Evaluation of a diagnostic pathway in heart failure in primary care, using electrocardiography and brain natriuretic peptide guided echocardiography

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Material and methods

Subjects

Between January 2010 and February 2011, 314 patients from primary care practices in the city of Glasgow, Scotland participated in the study. The median follow up time was 286.50 days (IQR: 157–371) minimum 52 days and maximum 474 days.

Patients attending their general practitioner (GP) with breathlessness of suspected cardiac cause, atrial fibrillation (AF) proven on ECG or murmur were subjects for the study. The GP completed a referral form including information on indication for referral, past medical history, risk factors and drug history. Patients with LVH on ECG with or without history of hypertension and patients with a prosthetic valve were excluded from referral to the service. Instead GP's were directed to the GGC hypertension guidelines and direct referral to a cardiologist was recommended.

Data from each patient were entered to a Microsoft access file. Clinical Sub Groups of the MCN (managed clinical network) consist of lead and senior cardiac physiologists, consultant cardiologists, cardiac redesign manager and laboratory manager and this group, developed the diagnostic pathway (Figure 1).

Data entered to the database during the pathway

Data entered in the database from the GP form is outline in table 2, followed by data entered from the day of the study in table 3.

Table 2. Data entered to the database.

General information	Name, surname, Community Health Index (CHI) number (a unique health care system identifier for all residents of Scotland), date of birth and date of referral.
Indication of referral	Clinical suspicion of heart failure, paroxysmal nocturnal dyspnoea, dyspnoea on exertion, dyspnoea at rest, orthopnoea or ankle oedema.
Blood test results	Haemoglobin and creatinine values and dates when these tests were performed.
Information on previous medical history	Myocardial infarction, unstable angina, angina, coronary artery bypass graft (CABG), percutaneous transluminal coronary angioplasty (PTCA), valve disease, valve surgery, atrial fibrillation, hypertension, chronic obstructive pulmonary disease (COPD) and asthma.
Previously seen by cardiologist	If and if so the date and hospital was noted.
Drug history	Thiazide diuretic, loop diuretic, combination diuretic, beta blocker, angiotensin converting enzyme inhibitor, angiotensin receptor blocker, spironolactone / eplerenone, digoxin, calcium channel blockers and/or antiarrhythmics.
Information on previous echocardiography,	Date, hospital and result.
Recording of echo results	Left ventricular systolic dysfunction and if mild, mild to moderate, moderate, moderate to severe, severe or not recorded.

Table 3. Data entered from the day of the study

Day of attendant	Date and if the patient attended or did not attend
EKG results	Normal, branch block, Q-waves, left ventricular hypertrophy, atrial fibrillation or other.
BNP test	Preformed or not and result (pg/ml).
Ankle oedema	Ankle oedema or not at referral
Echocardiogram	If preformed or not indicated
Referral from this point	Back to the general practitioner or to a cardiologist and if that was the case, the date of return to the cardiology clinic.

Further data collection

The database was collected and transformed into a excel file for further cleaning of the dataset. Further data listed in table 4 was collected to supplement the database. The echocardiography database at the Victoria Infirmary was searched for previous echocardiography results and these were also reviewed in the same manner described above.

Table 4. Additional information added to the database

Blood sample tests	Haemoglobin, platelets, urea, estimated glomeration filtration rate, TSH/T4, potassium, creatinine and the date of the test for those with missing values
Appointments	Cardiology appointments, respiratory appointments, the dates they were planned and whether or not the patient attended
Deceased	Yes or no
Echocardiography measurements	Ejection fraction, left ventricular hypertrophy (LVH), E/E' ratio, left ventricular end diastolic diameter (LVEDD), left ventricular systolic dysfunction (LVSD).
	Valve disease e.g. mitral stenosis, mitral regurgitation, tricuspid stenosis, tricuspid regurgitation, aortic stenosis and aortic regurgitation. Valve disease were classified in to mild, mild to moderate, moderate, moderate to severe and severe.
	Other findings on echocardiography were classified into *other* with a clarifying comment box attached to it e.g. moderate, moderate to severe and severe pulmonary oedema, bi-atrial dilatation, significant LV systolic impairment without LVSD and/or infarctions

Blood sample test was collected from the laboratory database. Information on appointments and if the patient had deceased were collected from hospital and primary care database. Echocardiography measurements were found in echocardiography reports from the Victoria hospital echocardiography database.

The pathway was designed to detect functional impairment of the heart in those with signs and symptoms of heart failure so that a diagnosis of HF could be made and then appropriate treatment started. HF is commonly due to LVSD and whilst HF with preserved ejection fraction does exist no effective treatments for it exist and its definition is debatable.

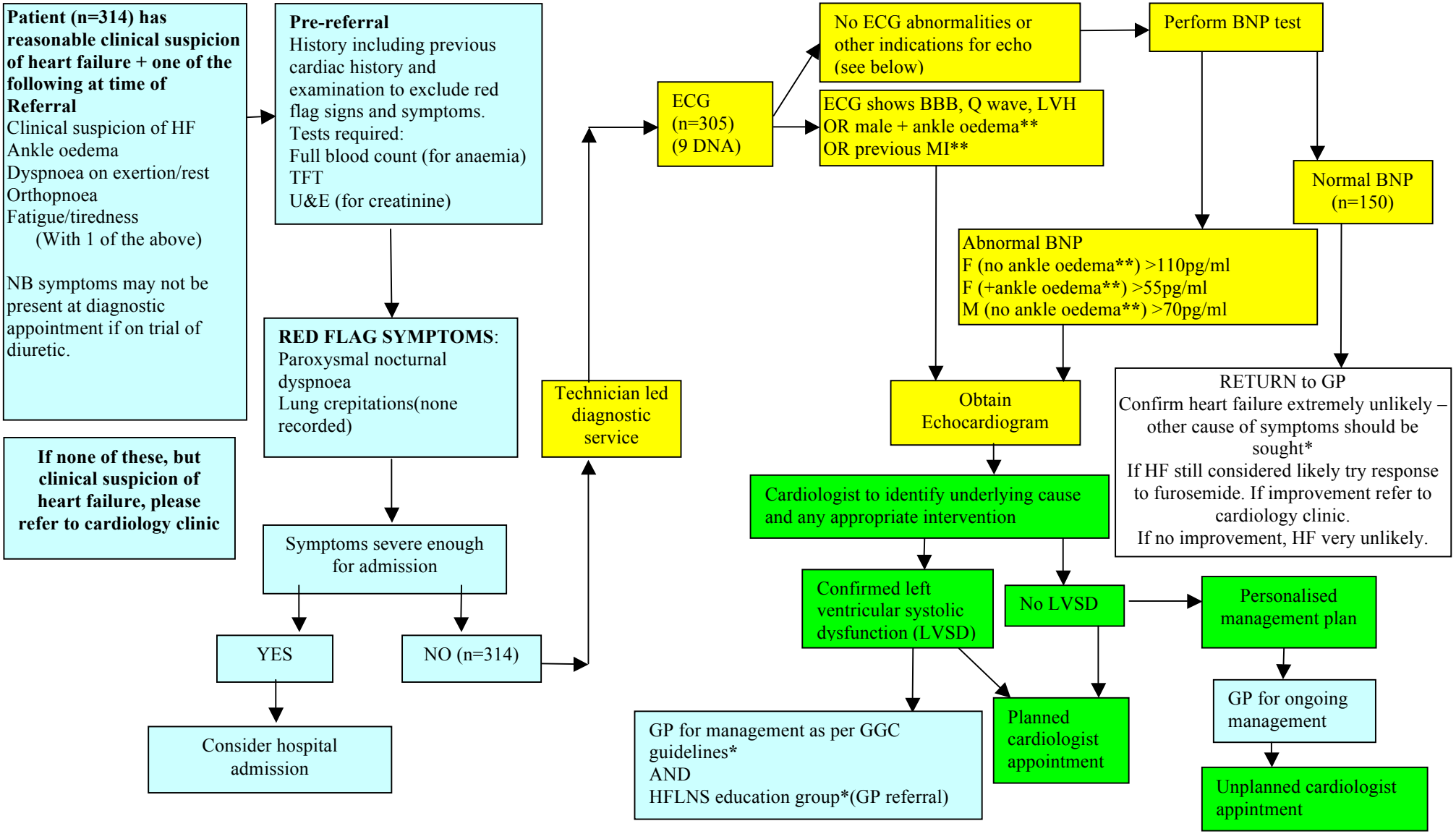

Figure 1: Suspected NEW Heart Failure Patient Diagnostic Pathway

O=GP **O**=cardiac physiologist **O**=cardiologist *=standard letter **=info from referral form

Abbreviations: LVSD; left ventricular systolic dysfunction, BBB; bundle branch block, LVH; left ventricular hypertrophy, GP; general practitioner, MI; myocardial infarction, HFLNS; Heart Failu Liaison Nurse Service, GGC; Greater Glasgow Clyde, TFT; Thyroid Function Test, U&E; Urea and electrolytes, CXR; Chest X-Ray, BNP; B-Type Natriuretic Peptide, DNA; did not attend

Study design

GPs were informed of the pilot via a letter from the MCN (Appendix 1).The Victoria Infirmary in Glasgow was chosen as the pilot site as it has a high number of GP Direct Access echocardiogram referrals. A senior physiologist held an educational meeting with all staff involved to explain and discuss the pathway. An Information sheet was developed to inform patients of the need to assess their symptoms via ECG and BNP (Appendix 2). Patients with an abnormal ECG had echocardiography carried out at the same visit, and those with normal ECG had an additional BNP measurement to determine if the patient needed same day echocardiography examination. A standard letter to GPs was agreed and sent out for the patients where and echocardiogram was not indicated (Appendix 3). All echocardiograms were reviewed by a consultant cardiologist and triaged to various recommendations at the end of the pathway or a cardiology outpatient appointment. Physiology staff collected the information on an access database supported by clinical effectiveness staff.

A retrospective study was performed on the existing database which held information on all patients who proceeded through the pathway. The movement of all patients through the pathway were studied.

There were currently five outcomes possible for the patients in the pathway:

1. Abnormal ECG/male and ankle oedema/previous MI and then echocardiography
2. Abnormal BNP and then echocardiography
3. Normal ECG and BNP and discharge back to GP
4. Did not attend or did not complete the pathway

Investigations

Electrocardiography (ECG)

All patients referred were triaged using an ECG performed by a special trained nurse with the pre-programmed computer interpretation. Patients with an abnormal ECG, males with ankle oedema and those with a myocardial infarction during the last year, proceeded straight to echocardiography. Those with normal results proceeded to BNP testing.

The machine used for ECGs was a GE MAC 5500 machine (General Electric, New York, USA). ECGs were considered abnormal if left bundle branch block (LBBB), atrial

fibrillation (AF), Q waves or left ventricular hypertrophy (LVH) were found. There was also an "other" category where other abnormalities were entered.

Brain natriuretic peptide (BNP)

BNP tests were performed on those patients referred from the GP who had a normal ECG or none of the other indications for echocardiography described above. Blood was taken immediately after the ECG test and sent directly to the laboratory for analysis.

Those with an abnormal BNP test continued on to a same day echocardiogram and the remainder (normal ECG and normal BNP) were referred back to their GPs with heart failure being an unlikely cause of their symptoms. The cut off values of BNP used to determine a normal value were decided by a group of cardiologists involved in the MCN after review of the literature. BNP was considered to be abnormal if:

Female without ankle oedema >110 pg/ml

Female with ankle oedema >55 pg/ml

Male with no ankle oedema >70 pg/ml

Patients with BNP result less than or equal to ten were set to a BNP result of ten when performing the statistics.

Echocardiography

Echocardiography was performed in patients with abnormal ECG (LBBB, LVH, AF), abnormal BNP test or based on referral symptoms and history (male plus ankle oedema or previous MI). A GE VIVID 7 echocardiography machine with a M4S probe, (Greenbrier, Tennessee, USA) was used. The left ventricular ejection fraction was measured using Simpson's biplane method wherever possible. Otherwise a subjective assessment of the left ventricular function was made by the echocardiographer who was an experienced technician. All echocardiogram results were reviewed by a cardiologist. The cardiologist was not blinded to the BNP result, in the cases where this test was performed. In case of normal echocardiography results the patient was referred back to the GP in the search for alternative cause of symptoms. If the echocardiography result was abnormal a cardiologist appointment was arranged. LVSD was divided according to local guidelines based on the ejection fraction (table 5):

Table 5. Cut offs used to categorise left ventricular function

Left ventricular function/	EF (%)
Hyper dynamic left ventricular function	>75
Normal left ventricular function	55-75
Mild LVSD	40-55
Mild – moderate LVSD	35-40
Moderate LVSD	30-35
Moderate – severe LVSD	25-30
Severe LVSD	<25

EF; ejection fraction, LVSD; left ventricular systolic dysfunction

Statistic methods and analysis

Continuous variables were compared using t-tests for independent samples (2-tailed). Proportions were compared using the Pearson Chi-Square test and where the assumptions of the test were violated, the Fisher's exact test (2-sided). A P-value <0.05 was used to indicate statistical significance. All analyses were conducted using SPSS version 18.0.

Missing data

Age was calculated as the date of birth minus date of referral. If the information on date of referral was missing in the database the date of attendance was used. If the date of referral was missing and the patient did not attend, the date of referral was set to 01/01/2011 to be able to calculate the patient's age. Estimated glomerular filtration rate was recorded as >60 mL/min or the actual value if under this. Those individuals with an estimated glomerular filtration rate of >60 were designated as having a value of 60.

Ethical considerations

The evaluation was approved by the audit sub-committee of the Glasgow MCN in heart disease. No further ethical approval is required for the current study as it involves the analysis of secondary fully anonymous data for the purposes of the evaluation of a clinical service.

Results

Subjects

Patients were referred to the diagnostic pathway for various reasons outlined in Figure 2, mostly for a clinical suspicion of heart failure. Only one person was admitted with the red flag symptom of paroxysmal nocturnal dyspnoea and none of the patients attending the pathway had symptoms severe enough for direct admission to hospital. Two patients, one patient attending the pathway with pericardial and pleural fluid and one with gross ankle oedema, had severe LVSD on echocardiogram investigation and were admitted to the Victoria Infirmary. One patient attending the pathway was incorrectly referred having dilated cardiomyopathy previously and was sent back to their GP after echocardiography.

The mean age of the participants was 69.61 (SD 11.8), and the median was 71 years (IQR 62-78). Mean age was slightly higher in patients with abnormal ECG and BNP, 73 years (SD 10) and 73 years (SD 11) respectively, and in the group of patients with left ventricular systolic dysfunction the mean age was 72 years (SD 10). Of all attendees 132 (42%) were male and 182 (58%) were female. Six patients died during follow up, three of which did not have an echocardiogram and three which had. One of the deceased had confirmed left ventricular systolic dysfunction.

Of the 231 who had a normal ECG, 32 were also male with ankle oedema or had had a previous myocardial infarction. Of the 199 patients with a normal ECG, 190 had a BNP test. In addition 28 from the group with an abnormal ECG or males with ankle oedema or previous myocardial infarction and 8 from the group with “other” abnormalities on ECG had a BNP test. Therefore, some patients are counted more than once in the flowchart. 150 (49.2%) patients had normal ECG testing and normal BNP. Most of them were discharged back to their GP for alternative cause of symptoms (Figure 2).

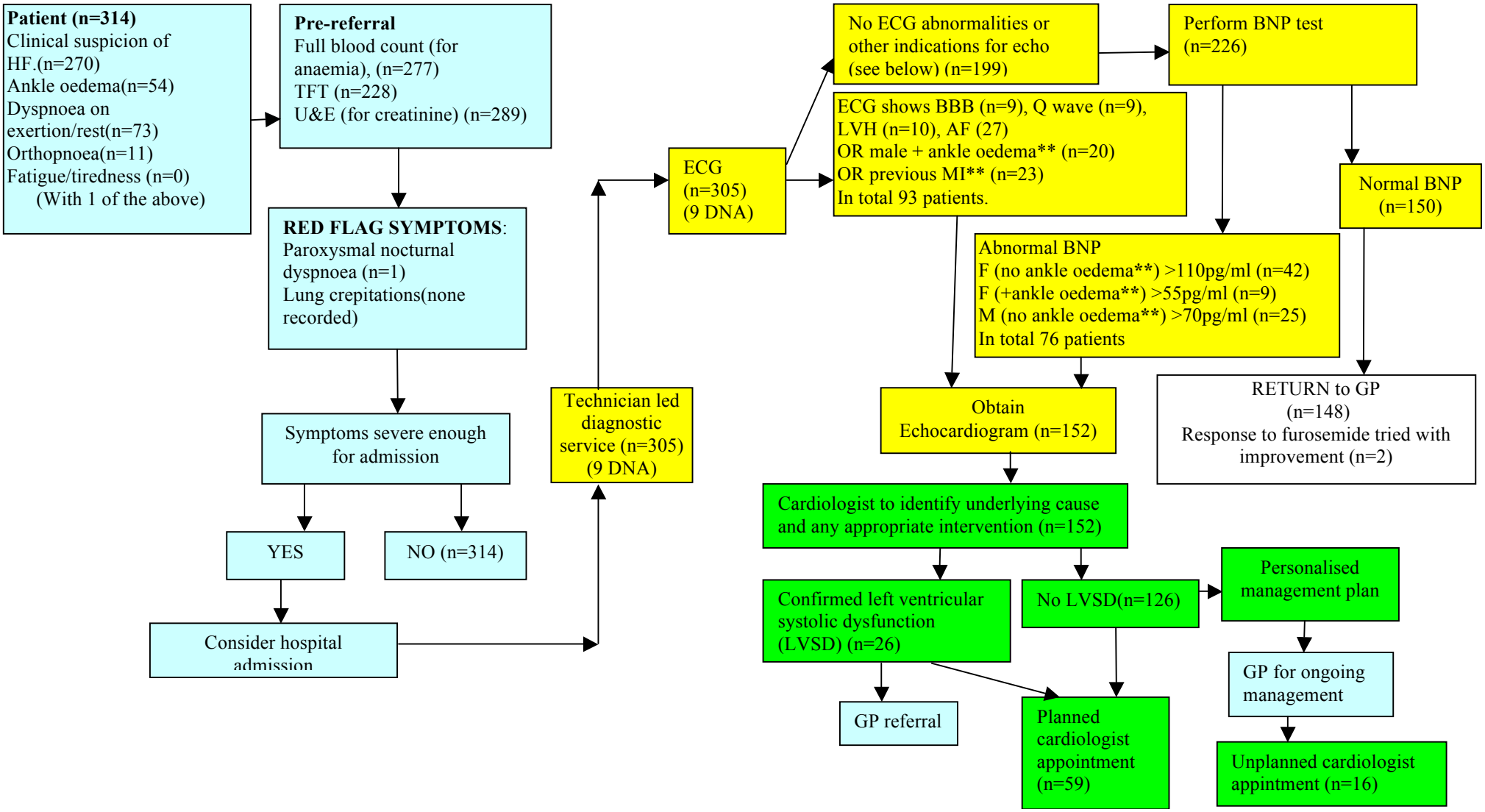

Figure 2: Suspected NEW Heart Failure Patient Diagnostic Pathway

O=GP O=cardiac physiologist O=cardiologist *=standard letter **=info from referral form

28 from the group with an abnormal ECG or males with ankle oedema or previous myocardial infarction and 8 from the group with "other" abnormalities on ECG had a BNP test.

Abbreviations: LVSD; left ventricular systolic dysfunction, BBB; bundle branch block, LVH; left ventricular hypertrophy, GP; general practitioner, MI; myocardial infarction, HFLNS; Heart Fail Nurse Service, GGC; Greater Glasgow Clyde, TFT; Thyroid Function Test, U&E; Urea and electrolytes, CXR; Chest X-Ray, BNP; B-Type Natriuretic Peptide, DNA; did not attend

Investigations

ECG

Of the 314 patients referred to the diagnostic pathway, 305 attended to have an ECG performed. Comparisons between patients with normal and abnormal ECG findings or other symptoms that required echocardiography can be found in Table 6. Patients with an abnormal ECG or other symptoms that required echocardiography were more likely to a history of coronary revascularisation and be receiving a beta blocker or ACE inhibitor reflecting the fact that this group included those with a history of MI.

On referral 7 patients had known atrial fibrillation, whereas an additional 19 were found to be in atrial fibrillation after the initial ECG. After ECG, these patients proceeded to echocardiography or BNP testing on the basis of the results and clinical features as described above in Figure 2. The disposition of the patients is outlined in figure 3.

Table 6. Baseline characteristics of participants with normal compared to abnormal ECG.
For extended version see appendix 4.

		ECG n (%)		
		Normal 199 (65.2)	Abnormal ECG or Male with ankle oedema or previous MI 93 (30.5)	P-value
Age	Mean (SD)	68 (12)	73 (10)	
	Median (IQR)	70 (60-78)	74 (65-81)	
Gender	Male	64 (32.2)	59 (63.4)	
	Female	65 (32.2)	34 (36.6)	<0.0001
Indication for referral				
Dyspnoea on exertion		32 (16.1)	24 (25.8)	0.049
Dyspnoea at rest		6 (3.0)	8 (8.6)	0.037
Ankle oedema		21 (10.6)	32 (34.4)	<0.0001
Previous medical history				
MI		0	35 (37.6)	<0.0001
Unstable angina		0	2 (2.2)	0.038
Angina symptoms		12 (6.0)	19 (20.4)	<0.0001
CABG		7 (3.5)	14 (15.1)	<0.0001
PTCA		1 (0.5)	9 (9.7)	<0.0001
Previous valve surgery		0	0	
Atrial fibrillation		1 (0.5)	6 (6.5)	0.002
COPD		24 (12.1)	9 (9.7)	0.549
Asthma		10 (5.0)	2 (2.2)	0.249
Drug history				
Beta blocker		27 (13.6)	35 (37.6)	<0.0001
ACE I		39 (19.6)	42 (45.2)	<0.0001
ARA		0	1 (1.1)	0.143
Digoxin		1 (0.5)	6 (6.5)	0.002
CCB		42 (21.1)	29 (31.2)	0.061

Abbreviations', HF, heart failure; PND, paroxysmal nocturnal dyspnoea; MI, myocardial infarction; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty; COPD, chronic obstructive pulmonary disease; ACE I, Angiotensin converting enzyme inhibitor; ARA, Aldosterone antagonist; CCB, calcium channel blocker

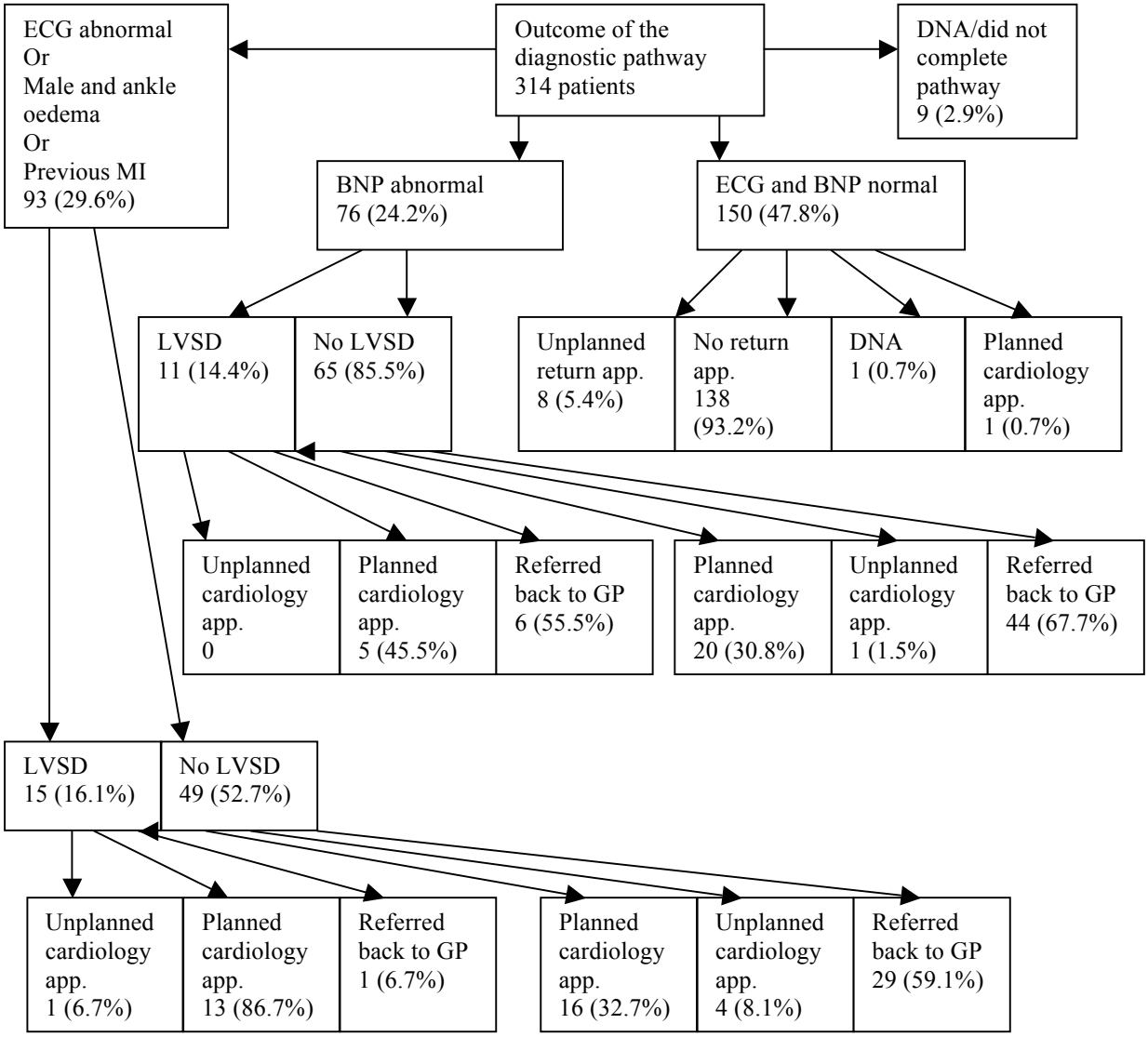

Figure 3 Summary of patient disposition.
MI; myocardial infarction, GP; general practitioner, LVSD; left ventricular systolic dysfunction, DNA; did not attend, app.; appointment

BNP

Patients without ECG abnormalities or other indications for echocardiography (males with ankle oedema or previous MI) proceeded to BNP testing. A normal BNP level was found in 150 patients and they were referred back to their GP. Of the male participants 25 (8%) had an abnormal BNP test, i.e. > 70 pg/ml, 42 women (13.4%), had a BNP value above 110 pg/ml and 9 women (2.9%) had ankle oedema and a BNP value above 55 pg/ml. The mean and median BNP levels in the patients who underwent BNP testing are outlined in Table 7.

Table 7. Results of BNP tests (pg/ml)

	All n=226 (72%)	**Men, n=78 (35%)**	**Women, n=148 (65%)**
Mean (SD)	127.30 (SD 290.156)	114.13 (SD 268.569)	134.24 (SD 301.564)
Median (IQR)	57 (32 - 125)	46 (22 – 133.25)	65.5 (36 – 120.75)

SD=; Standard deviation IQR= interquartile range

Patients with BNP results ≤10 were set to have a BNP result of 10. As it can be seen from Figure 4 the distribution of BNP levels was skewed. A BNP test value of 10 pg/ml or less were found in 14 patients (4.5%), and in 4 patients (1.3%) levels were ≥ 1000 pg/ml. Comparisons between patients with normal and abnormal BNP measurements can be found in Table 7. A history compatible with coronary disease (e.g. angina and previous revascularisation) were associated with having an abnormal BNP. The dispositions of patients with an abnormal BNP are shown in Figure 3.

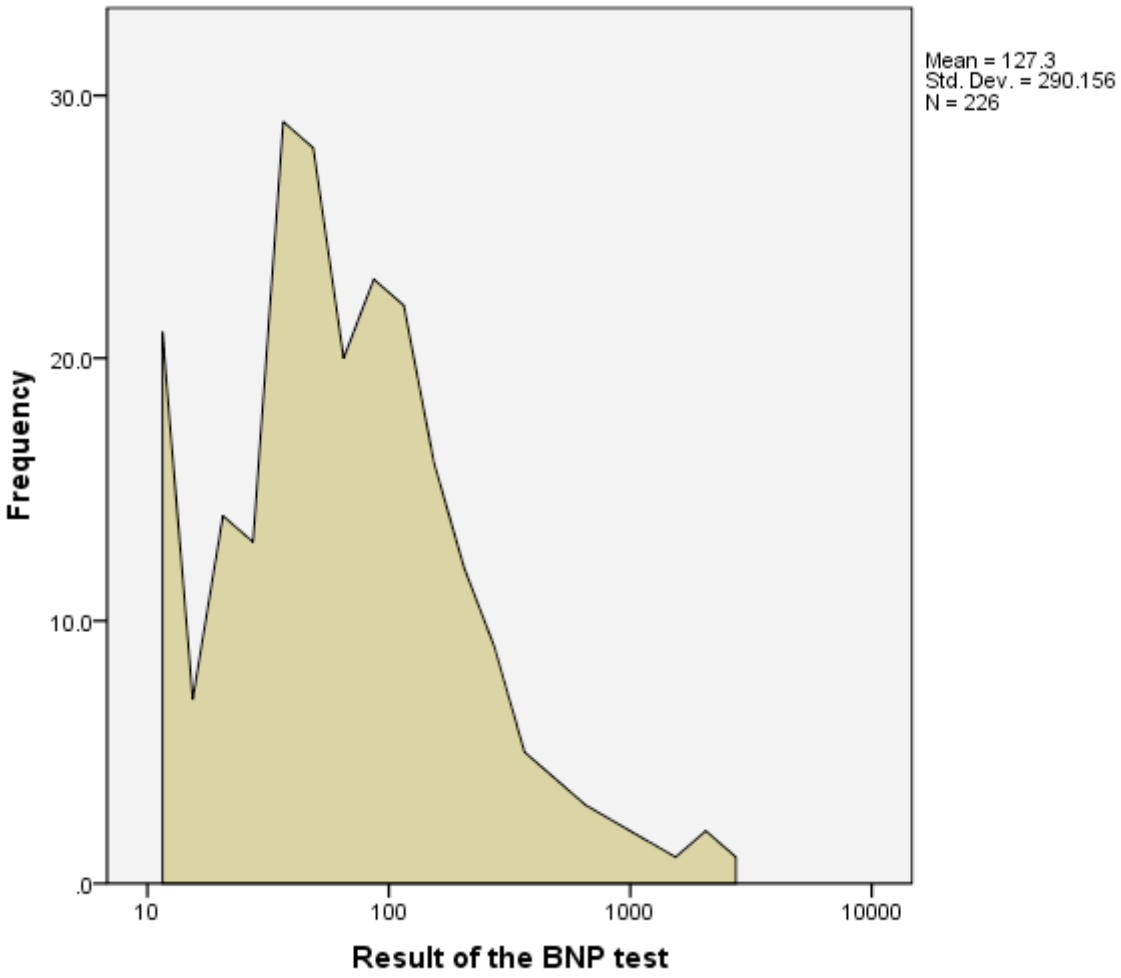

Figure 4. Histogram of the 226 brain natriuretic peptide (BNP) results with logarithmic x-axis. Positively skewed distribution of the BNP level in patients referred to the pathway. BNP was measured in pg/ml.

Table 7. Baseline characteristics of participants with normal compared to abnormal BNP levels.
For extended version see appendix 5.

		BNP n (%)		
		Abnormal 76 (33.6)	Normal 150 (66.4)	P-value
Age	Mean (SD)	73 (11)	66 (12)	
	Median (IQR)	76 (63-82)	67 (58-75)	
Gender	Male	26 (33.8)	53 (35.8)	
	Female	51 (66.2)	95 (64.2)	<0.0001
Indication for referral				
Dyspnoea at rest		1 (1.3)	4 (2.7)	0.003
Ankle oedema		12 (15.6)	12 (8.1)	<0.0001
Previous medical history				
MI		13 (16.9)	8 (5.4)	0.009
CABG		10 (13.0)	4 (2.7)	0.009
PTCA		2 (2.6)	2 (1.4)	0.027
Atrial fibrillation		0	1 (0.7)	0.001
COPD		8 (10.4)	18 (12.2)	0.741
Asthma		4 (5.2)	6 (4.1)	0.925
Drug history				
Beta blocker		21 (27.3)	13 (8.8)	<0.0001
ACE I		17 (22.1)	31 (20.9)	0.003
ARA		0	0	0.281
Digoxin		0	1 (0.7)	0.003
CCB		16 (20.8)	33 (22.3)	0.598

Abbreviations; HF, heart failure; PND, paroxysmal nocturnal dyspnoea; MI, myocardial infarction; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty; COPD, chronic obstructive pulmonary disease; ACE I, Angiotensin converting enzyme inhibitor; ARB, Angiotensin receptor blocker; ARA, Aldosteron antagonist; CCB, calcium channel blocker

Echocardiography

Of the 305 patients enrolled in this pathway 152 (49.8%) underwent echocardiography and 26 patients (8.5%) had LVSD. A comparison of patients with and without LVSD can be found in Table 8. Those with LVSD were more likely to have a history of MI or valve disease that was at least mild to moderate. One patient who underwent echocardiography had atrial fibrillation that was uncontrolled, therefore measurement of the ejection fraction was not possible and the patient systolic function was not categorized. The cardiologist who reviewed the echocardiogram images diagnosed diastolic dysfunction in seven patients, none of them had additional LVSD.

Table 8. Baseline characteristics of participants with and without left ventricular systolic dysfunction. For extended version see appendix 6.

		Left ventricular systolic dysfunction n (%)		
		No 126 (83.0)	Yes 26 (17.0)	P-value
Age	Mean (SD)	73 (11)	72 (10)	
	Median (IQR)	74 (66-81)	71 (66-79)	
Gender	Male	62 (49.2)	14 (53.8)	
	Female	64 (50.8)	12 (46.2)	0.667
Previous medical history				
MI		18 (14.3)	8 (30.8)	0.042
COPD		13 (10.3)	2 (7.7)	1.000
Asthma		6 (4.8)	1 (3.8)	1.000
Drug history				
ARA		1 (0.8)	0	1.000
CCB		35 (27.8)	6 (23.1)	0.623
Valve disease findings on Echo				
Mitral regurgitation		9 (7.2)	9 (34.6)	<0.0001
Mild to moderate valve disease		4 (3.2)	4 (15.4)	0.03

Abbreviations; HF, heart failure; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; ARA, Aldosterone antagonist; CCB, calcium channel blocker

Outcome following attendance

Nine patients who did not undergo echocardiography were referred to a cardiologist during the period of follow up. The diagnoses made by the cardiologist were as follows: Three patients had cardiovascular disorder unlikely or renal disease, four were diagnosed with new onset angina or chest pain, one patient had obesity and one had respiratory cause of shortness of breath.

Performance of the pathway

As no patients were found to have heart failure at re-attendance at clinic, all 26 cases of heart failure were identified in our pathway (Table 9). This gives a sensitivity of 100% for the period of follow up. Most patients with either ECG or BNP abnormality had normal findings on echocardiography. Therefore, the specificity was 54.3 % and accuracy was 58.3%. The negative predictive value was 100 % and positive predictive value 17.1%. It should be highlighted that these figures only relate to the median follow up period of 286 days and it is unknown whether these values will remain after further follow up.

Table 9. Performance of the pathway

		Echocardiography showing LVSD or return to clinic with heart failure	
		Yes	No
ECG or BNP abnormal	Yes	26	126
	No	0	150

LVSD; left ventricular systolic dysfunction