



Cardio-HART CARDIAC DIAGNOSTIC SYSTEM

www.cardiophoenix.com

The Challenge!

Cardiovascular diseases (CVD), Heart Failure and valve disease, remain the leading cause of disease burden in the world, afflicting tens of millions globally.

It affects a large spectrum of the population, occurs in **all ages, equally in both genders, increases with age, high blood pressure, obesity, and diabetes.**

In **Primary Care**, ECG and Natriuretic peptides testing plays a role in the clinical decision leading to a diagnosis, but they have limitations that contribute to **low detection rates, especially in the early phases.**

Although diagnosis by **echocardiography** is more effective, as it can diagnose significant diseases that ECG cannot, but Echocardiography is not indicated for use in Primary Care, accessed only through a referral, with wait times measured in many months, averaging 6 months, by which time disease progression has taken hold, and little can be done for these patients.

Yet Cardiovascular Disease (CVD) is the single biggest condition where lives can be saved, **early detection critical** to accessing appropriate and timely treatment to achieve the best possible outcomes. Echocardiography is not indicated for use in Primary Care

A Breakthrough Cardiac Diagnostic System

Cardio-HART^(TM) is a cardiac diagnostic system for the detection of most **common Cardiovascular Diseases (CVD**¹), including significant diseases such as **Heart Failure (HF) and Valve disease**.

Cardio-HART's aim is to improve access to testing that is **quick**, **non-invasive**, **and provides immediate results**, in any clinical care settings, even Primary Care.

Significantly, it's capabilities extend to the early detection of CVD onset.

The Current Limitations

Currently in widespread use in Primary Care, the Standard **12 Lead ECG**² provides only limited diagnostic evidence for many common heart problems, **less than 44**% - a surprise to many, especially patients.

ECG has limited capabilities for the early detection of CVD, as by its binary classification nature, reporting either "normal" or "abnormal", that cannot report the extent of the pathological condition.

ECG has limited capabilities for providing evidence of structural and functional abnormalities that define most of the common diseases of the heart, especially significant diseases, unlike Echocardiography.

As a result, ECG has low sensitivity or specificity for Heart Failure and Valve disease, relying instead on other methods such as Natriuretic Peptide (BNP) testing, itself also limited. ECG Limitations: no Early Detection,

no Heart failure no Valve disease



An Inconclusive ECG provides no diagnostic support

Neither ECG nor BNP is capable of estimating Left Ventricle Ejection Fraction (LVEF), a critical factor in a clinical determination of Heart Failure, much less the determination of Heart Failure phenotype, whether HFpEF, HFmrEF or HFrEF.

The result of these limitations means that often the ECG is inconclusive, leaving the practitioner without any diagnostic support at a critical patient pathway decision point.

There is a risk that an **inconclusive** ECG result might be incorrectly interpreted as 'Normal' or indicating an absence of pathology, instead of being recognized as 'Not Detectable' by ECG.

Similarly the risk for **BNP**, as obesity contributes to insensitivity of BNP, there is a risk of mistaking insensitivity for "Normal".

Both, increasing the risk of **failure to diagnose**.

For lack of a suitable medical device for use in Primary Care, an opportunity for the early detection of CVD, Heart Failure and Valve disease, is missed.

Cardio-HART can address these unmet needs.

		1	Heart	Failur	e Map				ECG Fin	dings		
70	70 Normal Mil		Aild Moderate				Severe		Rhythm	Atrial Fibrillation		
65-									Premature Beats	Prem. Atrial C. (PAC)		
60								EF.	PR interval	Uninterpretable		
			/		2	*		H	QT interval	Normal		
155-		/		LVE	EF%=5	6			Axis Deviation	Normal		
50				HFS	sc=7.4			— 出	Rwave Abnormality	Absence		
45			/					Fmr	QRS Voltage	Normal		
40								_ <u>+</u>	B. Branch Block	Absence		
35 -								E E	Fascicular Block	Absence		
30								I	ST-T deviation	ST-T deviation		
0	1 3	2 3 Es	4 stimat	5 ed Hi	67 Esco	8 re	9	10	Ventr. Hypertrophy Crit.	Absence		
									Atrial Abnormality Crit.	Absence		
Algorithm	LVH	LAE	WMA	DDIM	AS	PH	AFib	Score	ECG Signal Quality	Good Quality		
HE score	+0	+15	+13	+0	+0	+ 0	+46	= 7.4	ECG Summary	Abnormal ECG		

ECHO for Primary Care!

Cardio-HART^(tm) (a.k.a. "CHART") is a breakthrough technology that combines the diagnostic capabilities of **3 MEDICAL DEVICES**:

- 1) an AI reported 12 Lead ECG;
- 2) an eStethoscope; and,
- 3) an Echocardiogram.

Using novel **bio-signals** powered by **AI**, CHART can predict **14 significant cardiac abnormalities**, typically diagnosed only by **Echocardiography**.



HART Findings						
LV Hypertrophy	Absent					
Dilated Cardiomyopathy	Absent					
RV Enlargement	Absent					
LA Enlargement	Mild					
RA Enlargement	Absent					
LV Wall Motion Abn.	Mild					
LV Systolic Dysfunction	Absent					
Impaired Relaxation	Absent					
AV Stenosis	Absent					
MV Stenosis	Absent					
AV Insufficiency	Absent					
MV Insufficiency	Abnormal					
TV Insufficiency	Abnormal					
Pulm. Hypertension	Absent					

CHART covers ~93% of all common heart diseases, and its severity, including: Heart Failure (HFpEF, HFmrEF or HFrEF), and related structural (atrial and ventricular enlargement), functional (systolic and diastolic dysfunction), and Valve abnormalities (stenosis or regurgitation), reported as HART Findings.

Significantly, CHART can detect the early onset of heart disease.

Notably, CHART's findings are disease equivalent to **Echo-findings**.

HART Findings are disease equivalent to Echo-Findings



Quick, Non-invasive Immediate results

CHART's AI allows it to reach significantly **higher sensitivity and specificity for most common diseases**, clinically validated to **reduce false positives and false negatives** (Calcagno, S. et al., 2022)³. Validation study results confirm CHART's capability for the early detection of heart disease, in Primary Care.

CHART is quick, non-invasive and gives immediate results. Significantly, it does not require specialist input in carrying out the investigation and does not require specialist reporting.

CHART is Echo for any clinical setting when echocardiography is not available, but needed.

The Care Pathway

CHART is a direct replacement for 12-Lead ECG In clinical care settings and pathways. But CHART is far more... Not only does it provide all the same capabilities of an AI reporting ECG, in addition CHART also provides all the same capabilities of an AI reporting Echocardiograph. No changes to clinical workflows or standard of care.

Similarly to Echocardiography, CHART provides the evidence of the **structural and functional abnormalities of CVD**, as typically diagnosed only by Echocardiography. **CVD Findings** typically diagnosed only by **Echo**

Why?

Because HART Findings are disease equivalent to Echo-Findings.

Priority based on Severity & Urgency Similarly, to Echo-findings, HART findings provides information on disease severity, including Normal, Mild, Moderate and Severe Abnormal conditions. Critical to early detection, is the Mild condition, a digital bio-marker of early onset of heart disease. Treated early, through various pharmacological treatments available in Primary Care, disease progression could be quickly stabilized.

Early detection, means treatments are not only more effective, but more affordable. As much preventative as treatment.

Not only does it provide the same capabilities of an **AI reporting ECG**, in addition CHART also provides the same capabilities of an **AI reporting Echocardiograph**. No changes to clinical workflows or standard of care.



When Echocardiography is not available

In other secondary care settings, there is an ongoing, even urgent need to **reduce cardiac risks**, provide early indications of cardiac disease or its progression, and critically, detect cardiac-related comorbidities that may arise from the primary condition afflicting the patient, as only **Echocardiography can provide**.

But Echocardiography services are stretched thin, unable to respond to all but the most urgent of needs, even then.

Routine or frequent Echocardiography testing, a pipe dream, as already Echocardiography and Cardiology services are seriously overstretched, **backlogged with long wait-lists**.

CHART's unique capabilities can provide routine, frequent, and regular access to substantially equivalent Echocardiography capabilities, bundled in a test as easy as ECG.

Whether early detection, tracking disease progression, or at the very least, helping identify and triage urgent cases critically in need of Echocardiographic confirmation, that would otherwise go unnoticed.

CHART can address the unmet need for regular echocardiography services, when and where they are not available. Anywhere, Anytime, Echo capabilities are needed.

Secondary care uses include:

- Cardiac Oncology, for detecting early heart disease onset between radiation treatments;
- Pre-Surgery, where CHART's negative predictive value (NPV) means certainty that there are no heart related risks that might threaten the surgery;
- Emergency Department, to immediately triage whether the emergency is heart related or non-heart related, such as gastritis, keeping patients on the wrong treatment pathway can be very costly;
- Respiratory Care, for tracking COPD related cardiac co-morbidities with regular testing, including detecting early onset of heart problems resulting from respiratory disease, and, in the opposite case, able to indicate an unknown-early pulmonary problem through it's right heart related findings, and
- **Cardiology**, where it could provide daily "Echo-reports" for every patient in the ward, in lieu of the daily ECG, and much more...



The use of **CHART streamlines healthcare**, addressing many systemic inefficiencies, releasing their related costs for use elsewhere.

In **Primary Care**, savings in the hundred's of millions could be realized, over the next 10 years.

The Facts

Cardio-HART^(TM) is **CE Certified** | MHRA registered.

Cardio-HART carries **Medical Liability Insurance for the UK and the EU.** In the UK, it is registered with **NHS as DHMIA/2227/21.**

The Cardio-TriTest^(TM) device is made in the UK.

Current Usage

CHART is in use in select sites within the **NHS**, in adoption trials.

In EU, Portugal as part of a formal Clinical trial, and in clinical use in Spain, Italy & Denmark.

Evidence to date

A formal **Clinical Study** designed with the assistance of the **FDA**, proved that CHART was able to reduce both false positive and false negative referral decisions. The study compared referrals decisions for 550 patients.

GP using **CHART reduced false positive by 5%, and false negative by 15.8**% compared to GP using AI reporting ECG. In addition, GP's using **CHART increased positive diagnostic rate from 8.5% to 26.7%, uncertainty decreased from 24% to 1.7%**[4]

Poincare Plot 1.5 1.4 Other records urrent record 1.3 1.2 1.1 RR(i+1) 8.0 8.0 0.7 0.6 0.5 0.4 0.3 -0 RR(i 0.6 0.7

Clinically proven to reduce FP and FN.

Al significantly **increases** sensitivity and specificity.

HART-findings performance was estimated using clinically validated data that also included a dataset of ten's of thousands of patient recordings collected over 8 years, where the ground truth was Echocardiography based, as established by 5 cardiologists randomly selected to reduce bias, per recording, in consensus.

The **sensitivity of Heart Failure** prediction by HART-model is significantly increased **compared to the best ECG- finding criteria:**

- sensitivity jumps from 53% to 83%,
- specificity jumps from 85% to 87%, and
- positive predictive value (PPV) jumps from 57% to 70%.

CHART Advantage – Starts on Day 1!

Presentation to Primary Care

CHART's advantage starts on initial patient presentation to **Primary Care**.

On signs or suspicion of **CVD**, **Heart Failure or Valve disease**, clinician orders a CHART test.

A nurse immediately conducts, in-clinic, the non-invasive test, and **~15 minutes** later, the **CHART report** is available to the clinician.

The CHART report will assist the clinician understand the patient's overall cardiac status, reporting on a long list of co-morbidities and related common heart diseases and their condition/severity. The report will also indicate whether **Heart Failure** should be considered, including whether a BNP test should be considered.

If **Heart Failure** is diagnosed, the standard of care requires immediate referral to Echocardiography for determination of whether Valve disease is present, as when both are present, together there is an increased risk of sudden cardiac death. **Valve disease** is typically present in 60% of all instances of Heart Failure.







With **CHART**, **Valve disease** is part of the report, including **Aortic and Mitral (Stenosis and Regurgitation) (AS, MS, AR, MR), and Tricuspid Valve Regurgitation (TR), with or without pulmonary hypertension (PH).** Pulmonary valve is reported indirectly⁵.

As the **Positive Predictive Value (PPV)** is clinically meaningful, patient pathway can be **immediately determined**, with an appropriate priority based on urgency and severity to the next level of care, as appropriate.

CHART also helps the clinician determine whether a patient can safely remain and be treated in a Primary Care setting. With strong diagnostic evidence at hand, clinicians can **confidently initiate treatment**, e.g. standard disease modifying therapies for Heart Failure, reducing morbidity, slowing disease progression.

Similarly the CHART report that shows no pathology present.

CHART's Negative Predictive Value (NPV) is 99%, a clinician can be quite certain heart disease is not present.

Confidently Initiate Treatment

Referred to Secondary Care

A **CHART** welcome examination on initial patient presentation to secondary care, can help identify whether the patient is a **Negative**, not in need of an echocardiography examination, thereby **saving specialist time and associated costs**.

If **Positive**, the CHART report provides other advantages, such as identifying indications that might not have been included in the original

ECG GIODAI Measu	i ements		virtue	al Scale	
Heart Rate [bpm]	72	20	50	100	200
median RR [s]	0.86	0.3	0.6	1.3	3
RR std [ms]	223		0	100	1000
RMSSD [ms]	305		0	100	1000
PNN50 [%]	87		0	55	100
LF/HF (0.15Hz)	1.2	0	0.5	6	
QRS axis [deg]	-29	-180	-90-30	90	180
PQ interval [ms]	304	50	120	225	360
PRc (Soliman) [ms]	304	50	120	225	500
P interval [ms]	116	0	70	150	200
Paxis [deg]	-38	-180	0	85	180
P term.force [mVms]	0.18			6	15
QT interval [ms]	370	220	310	500	600
QTc (fram)	392	300	350	470	550
QTc-CHART	372	300	350	470	55
J⊺c	298	200	250	370	45
QRS interval [ms]	94		0	120	20
VAT	42		0	50	10
ST interval [ms]	80	0	50	170	30
ST axis [deg]	-53	-180	-30	105	18
Taxis [deg]	142	-180	-15	105	18
Rsum (V1:V6) [uV]	1366	0	2300	8500	1200
Sok-Lyon [mV]	2.2		0	4.6	15
Cornell Volt [mV]	1.4		0	2.8	1
Lewis index [mV]	1.7		0	17	3
LVH Score	501		0	500	1500
RVH Score	3.4		0	34	6

Ischemic ST-T	Non-extensive
Non-SIEMI	Borderline
STEMI	Absent
	Extensive

Туре	Location:	Ant	Inf	Lat	Pos	Sep
Ischemic ST-T	Moderate	*	*	*		*
Non-STEMI	Mild	*	*	*		*
STEMI	Absent					
Old MI	Mild	*				*

referral, including whether **Heart Failure, Valve disease, Myocardial Infarction (MI)**, are present or suspected prior to the Echo examination.

Critically and likely the most important benefit, the **CHART report** provides a "big-picture" **view of all of the co-morbidities** for this patient.

The big-picture, was clinically proven to help the specialist focus the **Echo examination**, reducing the time required to conduct it and reducing the potential of missed pathologies.

Missed diagnoses, leads to follow-up visits or to even costlier admission to hospital.

Missed diagnoses, allow disease progression to continue, putting the patient at increasing risk.

CHART addresses this unmet need.

Secondary Care, other hospital settings.

In other Secondary care settings, when Echo is not available, **Cardio-HART can provide highly relevant clinical information, disease equivalent to Echocardiography**, leading to more rapid access to further diagnostics and treatment as needed.



Unlike, CHART...

ECG

- Unlike ECG, CHART, can detect early onset of Heart Disease (CVD)
- Unlike ECG, CHART can detect ~93% of most common heart diseases, unlike ECG at only 44%
- Unlike ECG, CHART can detect 14 Echo-findings, typically only diagnosed using Echocardiography
- Unlike ECG, CHART provides HART findings that are disease equivalent to Echo-Findings
- Unlike ECG, CHART can detect Valve disease
- Unlike ECG, CHART can detect heart sounds, murmurs...
- Unlike ECG, CHART can detect the presence and absence of Heart Failure
- Unlike ECG, CHART can provide the structural and functional characteristics that define Heart Failure
- Unlike ECG, CHART can distinguish Heart Failure by phenotype, HFpEF, HFmrEF or HFrEF
- Unlike ECG, CHART considers the patients body size and body mass index (BMI), to provide more individual results
- Unlike ECG, CHART can estimate of LVEF
- Unlike ECG, CHART can provide the priority based on urgency and severity of CVD
- Unlike ECG, CHART's AI allows it to reach significantly higher sensitivity and specificity for most common heart diseases

BNP

- Unlike BNP, CHART test can be done immediately on patient presentation to Primary Care
- Unlike BNP, CHART test does not require to be done in an off-site lab, requiring a referral
- Unlike BNP, CHART provides immediate results, no need to wait weeks for lab-results

- Unlike BNP, CHART can provide the structural and functional characteristics that define Heart Failure
- Unlike BNP, CHART can distinguish Heart Failure by its 3 phenotype, HFpEF, HFmrEF, and HFrEF
- Unlike BNP, CHART can provide the priority based on urgency and severity of Heart Failure
- Unlike BNP, CHART does not have insensitivity to a sub-group of patients, with special reference to obesity, that can skew the results
- Unlike BNP, CHART can be the primary method of diagnosis of HF, BNP useful for confirming borderline cases in particular

Echo

- Unlike ECHO, CHART is indicated for use in Primary Care settings
- Unlike ECHO, CHART does not require specialist to conduct of an investigation
- Unlike ECHO, CHART does not require specialist reporting
- Unlike ECHO, CHART testing can be routinely and frequently performed, as easily as ECG
- Unlike ECHO, CHART is quick, provides immediate results
- Unlike ECHO, CHART can be used anywhere anytime echocardiography findings are required, but not available

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