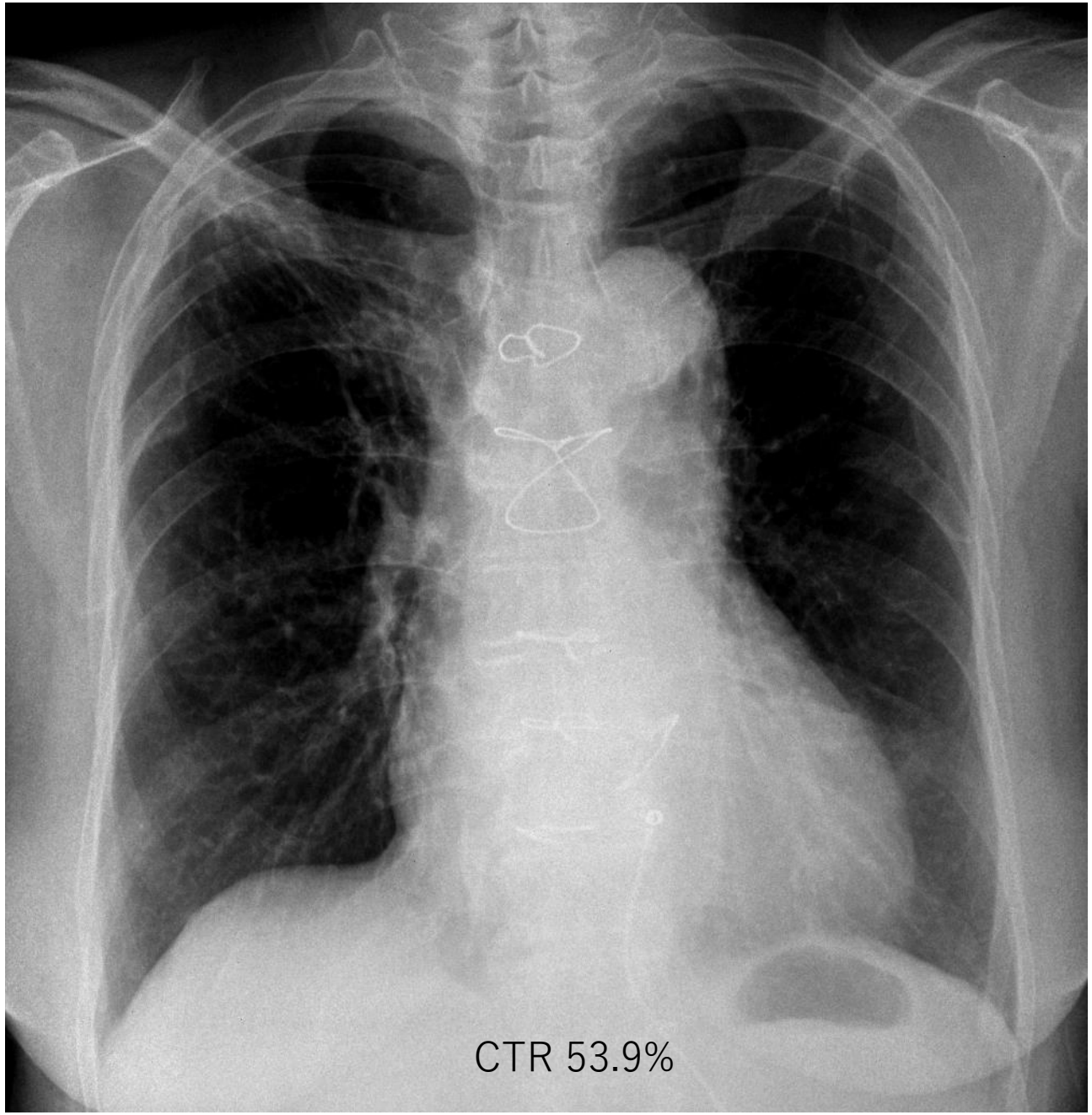
【測定範囲】
TTR エクソン1～4のコーディング領域
参照配列：NCBI Reference Sequence NG_009490.1

【検査の限界】
プライマー配列内にバリアントがある場合や、対象遺伝子を含む欠失等がある場合には、
正確な検査結果が得られないことがあります。

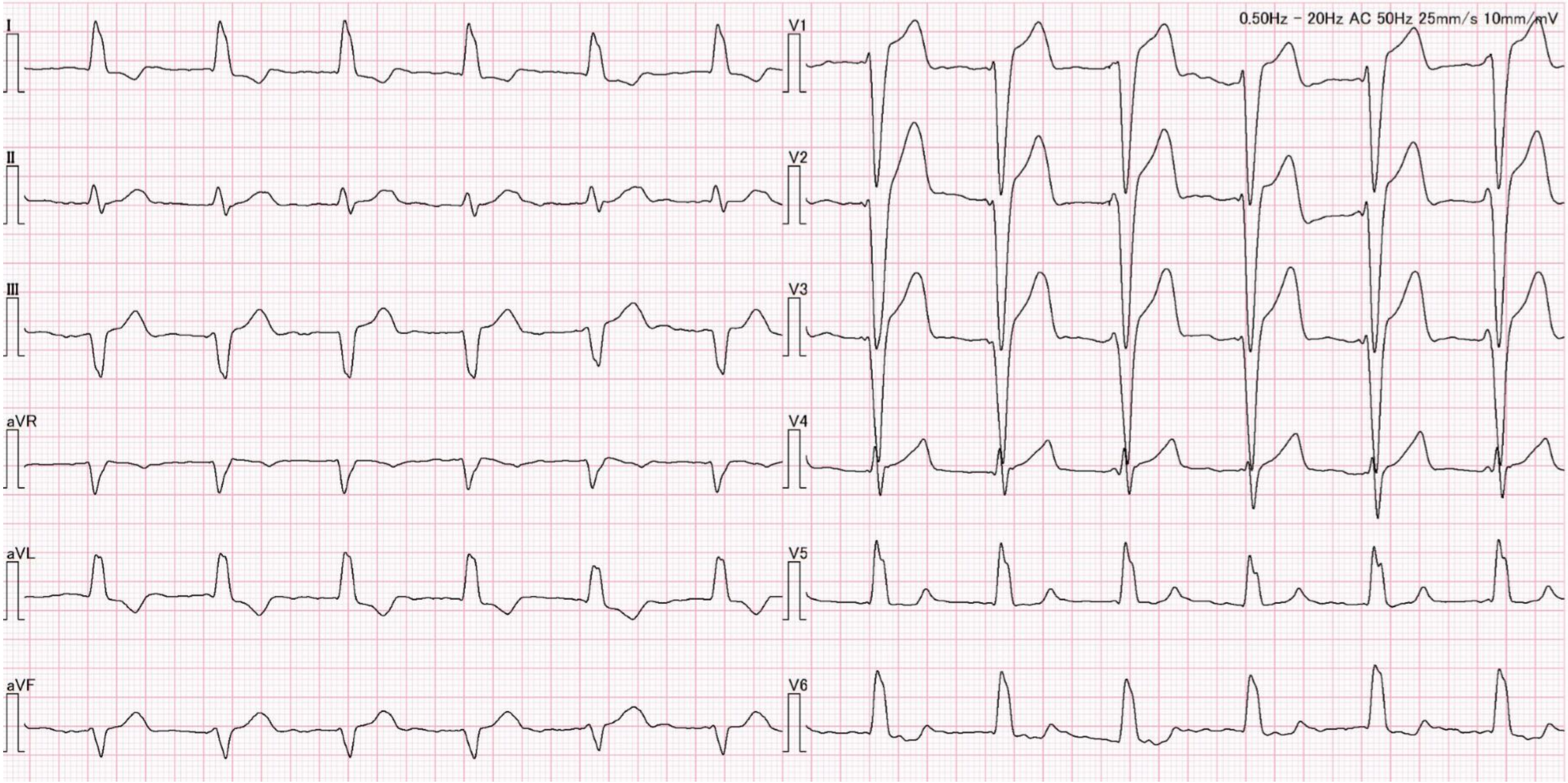
【方法】
本検査は検査室開発検査(LDT)です。

Case2 8221 89歳

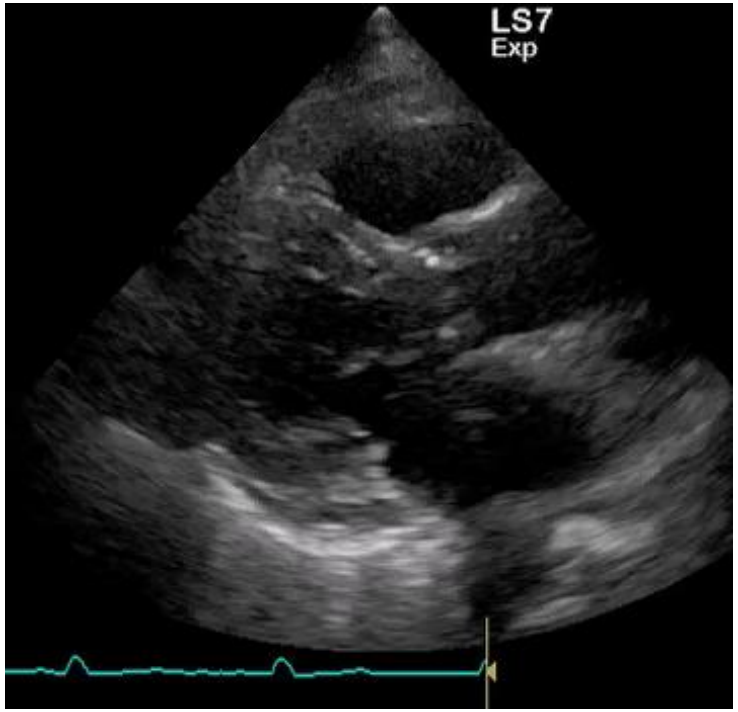
- 平成25年7月8日近医より心雑音を指摘され当院初診。Erb領域にmusical SM認め重症大動脈弁狭窄症の診断で〇病院心臓血管外科でAVR（mitroflow21）施行。術後も労作時の息切れが時々出現。

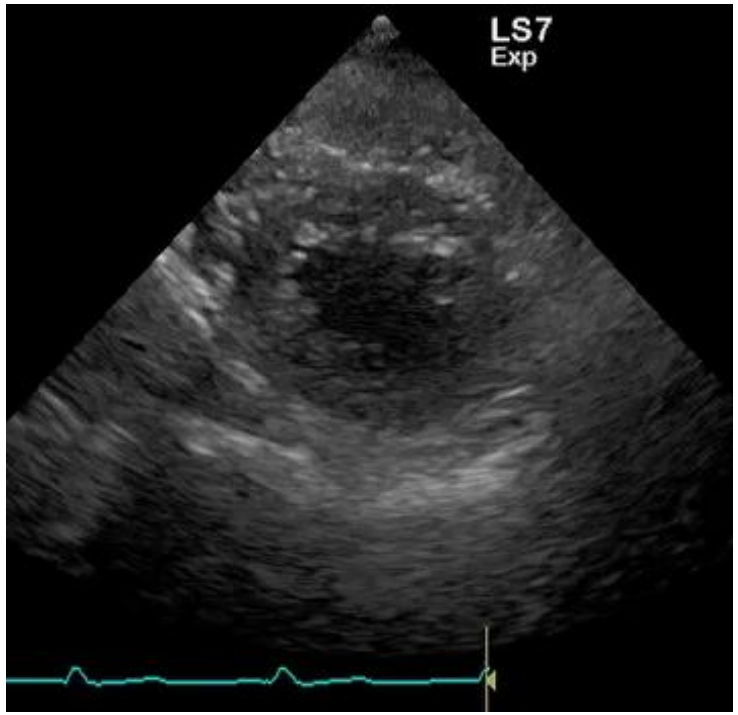


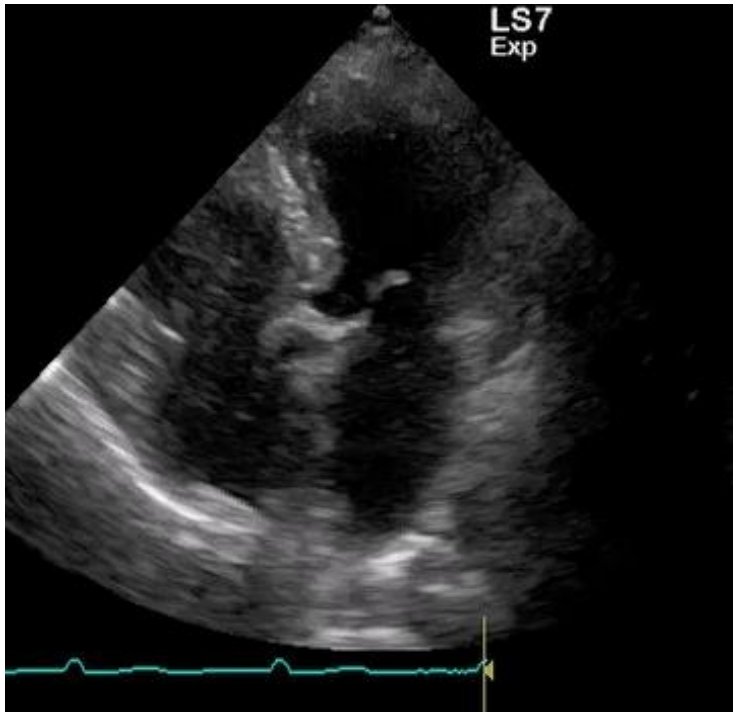
Case2 8221 89歳　♀



Case2 8221 89歳　♀





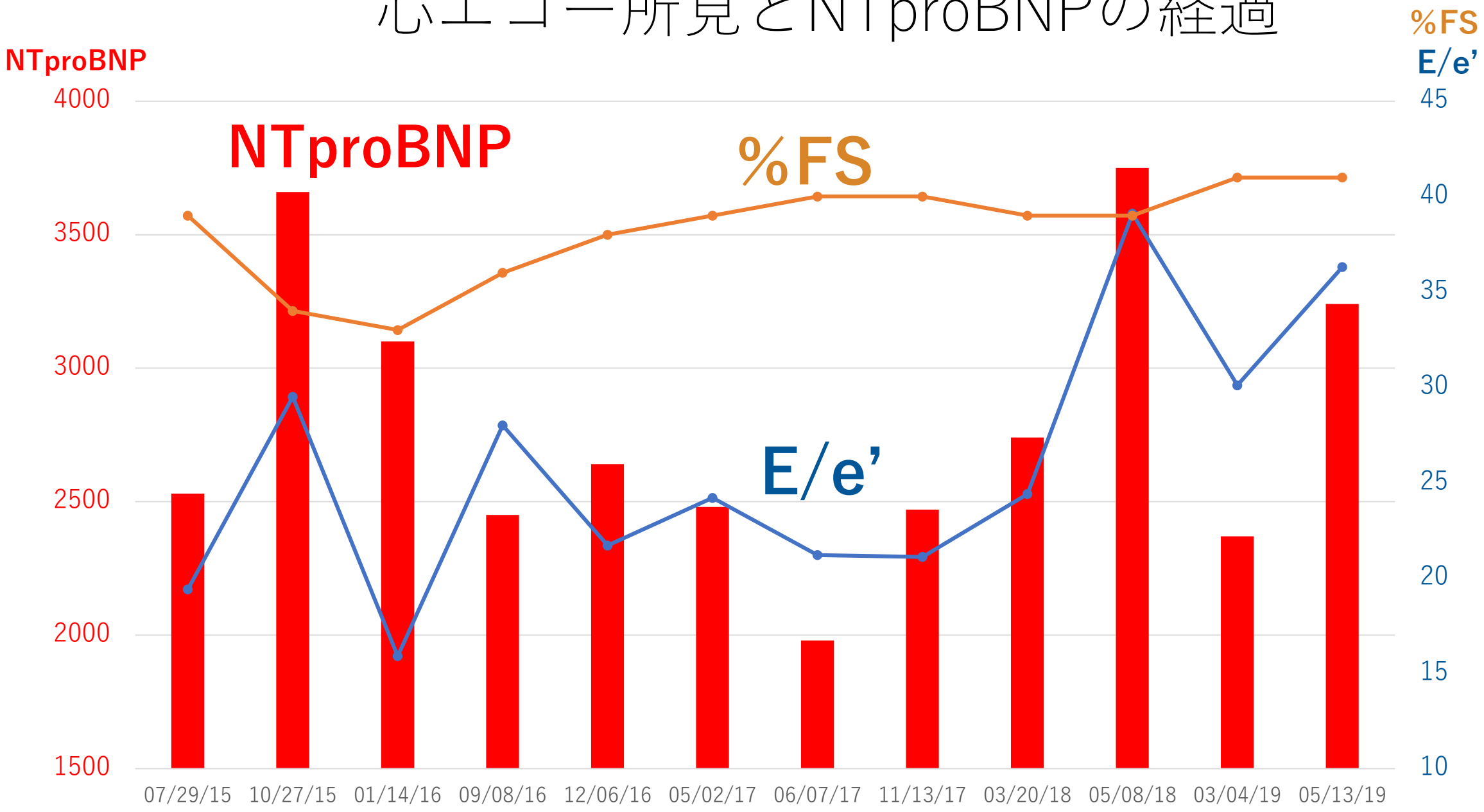


Case2 8221 89歳　♀

DATE	LVDd	LVds	IVS	PW	LAD	E/e'	IVC	AVFV	TRFV	EF	FS	NTproBNP
07/29/15	43.1	26.1	13.1	10.9	47.6	19.4	10.5	2.55	2.15	0.71	39	2530
10/27/15	43.3	28.4	13.2	11.0	45.6	29.5	9.2	2.55	2.55	0.63	34	3660
01/14/16	41.1	27.3	13.5	10.5	43.2	15.9	8.5	2.52	2.21	0.62	33	3100
09/08/16	42.8	27.1	13.6	11.1	42.6	28.0	10.3	2.52	2.15	0.66	36	2450
12/06/16	42.2	26.1	13.5	10.3	41.2	21.7	9.8	2.52	2.17	0.68	38	2640
05/02/17	42.2	25.5	13.6	9.7	42.1	24.2	11.8	2.52	2.23	0.70	39	2480
06/07/17	42	25.2	13.6	9.7	42.1	21.2	9.0	2.46	2.51	0.71	40	1980
11/13/17	43.9	25.9	12.8	10.3	40.1	21.1	8.7	2.46	2.56	0.71	40	2470
03/20/18	42.4	25.6	13.0	9.7	39.2	24.4	8.0	2.52	2.56	0.70	39	2740
05/08/18	42.1	26.1	13.0	9.6	39.2	39.1	9.9	2.71	2.52	0.70	39	3750
03/04/19	42.0	24.7	12.6	9.8	38.3	30.1	8.6	2.67	2.33	0.72	41	2370
05/13/19	43.3	25.5	12.8	10.0	38.3	36.3	10.1	2.64	2.25	0.72	41	3240

Case1 8372 84歳　♀

心エコー所見とNTproBNPの経過

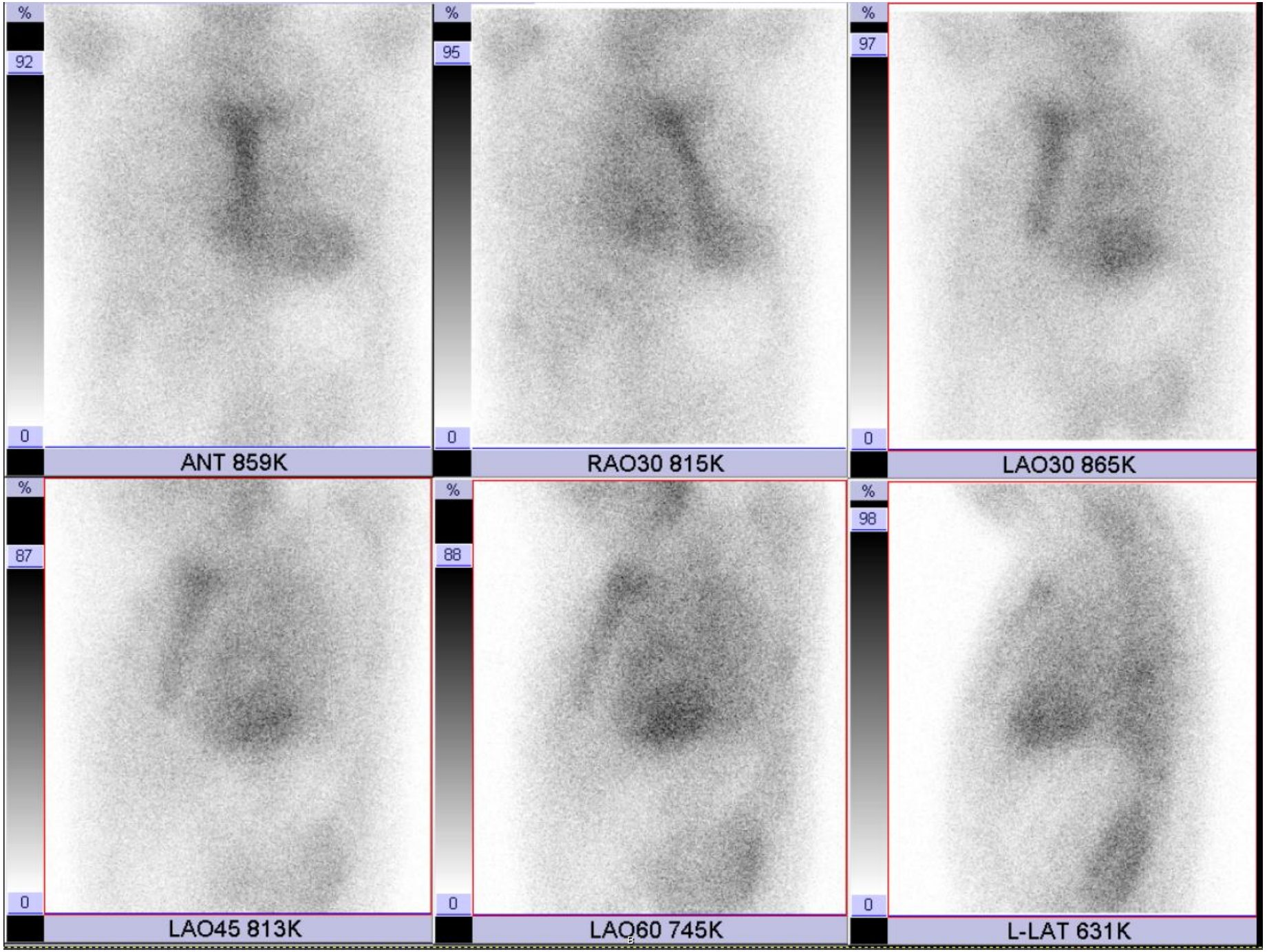


Case2 8221 89歳　♀

受付番号 2019/04/11 3-45004　報告 報告完了　担当医　オーダーNo
検体ｺﾒﾝﾄ　病棟階　診療科 ﾅｲｶ
依頼ｺﾒﾝﾄ ｺﾞ3H　院内区分　入院外来 外来　印刷

検査項目名	HL	検査結果	ｺﾒﾝﾄ	低	正常	高	単位	基準値
白血球数		4.8					10**3	4.0～8.0
赤血球数	▽	361					10**4	380～500
ﾍﾓｸﾞﾛﾋﾞﾝ	▽	10.4					G/DL	12.0～16.0
ﾍﾏﾄｸﾘｯﾄ	▽	33.6					%	36.0～48.0
MCV		93					FL	84～93
MCH		28.8					PG	27.0～32.0
MCHC	▽	31.0					%	32.0～36.0
血液像 好中球		55					%	45～74
血液像 ﾘﾝﾊﾟ球		32					%	20～45
血液像 単 球	▲	9					%	2～8
血液像 好酸球		3					%	0～6
血液像 好塩基球		1					%	0～3
血小板数		18.0					10**4	12.0～40.0
総蛋白		7.0					G/DL	6.7～8.3
尿素窒素		19.9					MG/DL	8.0～20.0
尿　酸		5.8					MG/DL	2.0～7.0
ｸﾚｱﾁﾆﾝ	▲	1.09					MG/DL	0.50～0.86
総ｺﾚｽﾃﾛｰﾙ		209					MG/DL	130～220
中性脂肪	▲	199					MG/DL	30～149
HDLｺﾚｽﾃﾛｰﾙ		62					MG/DL	40～100
Na		144					MEQ/L	137～147
K		4.2					MEQ/L	3.5～5.0
Cl		106					MEQ/L	98～108
Ca		8.9					MG/DL	8.4～10.2
燐	▲	4.7					MG/DL	2.5～4.5
LDLｺﾚｽﾃﾛｰﾙ		114					MG/DL	70～139
血清鉄		59					MIC/DL	50～160
ALP		313					U/L	105～330
AST(GOT)		36					U/L	8～38
ALT(GPT)		17					U/L	4～44
LD(LDH)	▲	265					U/L	120～245
ｱｰGT		17					U/L	30以下
ｺﾘﾝｴｽﾃﾗｰｾﾞ		270					U/L	213～501
CK(CPK)		81					U/L	40～170
総ﾋﾞﾘﾙﾋﾞﾝ		0.7					MG/DL	0.2～1.2
血清ｱﾐﾗｰｾﾞ1本		83					U/L	37～125
血 糖1本		98					MG/DL	70～109
ｱﾙﾌﾞﾐﾝ		4.0					G/DL	3.8～5.3
HbA1c(NGSP)		6.2					%	4.6～6.2
ﾌﾟﾚｱﾙﾌﾞﾐﾝ		23.3					MG/DL	22.0～40.0
CK-MB		1.7					NG/ML	5.0以下
ﾄﾛﾎﾟﾆﾝ-T	▲	0.025					NG/ML	0.014以下
BNP	▲	322.0					PG/ML	18.4以下

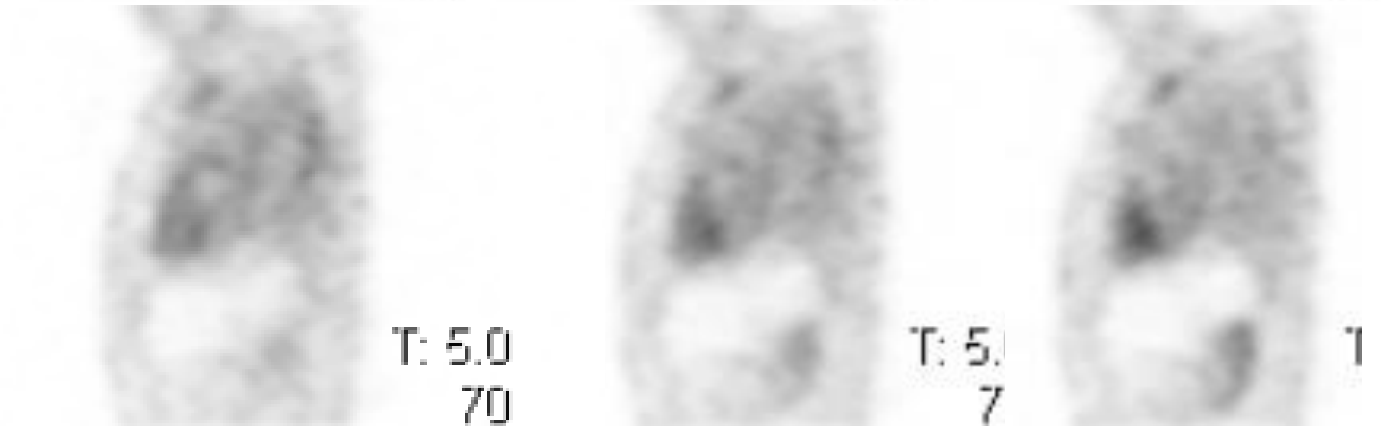
Case2 8221 89歳　♀
3/11/2019 ^{99m}Tc-PYP



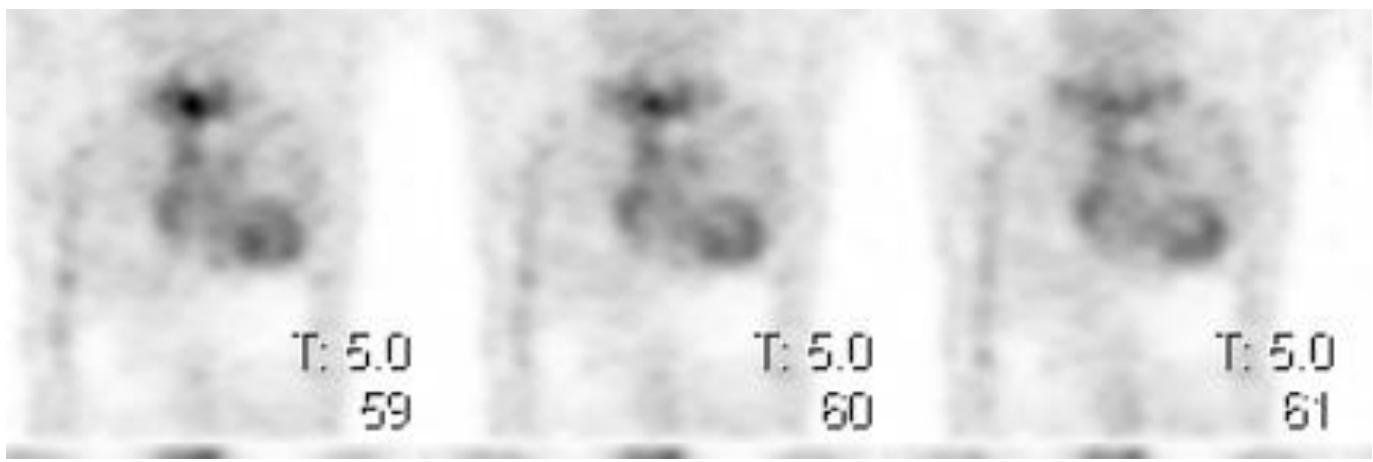
Case2 8221 89歳　♀
3/11/2019 ^{99m}Tc-PYP

Axial

Sagital



Coronal



Case2 8221 89歳　♀

臓器組織　皮膚　　臓器数：(　1

末　診　断　心臓アミロイドーシス S/O

病理組織学的判定

See the following description.

所見

標本物のサイズ：　約2.4×1.1×1.6cm

採取部位：　腹壁

真皮内にコンゴ赤染色（＋）ですが、HE染色標本上ではアミロイドの沈着は認められません。脂肪細胞は肥大し脂肪腫様の像を呈しています。

念のため、他の専門医の診断を仰ぎたいと思います。最終報告まで若干のお時間をいただければ幸いです。

【補足】

第一鏡検者の判断の通りで、真皮、脂肪隔壁あるいは血管壁に特異的な陽性所見を見出す事が出来ませんでした。

臨床診断　1.腹壁

病名 1:アミロイドーシス疑い

病理診断

Amyloidosis suspected, see comments please: Skin and subcutaneous tissue

所見

腹壁の生検 2 個です。

アミロイドーシスの有無を調べるために、アミロイド染色(DFS)とアミロイドの一種の transthyretin (TTR) の免疫染色を施行しました。

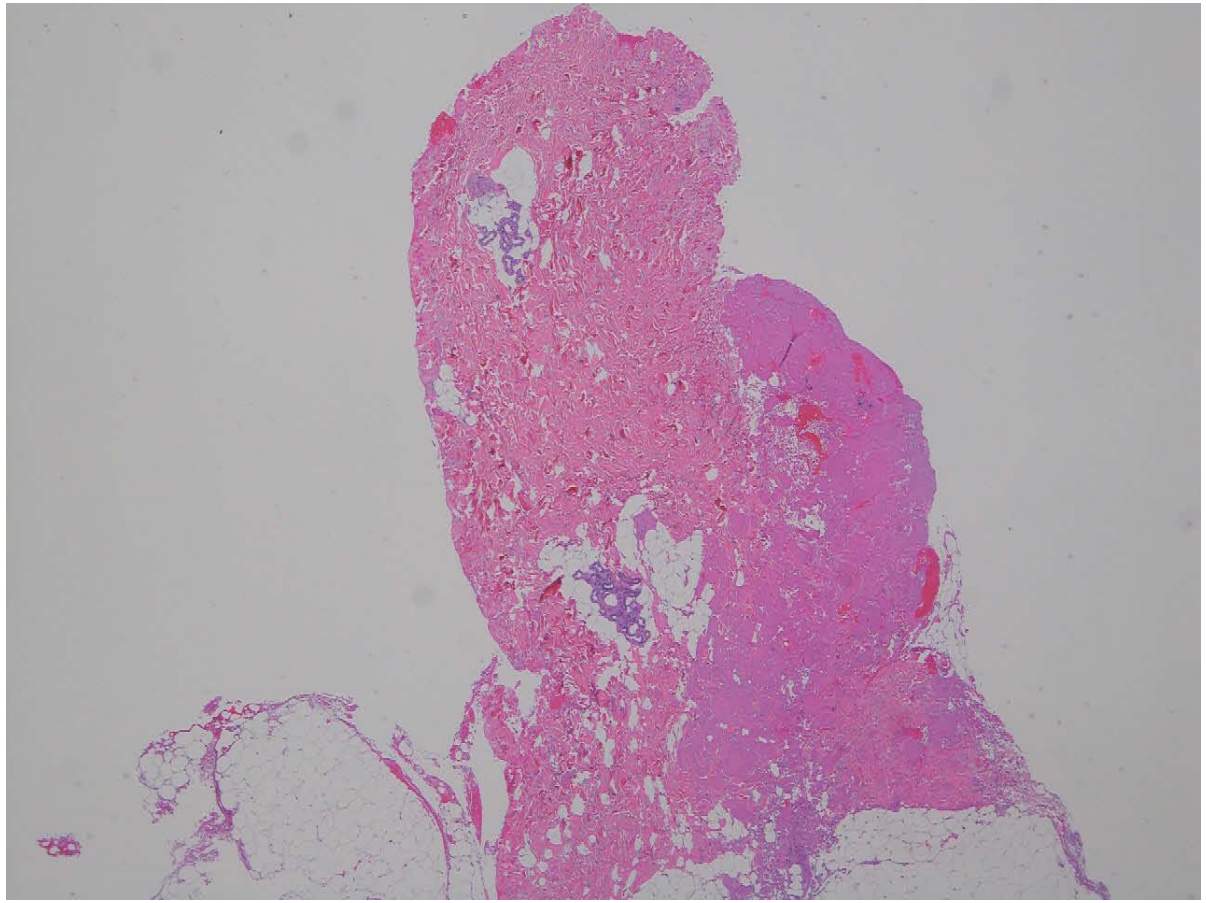
標本＃2の一部にアミロイドーシスを疑わせる amorphous な物質の沈着がみられます。DFS 染色では陽性のようにも見えますが、周囲の膠原線維が陽性にそまっており、偽陽性かもしれません。

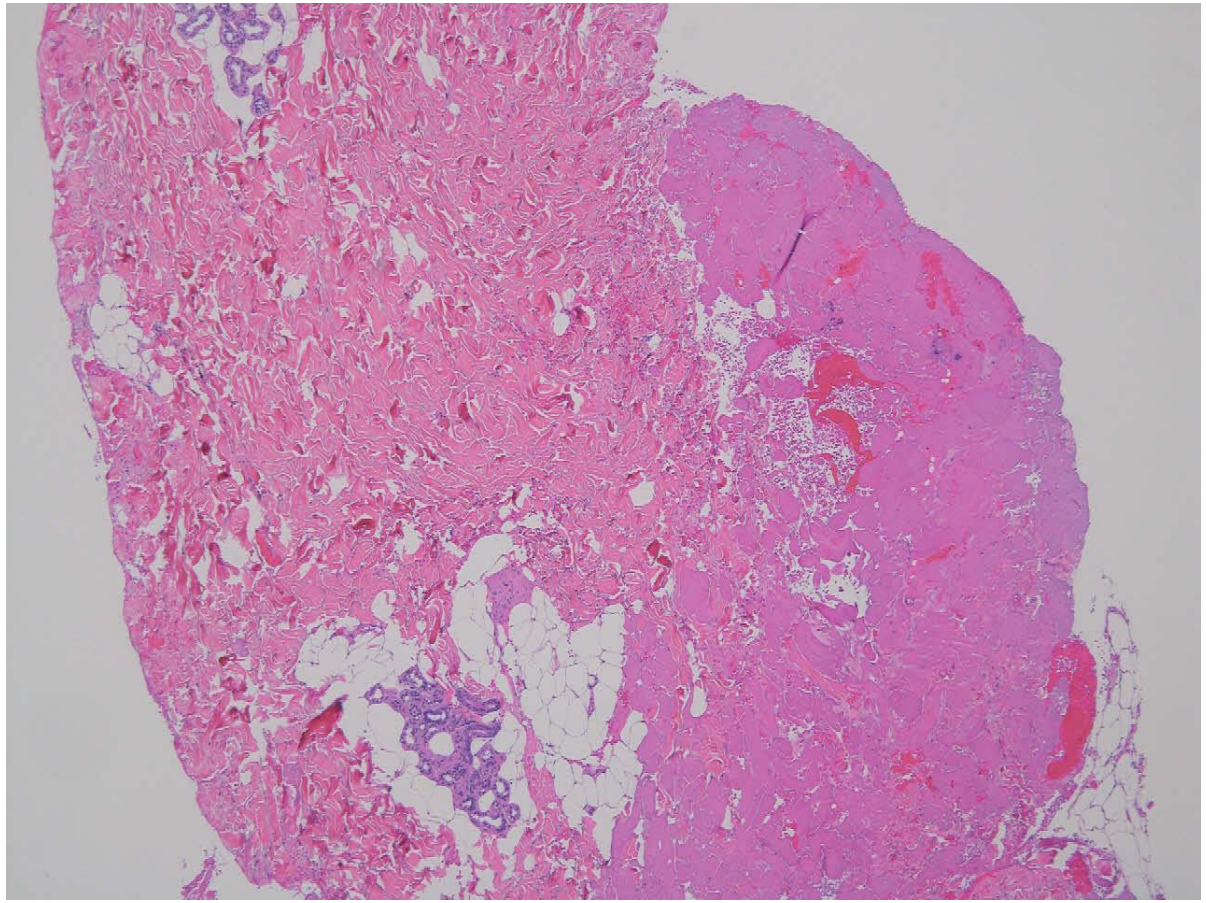
TTR 免疫染色ではアミロイド様に見える物質の辺縁にわずかに染まっておりますが、肝腎のアミロイド様の集塊が染まっておりません。同時に染色した陽性コントロールに比較すると痕跡的な染まり方です。

免疫染色は組織採取後の固定条件に大きく結果が左右されます。適切に処理された組織かどうかによりますので、本検体がどのように処理されたかにより、もっと染まるはずの組織だったのか、偽陽性なのかの判断ができません。

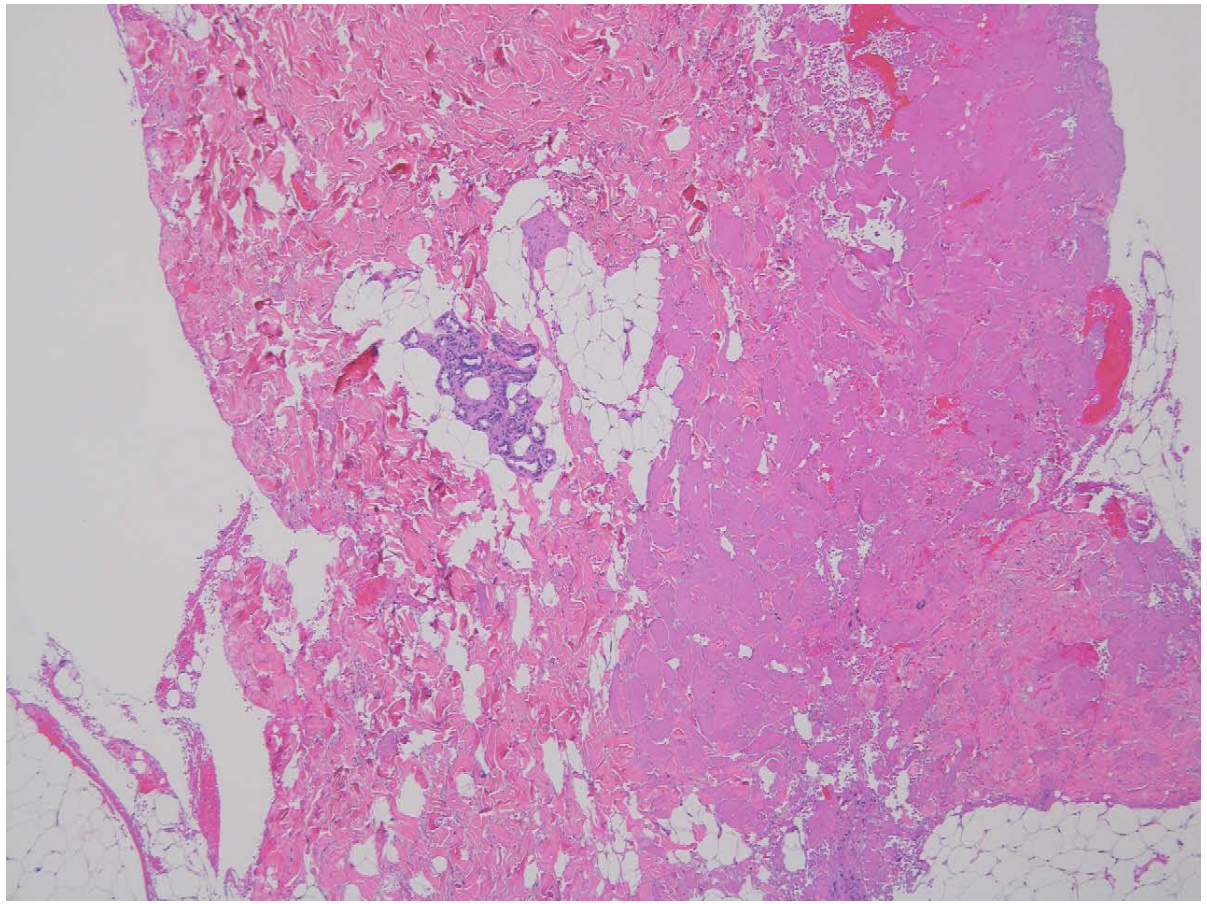
念のために写真を添付します。

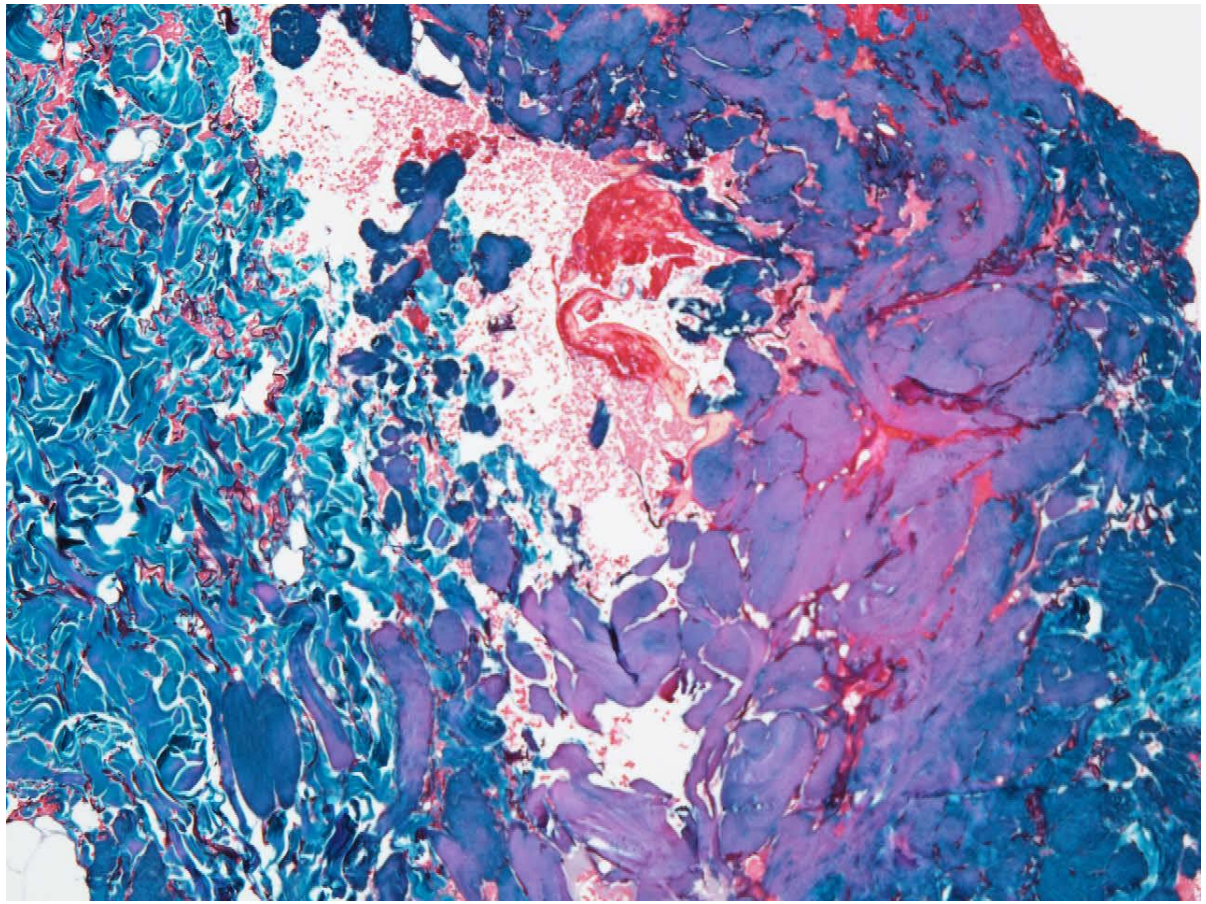
Case2 8221 89歳　♀



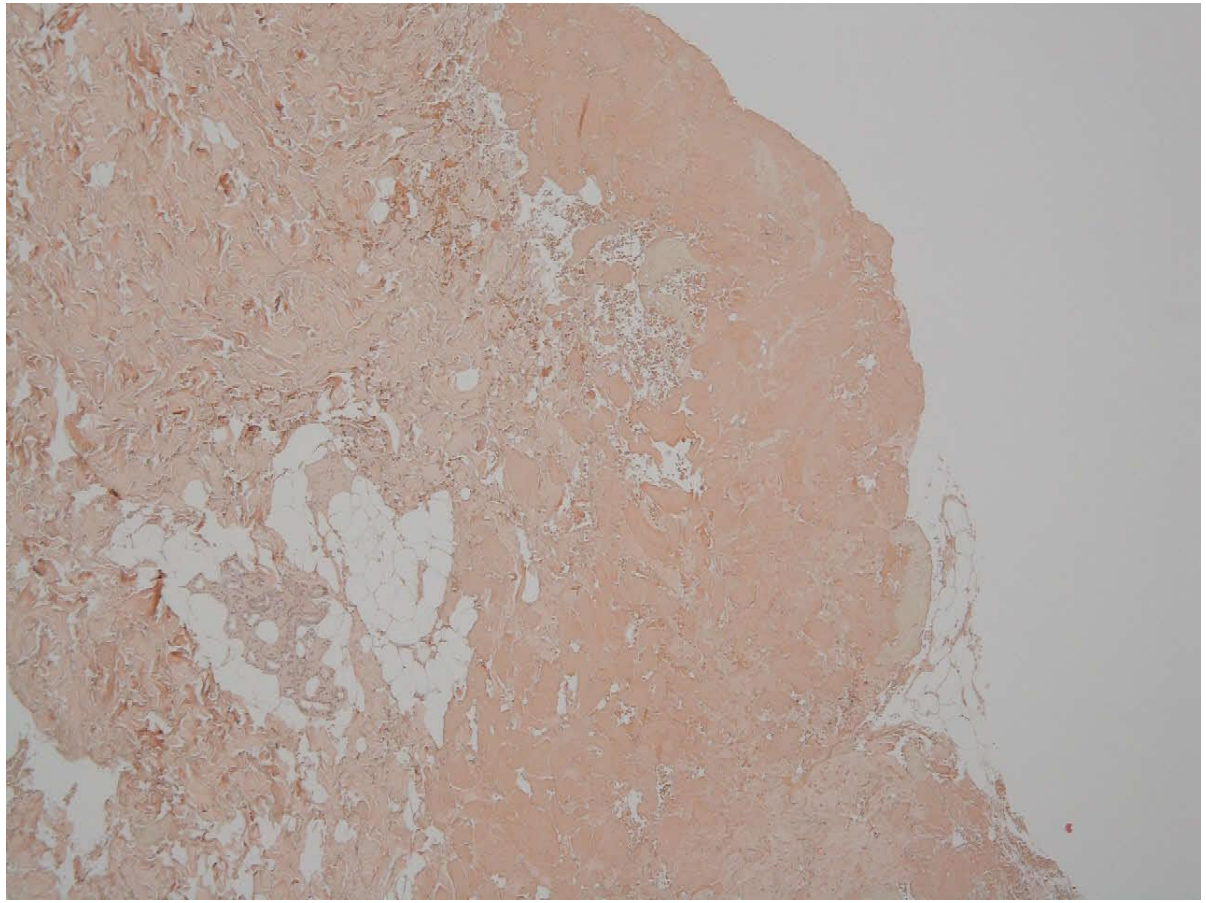


Case2 8221 89歳　♀

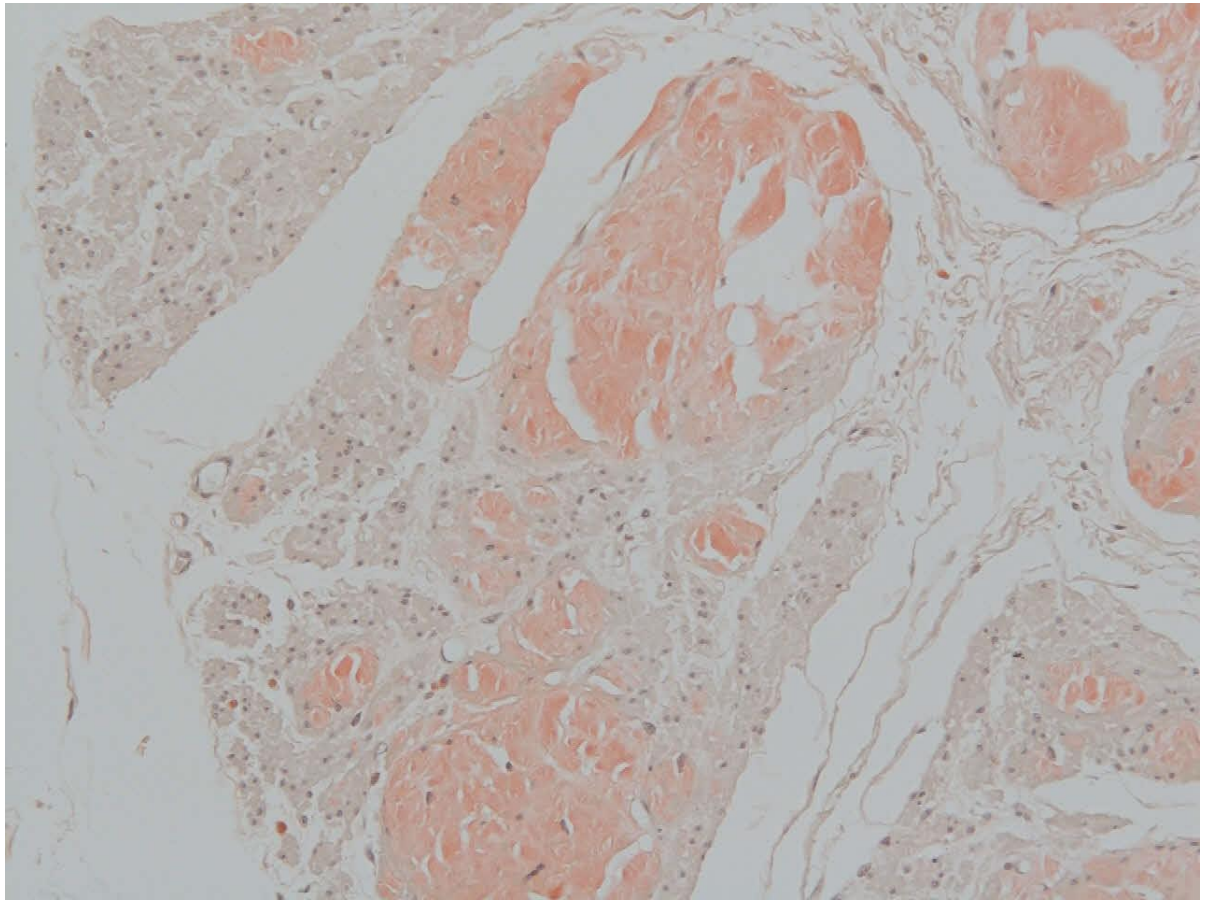




Case2 8221 89歳　♀



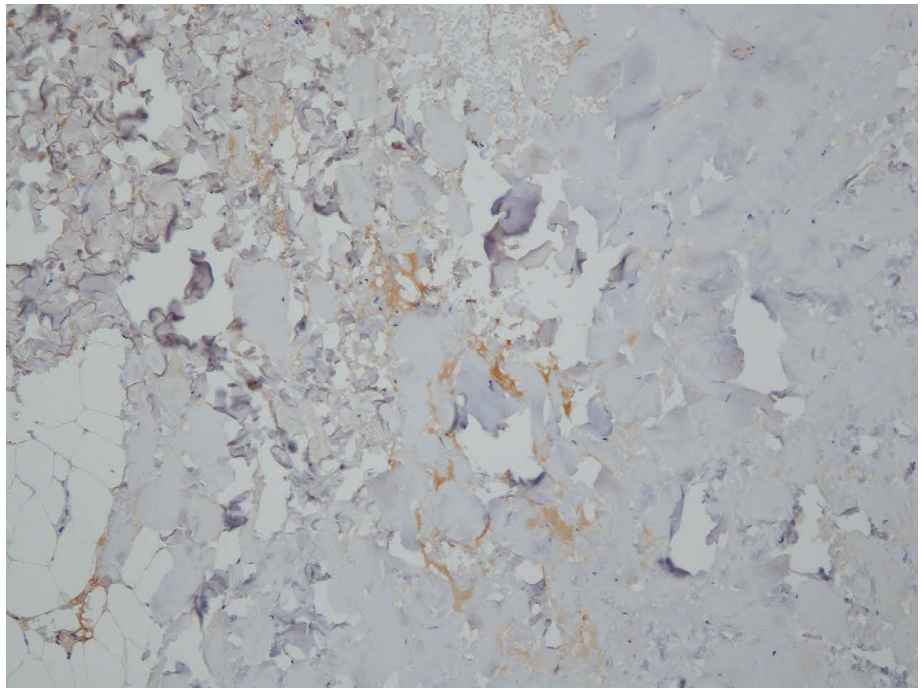
DSF染色

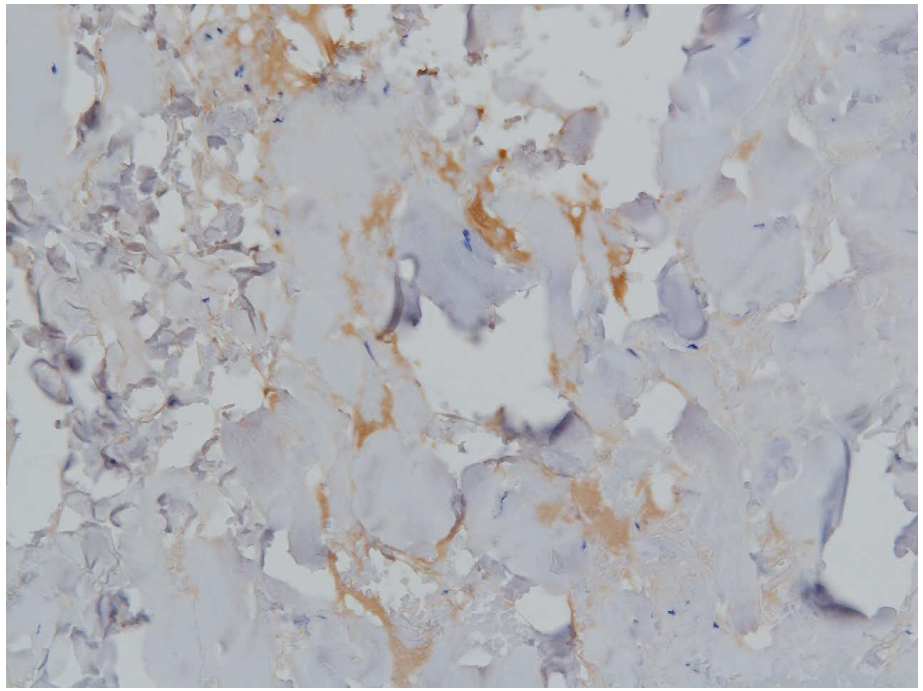


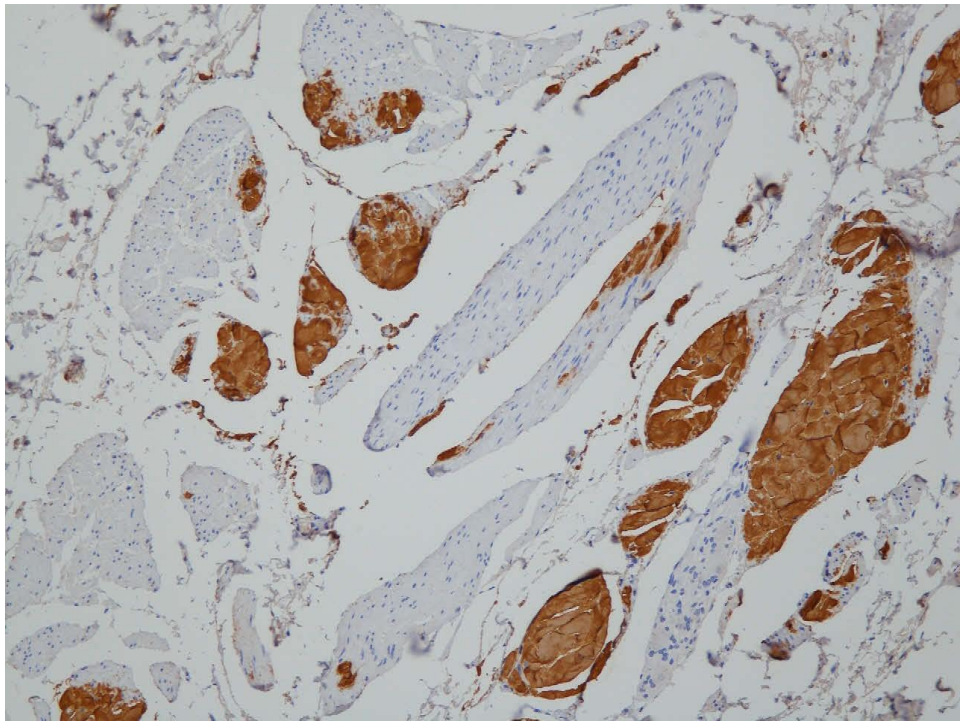
コントロール

Case2 8221 89歳♀

TTR免疫染色

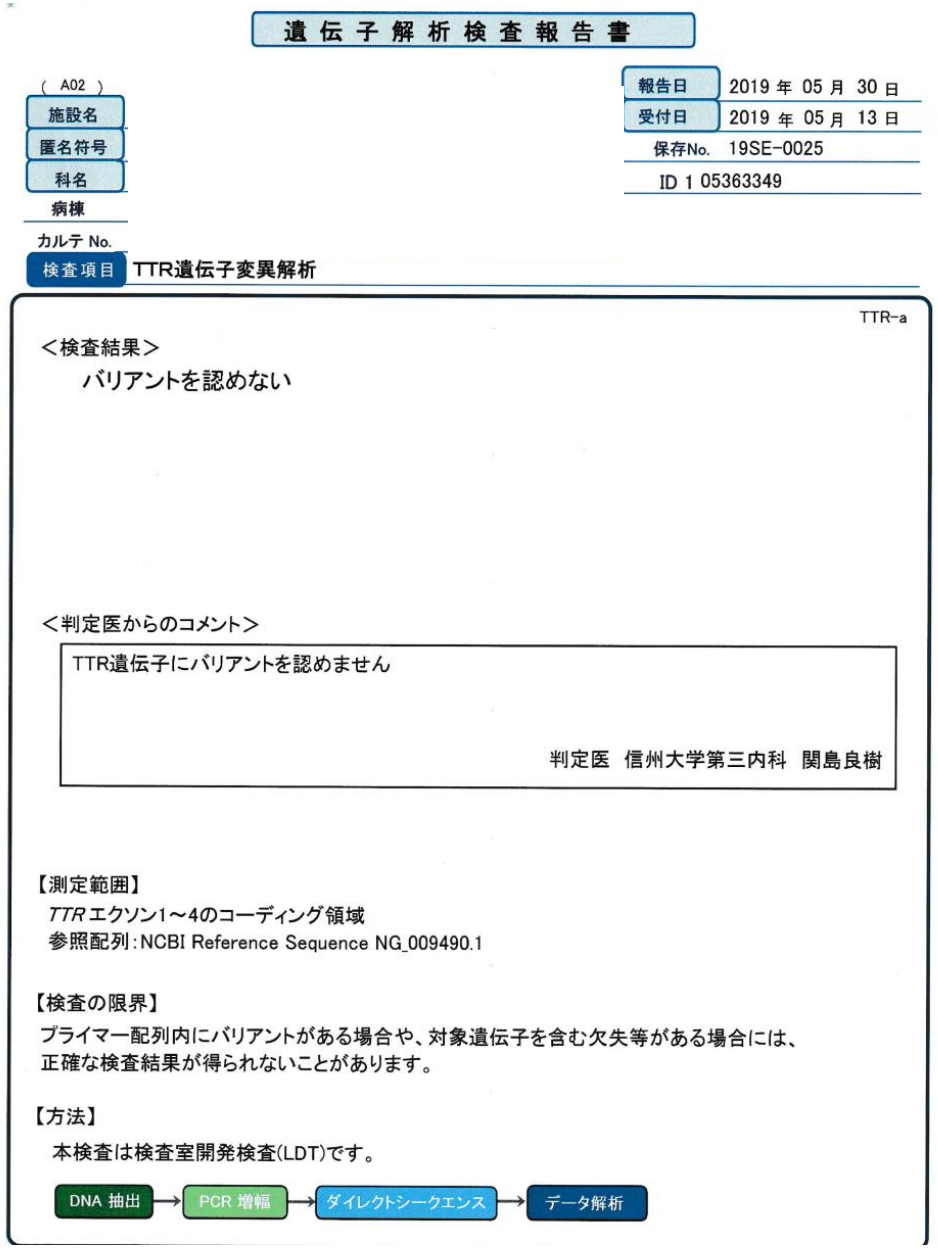






コントロール

Case2 8221 89歳



遺伝子解析検査報告書

(A02)
施設名
匿名符号
科名
病棟
カルテ No.

報告日 2019 年 05 月 30 日
受付日 2019 年 05 月 13 日
保存No. 19SE-0025
ID 1 05363349

検査項目 TTR遺伝子変異解析

TTR-a

＜検査結果＞
バリアントを認めない

＜判定医からのコメント＞
TTR遺伝子にバリアントを認めません

判定医 信州大学第三内科 関島良樹

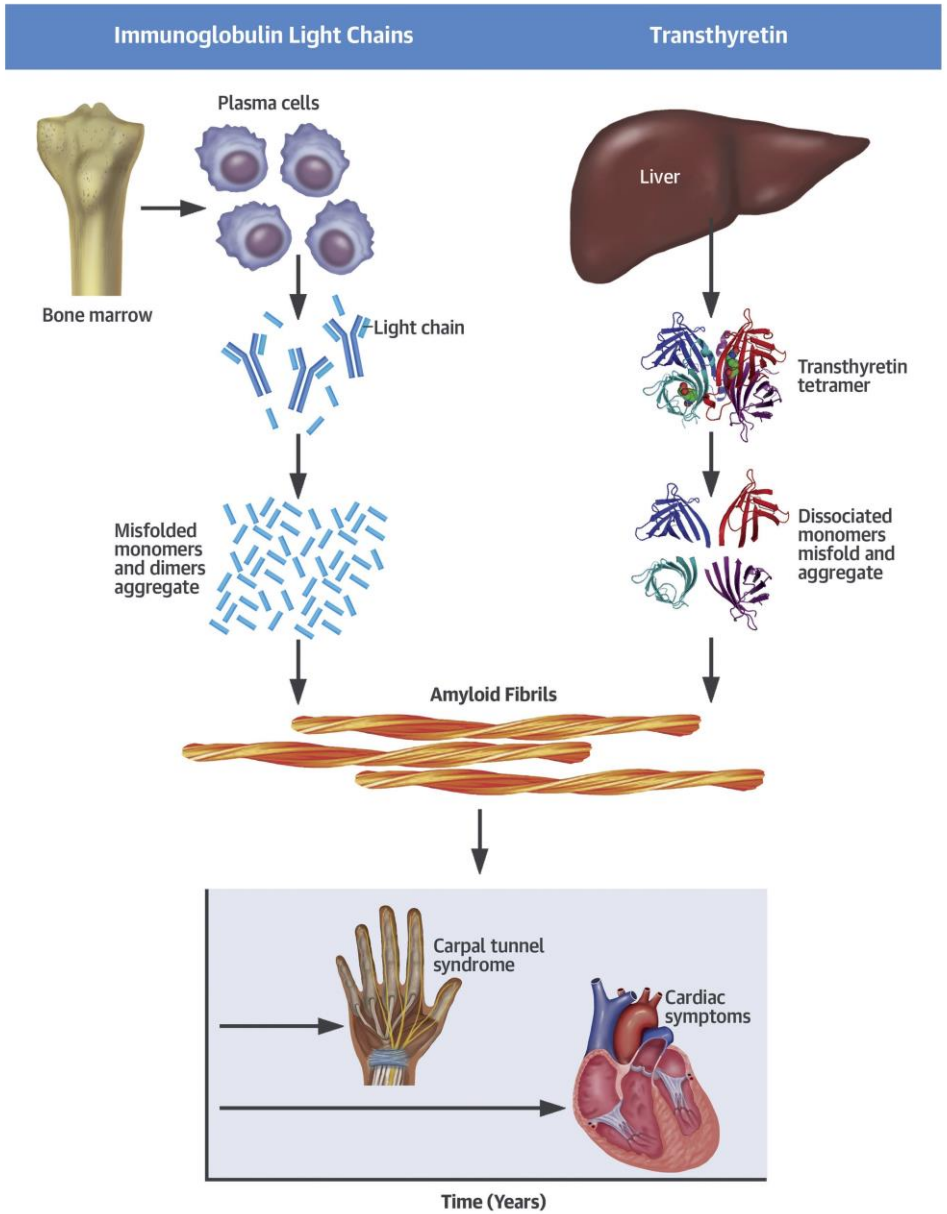
【測定範囲】
TTR エクソン1～4のコーディング領域
参照配列：NCBI Reference Sequence NG_009490.1

【検査の限界】
プライマー配列内にバリアントがある場合や、対象遺伝子を含む欠失等がある場合には、
正確な検査結果が得られないことがあります。

【方法】
本検査は検査室開発検査(LDT)です。

DNA 抽出 → PCR 増幅 → ダイレクトシークエンス → データ解析

CENTRAL ILLUSTRATION: Mechanism of Amyloid Deposition



Sperry, B.W. et al. J Am Coll Cardiol. 2018;72(17):2040-50.

老人性全身性アミロイドーシス

- 老人性全身性アミロイドーシスは、後天性の晩期発症型疾患。
- 正常型（野生型）タンパク 質由来のアミロイドの沈着が体内に蓄積。
- 最もよく知られているものは、高齢者の心臓に野生型トランスサイレチン（TTR）が蓄積する ことによって起こる。
- 家族性アミロイドーシスと異 なってTTR遺伝子の変異はみられず。
- 緩徐進行性の心疾患が症状を引き起こす。

European Heart Journal (2015) **36**, 2585–2594
doi:10.1093/eurheartj/ehv338

Wild-type transthyretin amyloidosis as a cause of heart failure with preserved ejection fraction

Esther González-López[1], Maria Gallego-Delgado[1], Gonzalo Guzzo-Merello[1], F. Javier de Haro-del Moral[2], Marta Cobo-Marcos[1], Carolina Robles[1], Belén Bornstein[3,4,5], Clara Salas[6], Enrique Lara-Pezzi[7], Luis Alonso-Pulpon[1], and Pablo Garcia-Pavia[1,7]*

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See page 2595 for the editorial comment on this article (doi:10.1093/eurheartj/ehv328)

Aims Heart failure with preserved ejection fraction (HFpEF) is a heterogeneous clinical syndrome with multiple underlying causes. Wild-type transthyretin (TTR) amyloidosis (ATTRwt) is an underdiagnosed cause of HFpEF that might benefit from new specific treatments. ATTRwt can be diagnosed non-invasively by ^{99m}Tc-3,3-diphosphono-1,2-propanodicarboxylic acid (^{99m}Tc-DPD) scintigraphy. We sought to determine the prevalence of ATTRwt among elderly patients admitted due to HFpEF.

Methods and results We prospectively screened all consecutive patients ≥60 years old admitted due to HFpEF [left ventricular (LV) ejection fraction ≥50%] with LV hypertrophy (≥12 mm). All eligible patients were offered a ^{99m}Tc-DPD scintigraphy. The study included 120 HFpEF patients (59% women, 82 ± 8 years). A total of 16 patients (13.3%; 95% confidence interval: 7.2–19.5) showed a moderate-to-severe uptake on the ^{99m}Tc-DPD scintigraphy. All patients with a positive scan underwent genetic testing of the *TTR* gene, and no mutations were found. An endomyocardial biopsy was performed in four patients, confirming ATTRwt in all cases. There were no differences in age, gender, hypertension, diabetes, coronary artery disease, or atrial fibrillation between ATTRwt patients and patients with other HFpEF forms. Although patients with ATTRwt exhibited higher median N-terminal pro-brain natriuretic peptide (6467 vs. 3173 pg/L; $P = 0.019$), median troponin I (0.135 vs. 0.025 μg/L; $P < 0.001$), mean LV maximal wall thickness (17 ± 3.4 vs. 14 ± 2.5 mm; $P = 0.001$), rate of pericardial effusion (44 vs. 19%; $P = 0.047$), and rate of pacemakers (44 vs. 12%; $P = 0.004$), clinical overlap between ATTRwt and other HFpEF forms was high.

Conclusion ATTRwt is an underdiagnosed disease that accounts for a significant number (13%) of HFpEF cases. The effect of emerging TTR-modifying drugs should be evaluated in these patients.

Keywords Heart failure with preserved ejection fraction • Diastolic heart failure • Cardiac amyloidosis • Transthyretin • Senile systemic amyloidosis • ^{99m}Tc-DPD scintigraphy

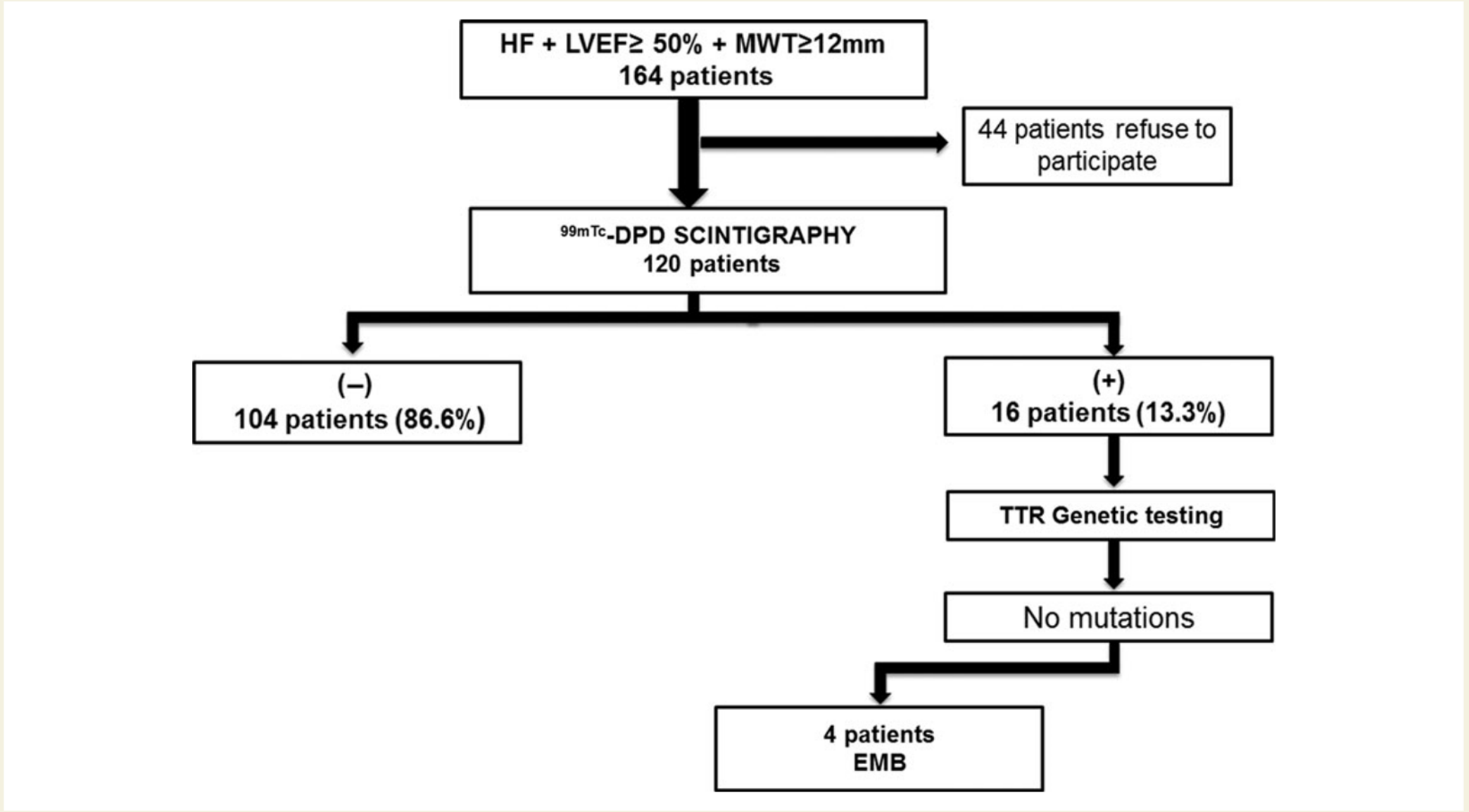

Figure 3 Assembly of the cohort and participant flow. LVEF, left ventricular ejection fraction; MWT, maximal wall thickness; EMB, endomyocardial biopsy; HF, heart failure; TTR, transthyretin.

Table 2 Clinical, epidemiological, analytical, electrocardiographic, and echocardiographic characteristics according to ^{99m}Tc-DPD scintigraphy results

	ATTRwt (^{99m}Tc-DPD+) (n = 16)	Other forms of HFpEF (^{99m}Tc-DPD−) (n = 104)	P-value
Age (years)	86 ± 6	81 ± 8	0.121
Male gender, n (%)	8 (50)	41 (39)	0.423
Median length of stay, days (range)	8 (6–14)	8 (6–15)	0.994
Mortality, n (%)	5 (31)	21 (20)	0.335
Survival			
At 3 months, % (95% CI)	87 (71–100)	90 (84–96)	0.76
At 6 months, % (95% CI)	87 (71–100)	83 (75–91)	0.76
At 12 months, % (95% CI)	73 (51–95)	76 (66–86)	0.76
Comorbidities			
Hypertension, n (%)	14 (88)	87 (84)	0.980
Diabetes mellitus, n (%)	4 (25)	41 (39)	0.267
CAD, n (%)	2 (13)	9 (9)	0.975
Treatment			
Loop diuretics, n (%)	16 (100)	104 (100)	1
Non-loop diuretics, n (%)	3 (18)	16 (16)	1
ACEI/ARB, n (%)	5 (31)	53 (52)	0.123
Beta-blockers, n (%)	5 (31)	48 (48)	0.224
Calcium channel blockers, n (%)	1 (7)	8 (8)	1
Aldosterone antagonists, n (%)	3 (19)	12 (12)	0.707
Amiodarone, n (%)	1 (7)	10 (10)	1
Anticoagulants, n (%)	12 (75)	68 (67)	0.746
Clinical features			
Systolic blood pressure (mmHg)	127 ± 19	136 ± 26	0.141
Diastolic blood pressure (mmHg)	74 ± 17	78 ± 22	0.407
Blood test			
Mean CCr (mL/min/1.73 m^2)	50 ± 17	59 ± 24	0.093
Mean haemoglobin (g/dL)	13 ± 1	12 ± 2	0.253
Median NTproBNP, pg/L (IQR)	6467 (2818–13 146)	3173 (1363–7139)	0.019
Median ultrasensitive troponin I (μg/L)	0.135 (0.017–1.91)	0.025 (0.017–1.74)	0.001
ECG			
AF, n (%)	13 (81)	67 (64)	0.184
Pacemaker, n (%)	7 (44)	12 (12)	0.004
Mean PR interval (ms)	177 ± 3	175 ± 41	0.934
Mean QRS interval (ms)	114 ± 25	101 ± 23	0.062
Low voltage, n (%)	5 (42)	26 (26)	0.434
Pseudo-MI, n (%)	4 (36)	15 (15)	0.185
Poor precordial R wave progression, n (%)	5 (45.5)	34 (35)	0.727
Median voltage-to-mass ratio, mm/cm^2/m^2 (IQR)	0.56 (0.3–0.85)	0.95 (0.65–1.47)	0.005
Echocardiography			
Mean LVEF (%)	60 ± 7	61 ± 8	0.501
Myocardial contraction fraction (%)	30 ± 14	43 ± 16	0.003
Mean LV end-diastolic diameter (mm)	41 ± 5.5	42 ± 8	0.796
Mean MWT, mm (IQR)	17 ± 3.4	14 ± 2.5	0.001
Median septal MWT, mm (IQR)	18 (15.7–21)	14 (13–16)	0.001
Median posterior wall, mm (IQR)	12.5 (11–17)	11.5 (10–13)	0.028
Symmetric hypertrophic pattern, n (%)	8 (50)	59 (57)	0.788
Asymmetric hypertrophic pattern, n (%)	8 (50)	45 (43)	0.788
E/A ratio	1.3 ± 0.6	1.1 ± 0.6	0.38
DT (ms)	191 ± 64	204 ± 80	0.639
Lateral E/E' ratio	20 ± 9	14 ± 7	0.600
Mean LV mass index (g/m^2)	161 ± 43	115 ± 34	0.001
Pericardial effusion, n (%)	7 (44)	19 (19)	0.047

Data are presented as mean ± SD or median (IQR).
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; AF, atrial fibrillation; pseudo-MI, pseudoinfarction pattern; LVEF, left ventricular ejection fraction; MWT, maximal wall thickness; DT, early deceleration time.

Occult Transthyretin Cardiac Amyloid in Severe Calcific Aortic Stenosis

Prevalence and Prognosis in Patients Undergoing Surgical Aortic Valve Replacement

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Background—Calcific aortic stenosis (cAS) affects 3% of individuals aged >75 years, leading to heart failure and death unless the valve is replaced. Wild-type transthyretin cardiac amyloid is also a disorder of ageing individuals. Prevalence and clinical significance of dual pathology are unknown. This study explored the prevalence of wild-type transthyretin amyloid in cAS by myocardial biopsy, its imaging phenotype and prognostic significance.

Methods and Results—A total of 146 patients with severe AS requiring surgical valve replacement underwent cardiovascular magnetic resonance and intraoperative biopsies; 112 had cAS (75±6 years; 57% men). Amyloid was sought histologically using Congo red staining and then typed using immunohistochemistry and mass spectrometry; patients with amyloid underwent clinical evaluation including genotyping and ^{99m}TC-3,3-diphosphono-1,2-propanodicarboxylic-acid (DPD) bone scintigraphy. Amyloid was identified in 6 of 146 patients, all with cAS and >65 years (prevalence 5.6% in cAS >65). All 6 patients had wild-type transthyretin amyloid (mean age 75 years; range, 69–85; 4 men), not suspected on echocardiography. Cardiovascular magnetic resonance findings were of definite cardiac amyloidosis in 2, but could be explained solely by AS in the other 4. Postoperative DPD scans demonstrated cardiac localization in all 4 patients who had this investigation (2 died prior). At follow-up (median, 2.3 years), 50% with amyloid had died (versus 7.5% in cAS; 6.9% in age >65 years). In univariable analyses, the presence of transthyretin amyloidosis amyloid had the highest hazard ratio for death (9.5 [95% confidence interval, 2.5–35.8]; P=0.001).

Conclusions—Occult wild-type transthyretin cardiac amyloid had a prevalence of 6% among patients with AS aged >65 years undergoing surgical aortic valve replacement and was associated with a poor outcome. **(*Circ Cardiovasc Imaging*. 2016;9:e005066. DOI: 10.1161/CIRCIMAGING.116.005066.)**

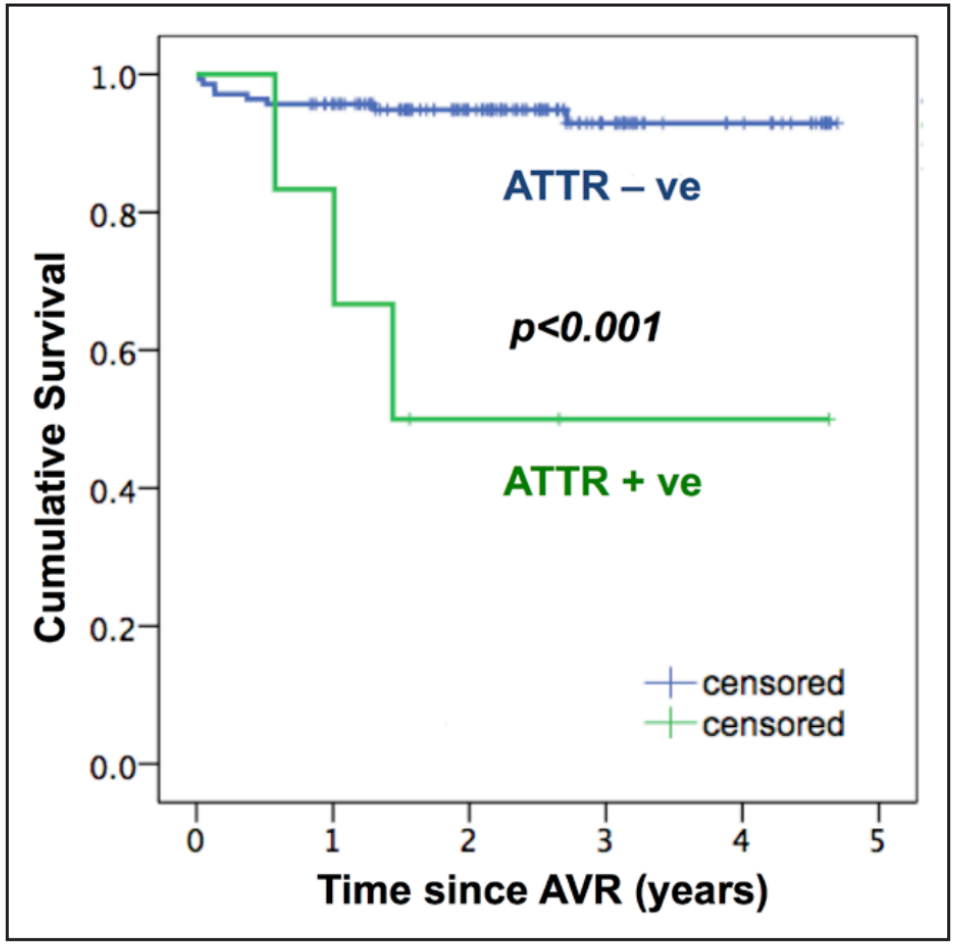

Figure 5. Kaplan–Meier plot of cumulative survival comparing aortic stenosis patients (n=146) with transthyretin amyloidosis (ATTR) amyloid on myocardial biopsy and those without. At median follow-up of 2.3 years (0.02–4.7), 11 patients with calcific aortic stenosis (cAS) had died, whereas all patients with bicuspid AS were alive. Three of 6 cAS with wild-type ATTR amyloid (50%) died compared with 8 of 106 (7.5%) in the remaining calcific AS cohort. AVR indicates surgical aortic valve replacement.

Table 1. Typical Echocardiographic Features of Cardiac Amyloidosis

Parameters	Comments
Characteristic granular/sparkling appearance of the LV myocardium	Not specific. Need to differentiate from hypertrophic and other infiltrative diseases*
Increased LV wall thickness	Results from amyloid infiltration of interstitial space and may relate to amyloid burden
Decreased LV end-diastolic volumes	Leads to reduced stroke volume despite near-normal LVEF
Typically preserved or mildly reduced LVEF	LVEF may decrease in end-stage disease
High *E*/*A* ratio	Is seen because of restrictive pathophysiology, but a reduced amplitude A wave may suggest poor atrial function and higher risk of thrombus formation*
Shortened mitral *E* deceleration time (restrictive filling pattern), high *E*/*e*′ ratio	High *E*/*e*′ suggests increased left atrial pressures
Increased left and right atrial volumes and reduced atrial function	A common feature. Also imaged on CMR Atrial strain can be significantly reduced
LS in the left ventricle is impaired and worse at the base and mid-ventricular regions when compared with the apex[4]	Specific patterns of LV LS may differentiate amyloid from aortic stenosis and hypertrophic cardiomyopathy[7,8]
RV thickening, reduced RV myocardial velocities on tissue Doppler imaging, and reduced RV LS[5,6]	TAPSE and RV LS are early indicators of cardiac involvement in patients with systemic AL amyloidosis[5,6]
Reduced tricuspid annular plane excursion despite normal RV end-diastolic dimension[5,6]	RV LS may be an independent predictor of cardiac death[5]
Valve thickening	Nonspecific
Pericardial effusion	Nonspecific
Atrial septal thickening	A characteristic feature of cardiac amyloidosis
Dynamic LV outflow tract obstruction	A less common feature but need to distinguish from hypertrophic cardiomyopathy

AL indicates amyloid light-chain; CMR, cardiac magnetic resonance; LS, longitudinal strain; LV, left ventricular; LVEF, LV ejection fraction; RV, right ventricular; and TAPSE, tricuspid annular plane excursion.

*Hypertrophic cardiomyopathy, hypertensive heart disease with or without renal failure, Anderson Fabry's disease, mucopolysaccharidosis, Friedreich ataxia.

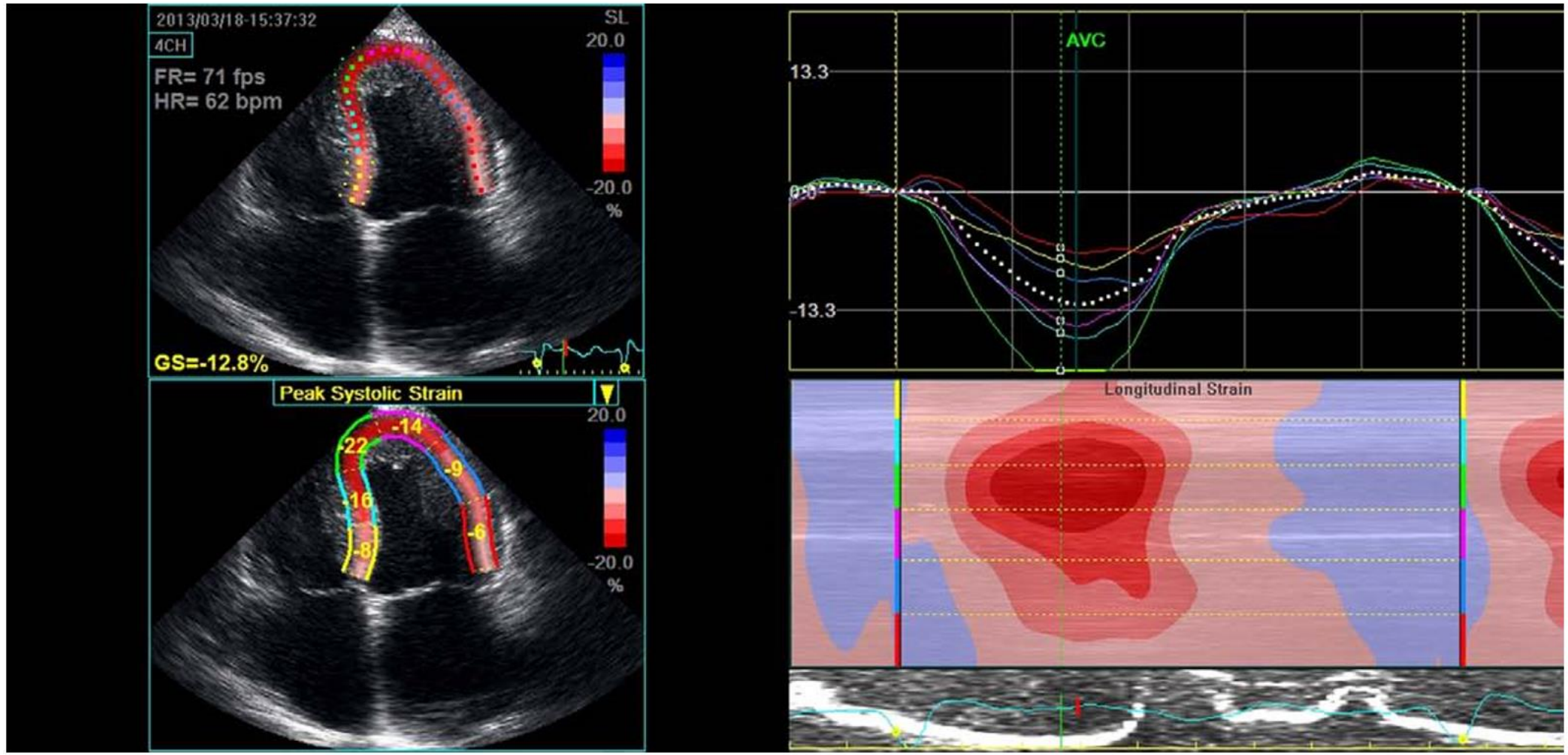

Figure 4. Left ventricular strain imaging in cardiac amyloidosis. Apical 4-chamber peak systolic strain image illustrating a classic strain pattern of relatively well-preserved apical strain (green and blue lines) with significant basal impairment (red and yellow lines). This is seen in the series of curves and the bull's-eye color-coded strain image. FR indicates frame heart; and HR, heart rate. Reprinted from Lubberink et al[34] with permission of the publisher. Copyright ©2013, the Society of Nuclear Medicine and Molecular Imaging, Inc.

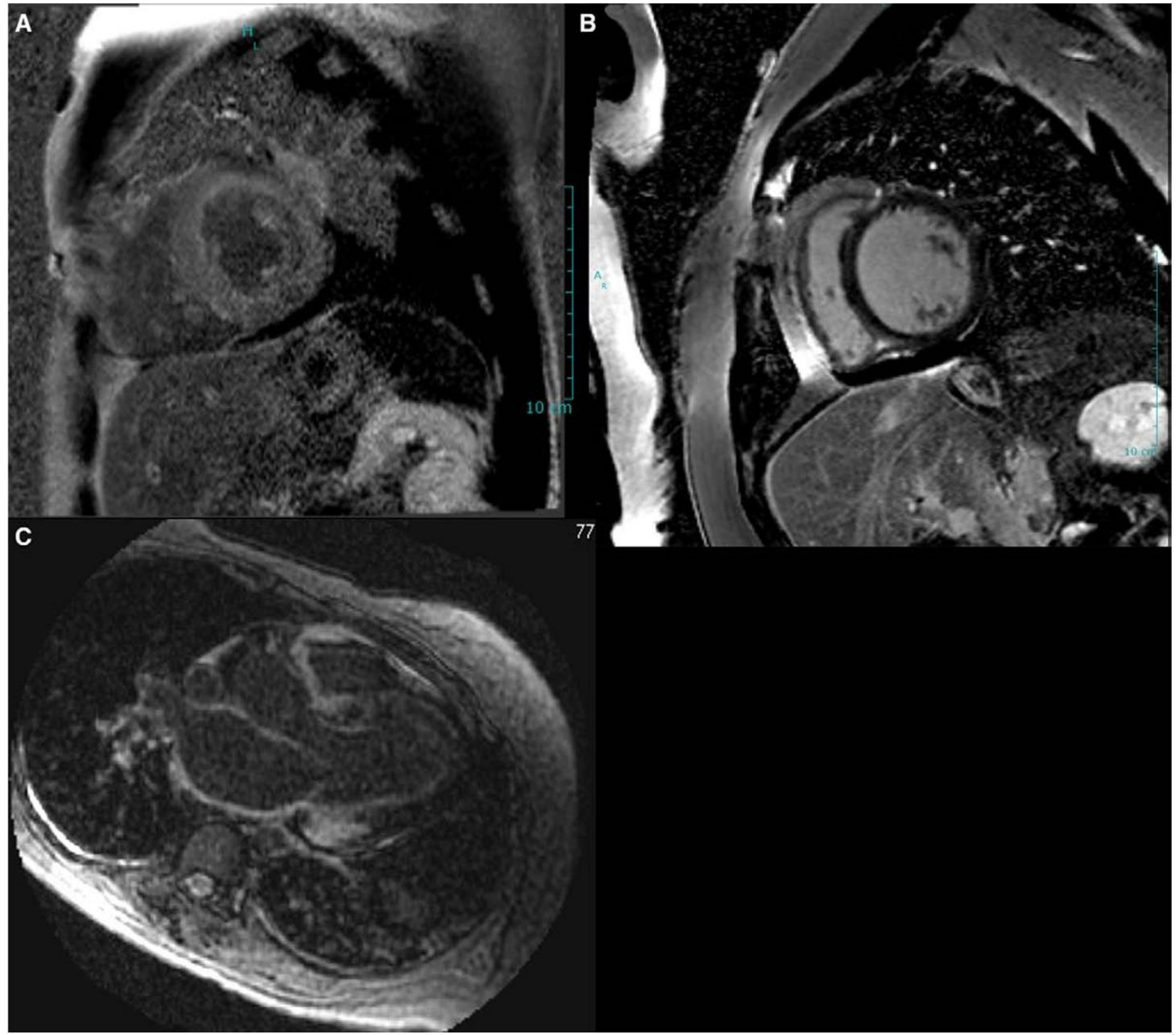

Figure 7. Typical rest cardiac magnetic resonance imaging features in a patient with familial transthyretin cardiac amyloidosis. Late gadolinium enhancement (LGE) images demonstrate diffuse LGE in the left ventricular myocardium (**A**) contrasted with dark myocardium in a normal patient (**B**). **C**, LGE in the atrial wall, a characteristic feature of cardiac amyloidosis.

Table 2. Typical CMR Features of Cardiac Amyloidosis

Parameters	Comments
Characteristic morphological features of cardiac amyloidosis/restrictive cardiomyopathy as listed in Table 1	Better resolution images than echocardiography No limitation of difficult echo windows
LV LGE	Diffuse and subendocardial LGE of the LV myocardium is more common than patchy focal delayed enhancement May be an early feature of cardiac involvement when compared with increased wall thickness
Atrial LGE and function	A characteristic feature of cardiac amyloidosis Atrial function can be studied well with CMR
T1 mapping	Subendocardial T1 relaxation time may be shortened in cardiac amyloidosis This is an early feature of cardiac amyloid involvement
Extracellular volume estimation based on T1 mapping and hematocrit measures	Extracellular volume expansion may permit an early diagnosis of cardiac amyloid even before overt LV LGE

CMR indicates cardiac magnetic resonance; LGE, late gadolinium enhancement; and LV, left ventricular.

Nonbiopsy Diagnosis of Cardiac Transthyretin Amyloidosis

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Background—Cardiac transthyretin (ATTR) amyloidosis is a progressive and fatal cardiomyopathy for which several promising therapies are in development. The diagnosis is frequently delayed or missed because of the limited specificity of echocardiography and the traditional requirement for histological confirmation. It has long been recognized that technetium-labeled bone scintigraphy tracers can localize to myocardial amyloid deposits, and use of this imaging modality for the diagnosis of cardiac ATTR amyloidosis has lately been revisited. We conducted a multicenter study to ascertain the diagnostic value of bone scintigraphy in this disease.

Methods and Results—Results of bone scintigraphy and biochemical investigations were analyzed from 1217 patients with suspected cardiac amyloidosis referred for evaluation in specialist centers. Of 857 patients with histologically proven amyloid (374 with endomyocardial biopsies) and 360 patients subsequently confirmed to have nonamyloid cardiomyopathies, myocardial radiotracer uptake on bone scintigraphy was >99% sensitive and 86% specific for cardiac ATTR amyloid, with false positives almost exclusively from uptake in patients with cardiac AL amyloidosis. Importantly, the combined findings of grade 2 or 3 myocardial radiotracer uptake on bone scintigraphy and the absence of a monoclonal protein in serum or urine had a specificity and positive predictive value for cardiac ATTR amyloidosis of 100% (positive predictive value confidence interval, 98.0–100).

Conclusions—Bone scintigraphy enables the diagnosis of cardiac ATTR amyloidosis to be made reliably without the need for histology in patients who do not have a monoclonal gammopathy. We propose noninvasive diagnostic criteria for cardiac ATTR amyloidosis that are applicable to the majority of patients with this disease. **(*Circulation*. 2016;133:2404-2412. DOI: 10.1161/CIRCULATIONAHA.116.021612.)**

Key Words: amyloid ■ cardiomyopathies ■ genetics ■ hypertrophy ■ radionuclide imaging

Table 2. Radionuclide 'Bone' Scintigraphy Findings Among 374 Patients With EMBs

	^{99m}Tc-PYP Scan Findings				
	Grade 0	Grade 1	Grade 2	Grade 3	n
No cardiac amyloid	7	1	1	0	9
Cardiac ATTR amyloid	1	10	7	67	85
Cardiac AL amyloid deposits	10	1	3	1	15
Cardiac ApoAI amyloid deposits	0	0	0	0	0
Cardiac amyloid deposits of unknown type	0	0	0	0	0
Total	18	12	11	68	109

Bisphosphonate Scintigraphy Patients were scanned after intravenous injection of ≈700 MBq 99mTc-PYP (n=199), providing an expected radiation dose of ≈5 mSv per patient. Wholebody planar images were acquired 1 hours after injection. 99mTc-PYP was scored by a single reader at each center using the following grading system:
grade 0=absent cardiac uptake; grade 1=mild uptake less than bone; grade 2=moderate uptake equal to bone; and grade 3=high uptake greater than bone.

Table 3. Sensitivity and Specificity of Radionuclide 'Bone' Scintigraphy Compared With EMB Histology

Positive Radionuclide Scan vs Cardiac Amyloid Deposits (n=374)			
	Positive Scan (Grade 1, 2, or 3), n	Negative Scan (Grade 0), n	Sensitivity and Specificity (CI), %
Cardiac amyloid deposits	289	38	88 (84–92) sensitive*
No cardiac amyloid deposits	6	41	87 (73–95) specific
	Positive Scan (Grade 1, 2, or 3), n	Negative Scan (Grade 0), n	
Cardiac ATTR amyloid deposits	259	2	>99 (97–100) sensitive
No cardiac ATTR amyloid deposits	36	77	68 (59–77) specific
	Grade 2/3 Scan, n	Grade 0/1 Scan, n	
Cardiac ATTR amyloid deposits	238	23	91 (87–94) sensitive
No cardiac ATTR amyloid deposits	15	98	87 (79–92) specific

CI indicates confidence interval; DPD, 3,3-diphosphono-1,2-propanodicarboxylic acid; EMB, endomyocardial biopsy; HDMP, hydroxymethylene diphosphonate; and PYP, pyrophosphate.

*The sensitivity of a positive radionuclide scan for detecting cardiac amyloid deposits of any type is likely to be falsely high owing to the high proportion of patients with ATTR amyloid in the sample.

^{99m}Tc-Pyrophosphate Scintigraphy for Differentiating Light-Chain Cardiac Amyloidosis From the Transthyretin-Related Familial and Senile Cardiac Amyloidoses

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Background—Differentiating amyloid light-chain (AL) from transthyretin-related cardiac amyloidoses (ATTR) is imperative given implications for prognosis, therapy, and genetic counseling. We validated the discriminatory ability of ^{99m}Tc-pyrophosphate (^{99m}Tc-PYP) scintigraphy in AL versus ATTR.

Methods and Results—Forty-five subjects (12 AL, 16 ATTR wild type, and 17 ATTR mutants) underwent ^{99m}Tc-PYP planar and single-photon positive emission computed tomography cardiac imaging. Scans were performed by experienced nuclear cardiologists blinded to the subjects' cohort assignment. Cardiac retention was assessed with both a semiquantitative visual score (range, 0; no uptake to 3, diffuse uptake) and by quantitative analysis by drawing a region of interest over the heart corrected for contralateral counts and calculating a heart-to-contralateral ratio. Subjects with ATTR cardiac amyloid had a significantly higher semiquantitative cardiac visual score than the AL cohort (2.9±0.06 versus 0.8±0.27; $P<0.0001$) as well as a higher quantitative score (1.80±0.04 versus 1.21±0.04; $P<0.0001$). Using a heart-to-contralateral ratio >1.5 consistent with intensely diffuse myocardial tracer retention had a 97% sensitivity and 100% specificity with area under the curve 0.992, $P<0.0001$ for identifying ATTR cardiac amyloidosis.

Conclusions—^{99m}Tc-PYP cardiac imaging distinguishes AL from ATTR cardiac amyloidosis and may be a simple, widely available method for identifying subjects with ATTR cardiac amyloidosis, which should be studied in a larger prospective manner. **(*Circ Cardiovasc Imaging*. 2013;6:195-201.)**

Key Words: ^{99m}Tc-PYP scintigraphy ■ AL amyloid ■ ATTR transthyretin cardiomyopathy ■ technetium

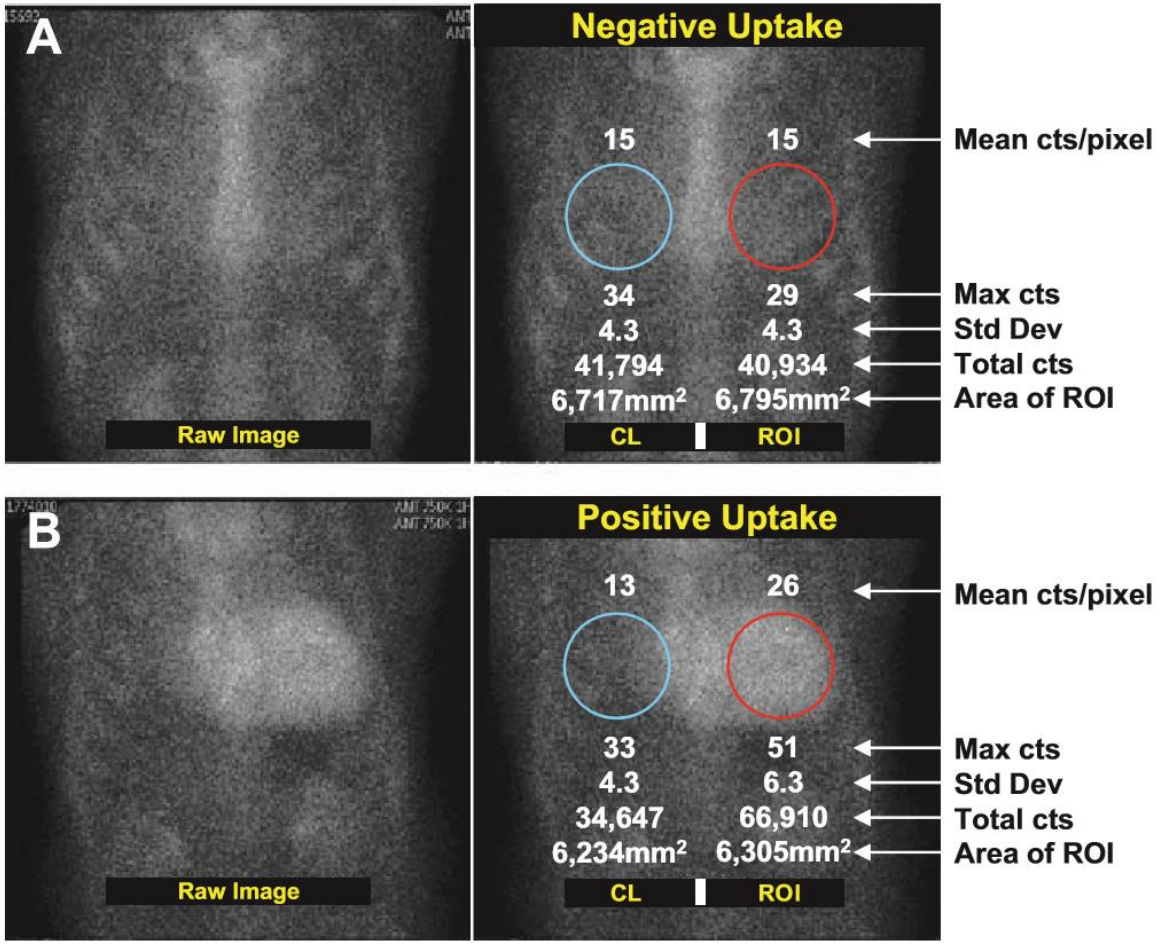

Figure 1. **A** and **B**, Semiquantitative method of calculating the distribution of ^{99m}Tc-pyrophosphate (^{99m}Tc-PYP) uptake. Raw images of a representative negative (**A**) and positive subject (**B**) are shown 1 hour after radiotracer infusion. ROI circles are depicted in red, and the contralateral comparison circle is depicted in blue. C/L indicates contralateral; cts, counts; ROI, region of interest; and Std Dev, standard deviation.

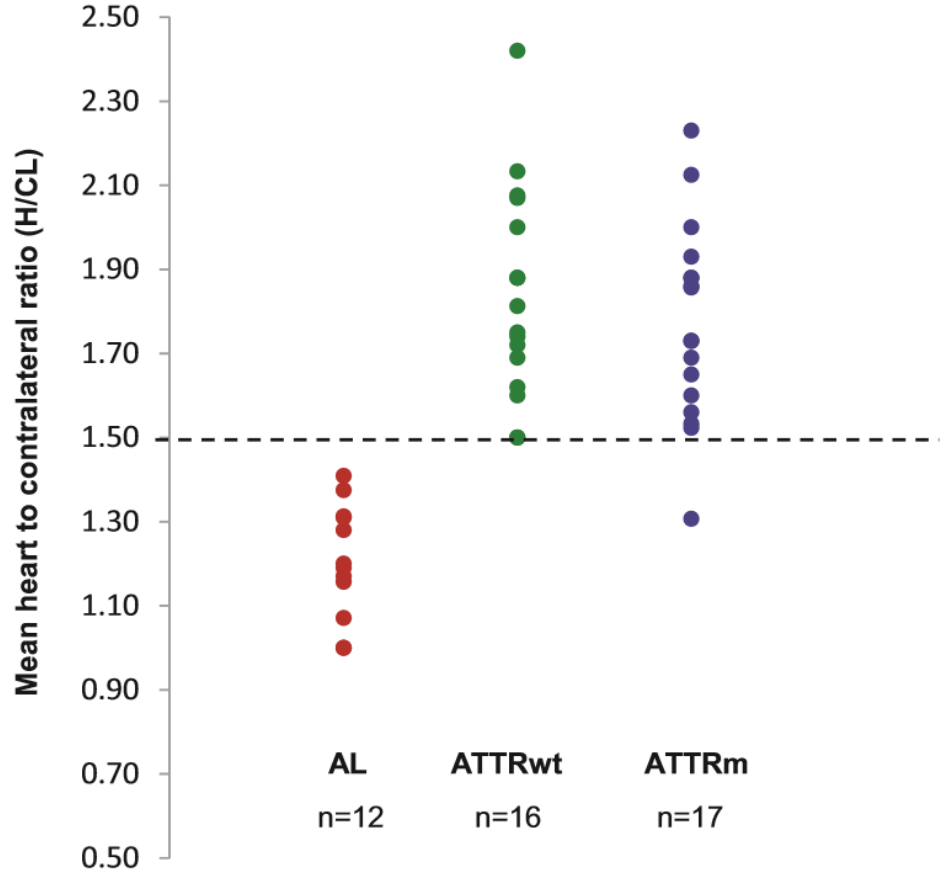

Figure 2. Mean heart-to-contralateral ratio according to amyloid subtype. Comparison of ^{99m}Tc-pyrophosphate (^{99m}Tc-PYP) mean heart-to-contralateral (H/CL) ratio between patients with amyloid light-chain (AL), wild-type transthyretin-related cardiac amyloidosis (ATTRwt), and mutant ATTR (ATTRm). AL and transthyretin-related amyloidoses are differentiated by mean H/CL ratio of 1.5. The outlier with H/CL 1.3 is an ATTRm patient with the unusual Thr59Lys mutation.

Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

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ABSTRACT

BACKGROUND

Transthyretin amyloid cardiomyopathy is caused by the deposition of transthyretin amyloid fibrils in the myocardium. The deposition occurs when wild-type or variant transthyretin becomes unstable and misfolds. Tafamidis binds to transthyretin, preventing tetramer dissociation and amyloidogenesis.

METHODS

In a multicenter, international, double-blind, placebo-controlled, phase 3 trial, we randomly assigned 441 patients with transthyretin amyloid cardiomyopathy in a 2:1:2 ratio to receive 80 mg of tafamidis, 20 mg of tafamidis, or placebo for 30 months. In the primary analysis, we hierarchically assessed all-cause mortality, followed by frequency of cardiovascular-related hospitalizations according to the Finkelstein–Schoenfeld method. Key secondary end points were the change from baseline to month 30 for the 6-minute walk test and the score on the Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS), in which higher scores indicate better health status.

RESULTS

In the primary analysis, all-cause mortality and rates of cardiovascular-related hospitalizations were lower among the 264 patients who received tafamidis than among the 177 patients who received placebo (P<0.001). Tafamidis was associated with lower all-cause mortality than placebo (78 of 264 [29.5%] vs. 76 of 177 [42.9%]; hazard ratio, 0.70; 95% confidence interval [CI], 0.51 to 0.96) and a lower rate of cardiovascular-related hospitalizations, with a relative risk ratio of 0.68 (0.48 per year vs. 0.70 per year; 95% CI, 0.56 to 0.81). At month 30, tafamidis was also associated with a lower rate of decline in distance for the 6-minute walk test (P<0.001) and a lower rate of decline in KCCQ-OS score (P<0.001). The incidence and types of adverse events were similar in the two groups.

CONCLUSIONS

In patients with transthyretin amyloid cardiomyopathy, tafamidis was associated with reductions in all-cause mortality and cardiovascular-related hospitalizations and reduced the decline in functional capacity and quality of life as compared with placebo. (Funded by Pfizer; ATTR-ACT ClinicalTrials.gov number, NCT01994889.)

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*The complete list of the ATTR-ACT Study Investigators is provided in the Supplementary Appendix, available at NEJM.org.

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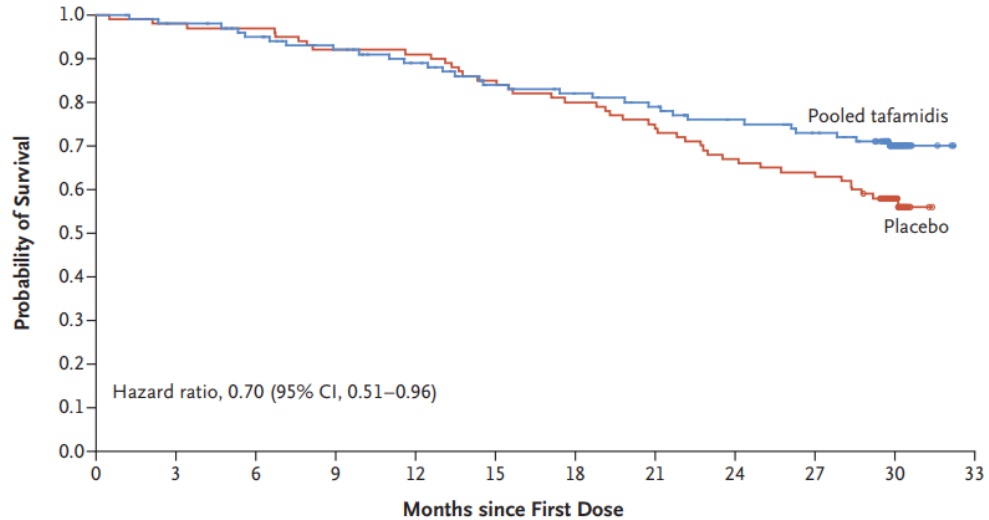
A Primary Analysis, with Finkelstein–Schoenfeld Method

	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			186 (70.5)	0.30
		<0.001	1.70 (1.26–2.29)		
Placebo	177			101 (57.1)	0.46

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)

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	

Figure 2. Primary Analysis and Components.

Panel A shows the results of the primary analysis as determined with the use of the Finkelstein–Schoenfeld method. Panel B shows an analysis of all-cause mortality for pooled tafamidis and for placebo, a secondary end point. Panel C shows the frequency of cardiovascular-related hospitalizations, also a secondary end point.

Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis

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ABSTRACT

BACKGROUND

Patisiran, an investigational RNA interference therapeutic agent, specifically inhibits hepatic synthesis of transthyretin.

METHODS

In this phase 3 trial, we randomly assigned patients with hereditary transthyretin amyloidosis with polyneuropathy, in a 2:1 ratio, to receive intravenous patisiran (0.3 mg per kilogram of body weight) or placebo once every 3 weeks. The primary end point was the change from baseline in the modified Neuropathy Impairment Score+7 (mNIS+7; range, 0 to 304, with higher scores indicating more impairment) at 18 months. Other assessments included the Norfolk Quality of Life–Diabetic Neuropathy (Norfolk QOL-DN) questionnaire (range, −4 to 136, with higher scores indicating worse quality of life), 10-m walk test (with gait speed measured in meters per second), and modified body-mass index (modified BMI, defined as [weight in kilograms divided by square of height in meters] × albumin level in grams per liter; lower values indicated worse nutritional status).

RESULTS

A total of 225 patients underwent randomization (148 to the patisiran group and 77 to the placebo group). The mean (±SD) mNIS+7 at baseline was 80.9±41.5 in the patisiran group and 74.6±37.0 in the placebo group; the least-squares mean (±SE) change from baseline was −6.0±1.7 versus 28.0±2.6 (difference, −34.0 points; P<0.001) at 18 months. The mean (±SD) baseline Norfolk QOL-DN score was 59.6±28.2 in the patisiran group and 55.5±24.3 in the placebo group; the least-squares mean (±SE) change from baseline was −6.7±1.8 versus 14.4±2.7 (difference, −21.1 points; P<0.001) at 18 months. Patisiran also showed an effect on gait speed and modified BMI. At 18 months, the least-squares mean change from baseline in gait speed was 0.08±0.02 m per second with patisiran versus −0.24±0.04 m per second with placebo (difference, 0.31 m per second; P<0.001), and the least-squares mean change from baseline in the modified BMI was −3.7±9.6 versus −119.4±14.5 (difference, 115.7; P<0.001). Approximately 20% of the patients who received patisiran and 10% of those who received placebo had mild or moderate infusion-related reactions; the overall incidence and types of adverse events were similar in the two groups.

CONCLUSIONS

In this trial, patisiran improved multiple clinical manifestations of hereditary transthyretin amyloidosis. (Funded by Alnylam Pharmaceuticals; APOLLO ClinicalTrials.gov number, NCT01960348.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Adams at the Department of Neurology, CHU Bicêtre, 78 rue du Général Leclerc, 94275 Le Kremlin-Bicêtre CEDEX, France, or at david.adams@aphp.fr.

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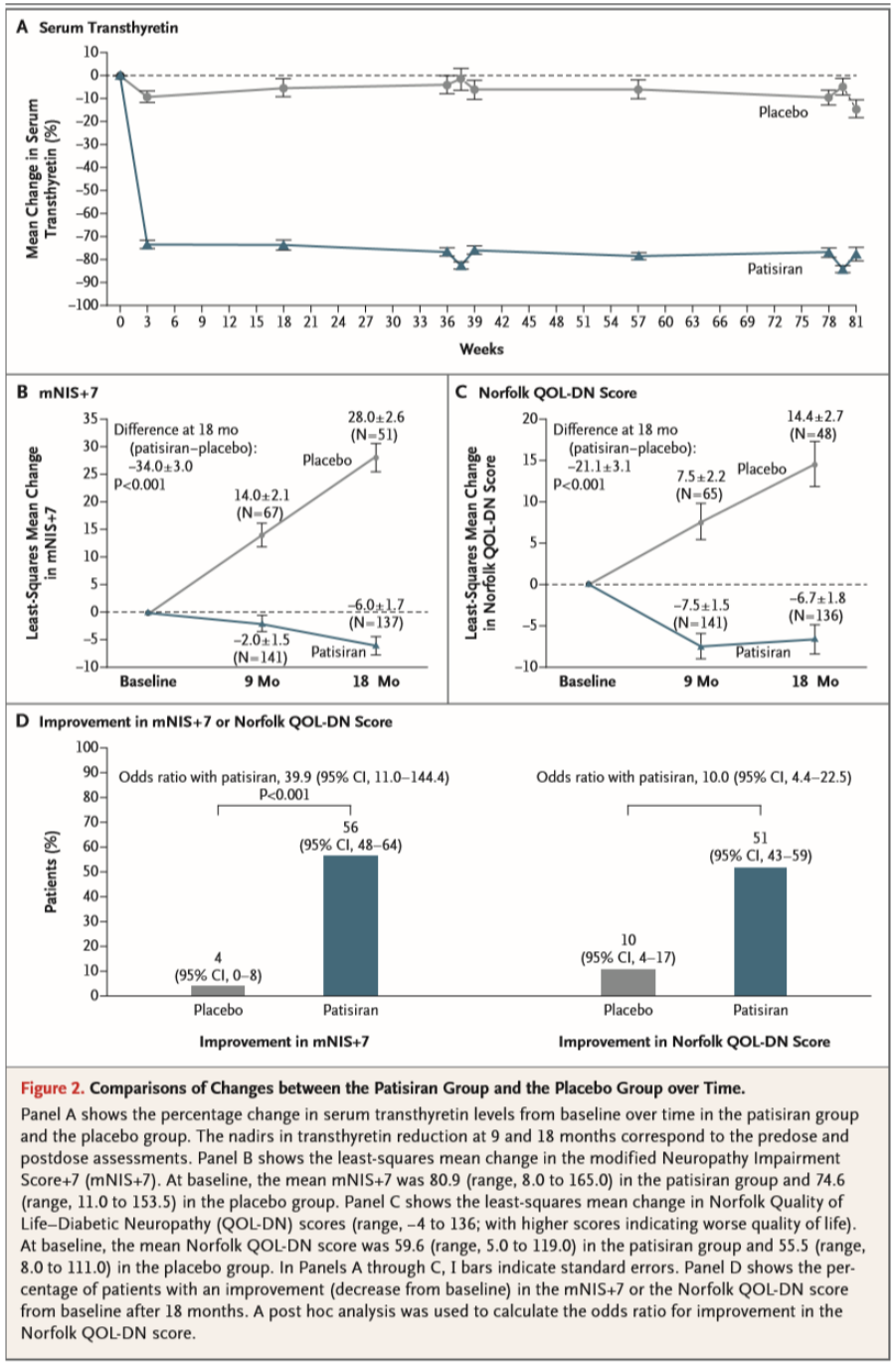

Figure 2. Comparisons of Changes between the Patisiran Group and the Placebo Group over Time.

Panel A shows the percentage change in serum transthyretin levels from baseline over time in the patisiran group and the placebo group. The nadirs in transthyretin reduction at 9 and 18 months correspond to the predose and postdose assessments. Panel B shows the least-squares mean change in the modified Neuropathy Impairment Score+7 (mNIS+7). At baseline, the mean mNIS+7 was 80.9 (range, 8.0 to 165.0) in the patisiran group and 74.6 (range, 11.0 to 153.5) in the placebo group. Panel C shows the least-squares mean change in Norfolk Quality of Life–Diabetic Neuropathy (QOL-DN) scores (range, −4 to 136; with higher scores indicating worse quality of life). At baseline, the mean Norfolk QOL-DN score was 59.6 (range, 5.0 to 119.0) in the patisiran group and 55.5 (range, 8.0 to 111.0) in the placebo group. In Panels A through C, I bars indicate standard errors. Panel D shows the percentage of patients with an improvement (decrease from baseline) in the mNIS+7 or the Norfolk QOL-DN score from baseline after 18 months. A post hoc analysis was used to calculate the odds ratio for improvement in the Norfolk QOL-DN score.

トランスサイレチン型心アミロイドーシス症例に対するビンダケル適性投与のためのステーテメント

日本循環器学会発表 平成 31 年 3 月 30 日

(1) 患者要件

１） NYHA 心機能分類Ⅰ～Ⅲ度。

２） 次の①又は②のすべての要件を満たした場合。

① 野生型

心不全による入院歴又は心不全症状を有する
心エコーによる拡張末期の心室中隔厚が 12mm を超える
組織生検によるアミロイド沈着が認められる
免疫組織染色によりTTR 前駆タンパク質が同定される

② 変異型の場合

TTR 遺伝子変異を有する
心不全による入院歴又は心不全症状を有 する
心エコーによる拡張末期の心室中隔厚が12mm を超える
組織生検によるアミロイド沈着が認められる

トランスサイレチン型心アミロイドーシス症例に対するビンダケル適性投与のためのステーテメント

日本循環器学会発表 平成 31 年 3 月 30 日

（2） 施設要件 ①～⑥のすべての条件を満たす施設

① 日本循環器学会認定専門医研修施設

② 日本医学放射線学会認定放射線専門医総合修練機関

③ 日本病理学会病理専門医研修認定施設

④ 日本血液学会専門研修認定施設

⑤ 日本神経学会認定教育施設

⑥ 心筋生検を年間 15 例以上実施している施設

※心臓超音波検査を専門とする循環器専門医が在籍する施設

注）国立循環器病研究センターは導入を認める。

トランスサイレチン型心アミロイドーシス症例に対するビンダケル適性投与のためのステーテメント

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(3)　医師要件

①ビンダケルの適応拡大承認日以前に変異型トランスサレチン型アミロイドーシスに対してビンダケルの使用経験がある。

②生検組織からトランスサイレチン前駆タンパク質を免疫組織染色で同定し、トランスサイレチン型心アミロイドーシスと診断した経験が3例以上。

③ 投与症例の全例登録 一旦導入された患者への継続処方 については後方病院でも可。

結語

- 老人性全身性アミロイドーシスの頻度は、これまで考えられてきたよりも高いと推定される。
- 早期診断のためには^{99m}Tc-PYPが最も有用だが、Cut-offの設定には注意が必要である。
- 組織診断にはコンゴレッドもしくはDSF染色に加えてトランスサイレチン免疫染色が必要である。
- 将来的には函館地区でのビンダケル投与のための施設要件の充足が必要？