PLASMA NOREPINEPHRINE IN PATIENTS ADMITTED IN CONGESTIVE HEART FAILURE TO THE KENYATTA NATIONAL HOSPITAL.

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DECLARATION

CANDIDATE:

This thesis is my original work and has not been presented for a degree in any other University.

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SUMMARY

Plasma norepinephrine was assayed in fifty one patients admitted to the Kenyatta National Hospital in congestive heart failure and in a total of thirty normal persons.

It was found that plasma norepinephrine was markedly elevated in patients in congestive heart failure and that the higher the levels were the poorer the functional ability of the patients was. High plasma norepinephrine was also associated with a high mortality.

PLASMA LEVELS OF NOREPINEPHRINE IN PATIENTS ADMITTED TO KENYATTA NATIONAL HOSPITAL WITH CONGESTIVE HEART FAILURE.

INTRODUCTION

The role of sympathetic nervous system in both compensated and decompensated heart failure is not well understood. It is however known that the activity of the sympathetic nervous system is increased in patients with congestive heart failure. The increased activity of the autonomic nervous system in turn leads to release of endogenous norepinephrine which acts on the heart to increase the heart rate and contractility (1, 2, 3, 4, 5, 11, 15). It has also been demonstrated that plasma levels of norepinephrine increase on exercise without alteration in the levels of epinephrine in plasma and urine and this implies that sympathetic beds other than the adrenal medulla are responsible for the increased norepinephrine activity (1, 19, 22, 23, 25, 26).

Biopsy specimens of tissue taken from atrial appendage have in fact been demonstrated to be depleted of norepinephrine stores and this has reasonably been attributed to enhanced release of norepinephrine from nerve endings as a result of stimuli from sympathetic nerves (6,7,8,16,17).

At a cellular level, the combination of norepinephrine and membrane bound cyclic adenosine monophosphate promotes myocardial contractility perhaps by facilitating transmembrane calcium influx (4,5,9.20,23).

Whereas norepinephrine in circulation is derived from the sympathetic nerve endings since the excretion of this catecholamine is not altered after adrenalectomy, it is believed that a considerable amount of it is metabolised before reaching circulation (7). The amount reaching circulation is dependent on a number of factors:

(a) The rate of release.

(b) The density, distribution and width of neuroeffector junction.

At narrow junctions the action of released norepinephrine is mainly terminated by reuptake into the nerve ending and is subsequently deaminated by the enzyme catechol methyl -O- transferase. At wider junctions there is diffusion into sorrounding tissues and early entry into circulation in predominant.

Smooth muscle in the walls of arteries and veins seen to have relatively wide neuromuscular junctions. It seems likely therefore that wide neuromuscular junctions such as those found in the vascular smooth muscle may be a more important source of plasma norepinephrine (7).

Studies done in the recent past indicate that norepinephrine may be used as an indicator of the activity of the sympathetic nervous system since blood norepinephrine levels rise promptly in response to orthostasis and exercise (8).

In the syndrome of heart failure a high level of norepinephrine in the blood in itself has been associated with a high mortality (5, 9, 10,26,27).

Furthermore, therapeutic agents associated with a reduction in blood norepinephrine e.g. captopril have been associated with a marked acute improvement in a failing heart and subsequent mortality has been greatly improved (11, 12). The normal plasma level of norepinephrine appears to vary depending on the assay method used. The normal plasma level is 0.18 ± 0.07 ng/ml when radioimmunoassay method is used (5); it is 0.097 ± 0.21 ng/ml when "High perfomance" liquid chromatography is used (12) and it is 0.58 ± 0.11 ng/ml when a fluorometric procedure is used (13).

In this study a fluorometric procedure is used on both patients and controls.

AIM: To find out if there is any relationship between (i) the plasma level of norepinephrine and the functional grade of failure and (ii) to see if it is also related to subsequent mortality.

MATERIALS AND METHODS

This study is a prospective one covering the period between May 1985 to December 1985. The study was done on patients admitted on the medical wards of Kenyatta National Hospital because of congestive heart failure. Most of the patients were admitted via the casualty department either as referrals from Provincial Hospitals of this country because of refractory congestive heart failure or as known cardiac patients who had gone into decompensation. A few patients were admitted as newly diagnosed cardiac patients who had gone into decompensation because of valvular lesions resulting from rheumatic fever. All admitted patients were eligible for admission into the study irrespective of age.

The controls were healthy adults accompanying the patients and blood donors at the out-patient department. Prior to venepuncture the donor was rested on a couch and examined to rule out any cardiovascular disease. The age, heart rate and blood pressure were noted. A verbal consent was obtained before blood was taken in both cases of controls and patients.

For the patients on the ward, their history was taken and the following symptoms were asked for

1. Dyspnoea on exertion
2. Palpitations
3. Fatique
4. Angina

It was also recorded as to whether these symptoms occurred at rest, during ordinary or less than ordinary exercise. By using these symptoms it was possible to classify the patients functional limitation in accordance with the New York Heart Association classification (appendix II (14).

The patients were then examined by the author for evidence of congestive heart failure. (appendix III). This was done at admission and discharge.

The etiology of the heart failure was often based on clinical findings but in a number of cases supportive evidence from electrocardiogram and m-mode echocardiogram was available. Towards the latter months of study these were unavailable due to technical problems pertaining to the recording machines.

Twenty millilitres of blood was taken at admission and at discharge and as soon as possible separated by centrifugation. The plasma was then stored at minus twenty degrees centigrade. At the end of each week this blood was analysed for norepinephrine using the method of Anton and Sayre (appendix I (19). The anticoagulant used as a solution of 1 gm ethylene diamine tetra-acid acid and 2 gm sodium thiosulphate per 100 millilitre at pH 7.4.

RESULTS

The total number of patients studied was 51 with a control of 30 normal persons.
For the patients studied the male: female ratio was 0.51: 0.49. The age range was 13 years to 78 years with a mean of 45.9 ± 2.6 years. The age range for controls was 13 years to 78 years with a mean age of 27.4 ± 0.60. The characteristics of the patients and controls are shown on Table Ia, Ib, Ic and Table II.

The results of analysis of the characteristics of the patients can be summarized as follows:-

PATIENTS IN CLASS IV

Irrespective of the sex of the patient there is a significant decrease in norepinephrine at discharge as compared to the level at admission ($p < 0.17$).

When compared for sex, the fall in plasma norepinephrine for both male and female patients is even more significant ($P < 0.001$ and P 0.0001 respectively).

There is no significant difference in plasma norepinephrine level between male and female patients in this class at admission and at discharge. Levels at discharge for both female and male patients are significantly less at admission ($P < 0.05$ for both sexes). There were many deaths in both female and male patients in this class and statistics at discharge must be seen in this light. (Seven female deaths and four male deaths).

PATIENTS IN CLASS III

At 90 per cent confidence interval ($P < 0.1$) the plasma norepinephrine at discharge is less than that at admission for both female and male patients. This is a significant drop in the level of norepinephrine.

When compared for sex, patients in this class at admission are found to have plasma levels that are markedly elevated. This is true at 98 per cent confidence interval ($P < 0.02$) for both female and male patients.

At discharge the level of norepinephrine in the female patient compared for sex is less than that at admission and this is a significant difference ($P < 0.09$). The fall in the male patient in this class compared for sex is less remarkable ($P < 0.13$) but nevertheless significant.

There is no significant difference in level of plasma norepinephrine between male and female patients at discharge but at admission the level in the female patient is higher than that of the male patient ($P < 0.30$).

CLASS II

The plasma level of norepinephrine at discharge was less than that at admission ($P < 0.2$). The sample size in this class however is too small.

COMPARISON OF NOREPINEPHRINE BETWEEN CLASSES:

CLASS II AND CLASS III: The difference in plasma norepinephrine at discharge is insignificant.

Class III and IV: The levels of plasma norepinephrine at discharge is significantly higher in class IV than in Class III ($P < 0.2$).

TABLE I: MEAN LEVEL OF PLASMA NOREPINEPHRINE(ng/ml) FOR MALE AND FEMALE PATIENTS IN CLASS III AND IV.

	Male		Female	
CLASS	Adm.	Disc.	Adm.	Disc.
	mean ± S D	mean ± S D	mean ± SD	mean ± SD
III	1.27 ± 0.65	0.93 ± 0.50	1.44 ± 1.11	0.74 ± 0.61
IV	1.39 ± 0.63	0.67 ± 0.21	1.28 ± 0.80	0.71 ± 0.42

Key

Adm. = Admission

Disc. = Discharge

TABLE 2: COMPARISON OF NOREPINEPHRINE (ng/ml) BETWEEN SURVIVORS AND THOSE WHO DIED.

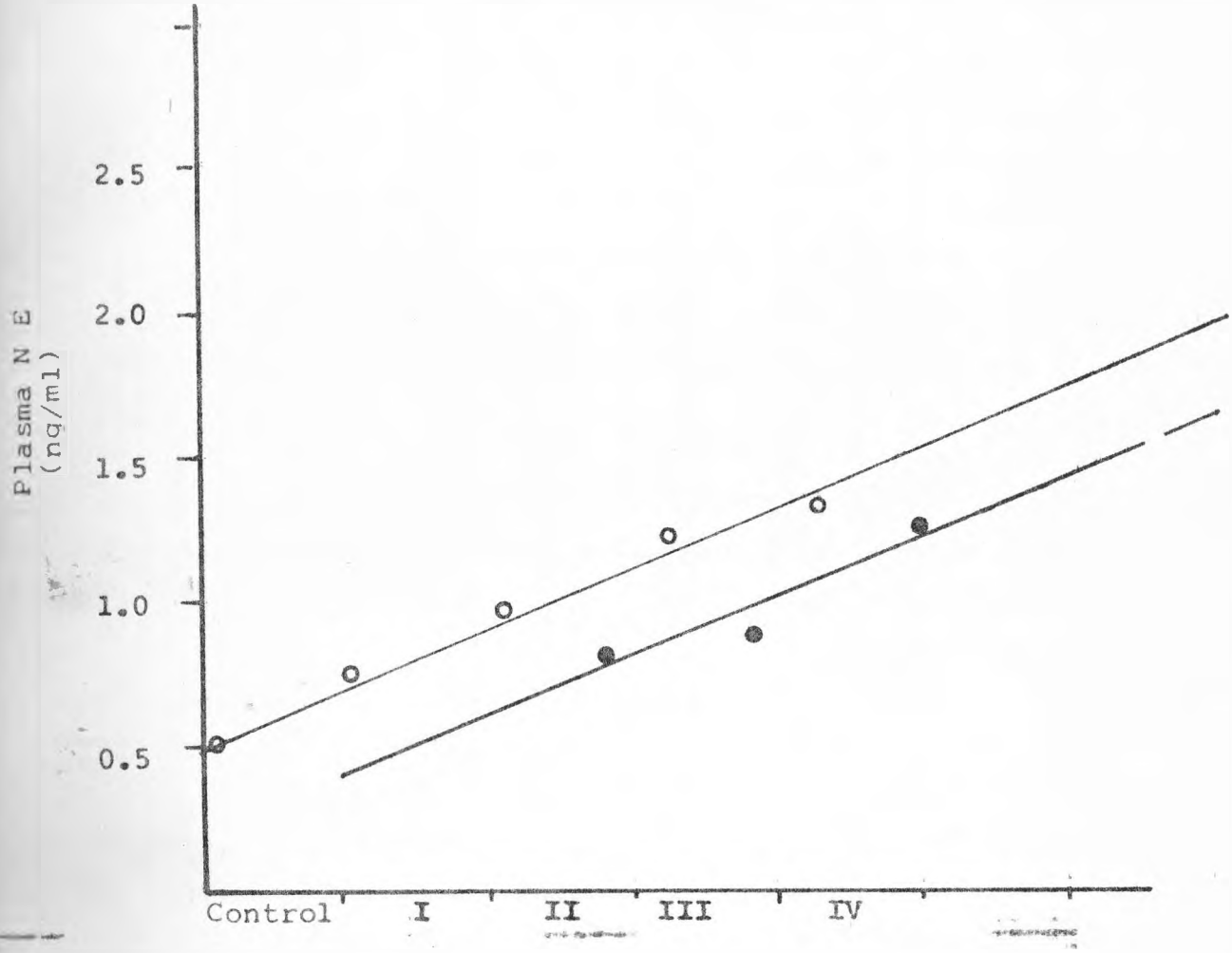
	SURVIVED	DIED
CLASS	Mean ± S D	Mean ± S D
III	1.51 ± 0.93	0.85 ± 0.33
IV	1.15 ± 0.64	0.64 ± 0.76

The above table shows that the patients in class III who survived had a greater amount of circulatory norepinephrine at admission than those who died ($P < 0.02$) and the opposite in class IV was true where the survivors had a lesser amount of norepinephrine than those who died ($P < 0.03$).

CARDIOTHORACIC RATIO (CTR)

At 70% confidence interval the CTR in class III is significantly different from that of class IV ($P < 0.03$). The sample size in class II was too small for genuine comparison with the other two classes but when one does so it is noticed that the difference is significant in comparison to class III and IV. ($P < 0.1$ for class II and III and $P < 0.3$ for class II and IV). On comparing the sexes one notices that the CTR in class IV is higher in the male patients than in the female patients. This is also true in class III ($P < 0.15$, and $P < 0.16$ respectively).

FIGURE I: FUNCTIONAL CARDIAC STATUS vs PLASMA NOREPINEPHRINE (ng/ml)



Functional cardiac status

N E = NOREPINEPHRINE ng/ml = nanogramme per millilitre

The above is a graphical presentation of the mean for each class at admission and at discharge.

Open circle - admission.

Closed circle - discharge.

HEART RATE

The heart rate in grade IV patients is significantly higher than in grade III patients ($P < 0.01$) i.e the worse the functional failure, the higher the heart rate. Since plasma norepinephrine in grade IV patients is higher than in grade III ($P < 0.2$) it follows that the heart rate changes in proportion to the plasma norepinephrine concentration.

TABLE 3: MORTALITY RATE AS COMPARED TO MEAN PLASMA NOREPINEPHRINE AT ADMISSION.

CLASS	MORTALITY (%)	Mean (NE) ± SD (ng/ml)
II	25	1.00 ± 0.29
III	26.7	1.34 ± 0.41
IV	38.7	1.32 ± 0.14
Mean	33.3%	1.33 ± 0.28

The results in figure 1 can be summarized as follows:

The plasma norepinephrine concentrations exhibit a progressive increase as the degree of heart failure worsens. All the three classes had plasma norepinephrine levels that were significantly different from control valuesat the time of admission.

But for class III and IV the discharge level of norepinephrine remained significantly elevated above the control level at the time of admission. This is presented graphically in Fig. I. At the beginning and end of the observation period it was observed that the plasma level of norepinephrine correlated directly with the functional cardiac status and reflected the degree of cardiac decompensation.

TABLE 1a: CLASS II: CHARACTERISTICS OF PATIENT GROUPS ACCORDING TO SEVERITY OF FAILURE ON ADMISSION

Case No.	Age (yr) Sex	H R (BPM)	B P (MM Hg)	CTR (%)	DIAG.	NYHA CLASS		N E	
						Adm.	Disc.	Adm.	Disc.
1	60 M	120	100/60	67	CCM	11	1	0.92	0.62
2	22 M	120	110/70	65	MVD (RHD)	11	1	0.62	0.32
3	75 M	96	150/90	66	CCM	11	11	0.62	1.54
4	32 M	224	140/100	45	MVD	11	+	1.85	+
Mean	47.3	140		65.8				1.00	0.82
± SEM	12.3	28.7		0.83				0.29	0.37

TABLE Ib CLASS III CHARACTERISTICS OF PATIENT GROUPS ACCORDING TO SEVERITY OF FAILURE ON ADMISSION

Case No.	Age (yr) and Sex	H R (BPM)	B P	CTR	Diag.	NYHA Class Adm.	NYHA Class Disc.	N E Adm.	N E Disc.
1	20 F	120	120/70	60	MVD (MS)	III	II	3.70	1.85
2	63 M	100	110/60	60	CCM	III	II	1.54	1.23
3	59 M	100	110/70	75	CCM	III	+	0.32	+
4	55 M	100	120/70	70	CCM	III	II	2.46	1.85
5	58 M	100	110/70	65	CCM	III	I	1.85	0.62
6	70 F	36	100/60	75	CCM	III	+	1.23	+
7	50 M	100	170/90	75	CCM	III	+	0.92	+
8	45 M	100	100/60	60	CCM	III	II	1.85	0.62
9	50 F	100	110/80	60	CHF ANEMIA	III	I	0.62	0.30
10	40 F	120	130/80	63	MVD	III	II	1.85	0.92
11	13 M	80	120/70	80	MVD + AI	III	II	0.62	0.31
12	70 M	100	120/70	55	CCM	III	+	0.92	+
13	21 F	100	90/60	66	MVD + $_{AS}$AI,	III	II	0.62	0.32
14	38 M	114	130/80	60	CCM	III	II	0.92	0.92
15	58 F	64	150/70	80	CCM	III	II	0.62	0.30
Mean	47.3	95.6		68.3				1.34	0.84
± SEM	4.47	5.56		2.00				0.41	0.13

TABLE Ic.CLASS IV CHARACTERISTICS OF PATIENT GROUPS ACCORDING TO SEVERITY OF FAILURE ON ADMISSION

Case No.	Age (yr) And Sex	H R (BPM)	B P (MMHg)	CTR (%)	Diag.	NYHA Adm.	Class Disc.	N E ADM.	DISC.
1	70 F	100	90/40	56	CCM	IV	III	1.54	1.23
2	22 M	118	160/80	66	MVD	IV	II	1.54	0.92
3	29 F	80	110/80	66	MVD	IV	III	0.32	0.31
4	28 F	128	110/70	60	MVD	IV	IV	0.62	0.62
5	70 F	88	120/70	81	COR PULNONALE	IV	II	0.32	0.32
6	28 F	128	90/60	66	MVD	IV	+	0.92	+
7	25 F	120	100/60	77	MVD	IV	+	2.46	+
8	16 F	120	130/50	54	MVD (AI + AS)	IV	+	0.62	+
9	21 F	132	130/90	52	MVD	IV	I	1.85	1.23
10	50 F	120	120/80	66	CCM	IV	II	0.62	0.32
11	27 F	88	UNRECORDABLE	70	MVD	IV	+	1.20	+
12	65 F	120	130/80	66	CCM	IV	II	0.92	0.32
13	45 M	110	120/80	56	COR PULMONALE	IV	II	0.92	0.92
14	70 M	80	UNRECORDABLE	70	CCM	IV	+	1.54	+
15	60 F	80	90/70	68	CCM +? SBE	IV	+	0.92	+
16	25 F	116	120/70	66	MVD	IV	II	1.85	1.54
17	41 M	140	110/60	66	CCM	IV	+	1.23	+
18	46 F	80	120/70	60	MVD	IV	II	2.15	0.62
19	48 F	72	110/50	84	MVD	IV	II	1.23	1.23
20	30 M	108	150/60	63	MVD	IV	+	1.54	+
21	42 M	100	120/50	60	MVD	IV	+	2.50	+
22	60 F	100	160/100	70	CCM	IV	III	0.92	0.62
23	16 M	120	130/90	85	VSD	IV	+	1.85	+
24	78 M	80	130/80	54	CCM	IV	II	1.23	0.63
25	75 F	64	110/70	75	CCM	IV	+	3.38	+
26	70 M	54	110/60	75	CCM	IV	-	0.62	ABSCONDED

TABLE IcCLASS IV (contd).

Case No.	Age (yr) Sex	H R (BPM)	B P (MMHg)	CTR (%)	Diag.	NYHA Class ADM.	NYHA Class DISC.	N E ADM.	N E DISC.
27	48 M	80	130/80	72	CCM	IV	II	0.62	0.62
28	37 F	100	110/70	60	MVD	IV	+	1.54	+
29	38 F	112	UNRECORDABLE	72	CCM (PERIPARTAL)	IV	II	1.80	0.60
30	50 F	88	130/70	60	CCM	IV	II	0.31	0.32
31	52 M	72	110/70	66	AVD (AI+AS)	IV	II	2.46	0.31
32	60 M	96	110/70	80	CCM	IV	II	0.62	0.62
Mean	42.2	110.4		66.9				1.32	1.20
± SEM	3.30	16.9		1.68				0.14	0.05
TOTAL Mean	45.9	101.7		66.9				1.3	0.8
± SEM	2.6	3.8		1.2				0.1	0.1

HR = HEART RATE BP = BLOOD PRESSURE CTR = CARDIOTHORACIC RATIO
NYHA = NEW YORK HEART ASSOCIATION CLASS ADM = ADMISSION DISC. = DISCHARGE
NE = NOREPINEPHRINE M = MALE F = FEMALE SEM = STANDARD ERROR OF THE MEAN
CCM = CONGESTIVE CARDIOMYOPATHY MVD = MITRAL VALVE DISEASE RHD = RHEUMATIC HEART DISEASE
CHF = CONGESTIVE HEART FAILURE AI = AORTIC INCOMPETENCE AS = AORTIC STENOSIS
AVD = AORTIC VALVE DISEASE + = DIED BPM = BEATS PER MINUTE.

TABLE II: CHARACTERISTICS OF CONTROL SUBJECTS

Case No.	Age (yr) sex	N E ng/ml	HR	B P
1	30 F	0.31	90	120/80
2	25 F	0.62	80	110/70
3.	22 F	1.23	100	110/60
4.	22 F	0.31	72	110/70
5	26 F	0.31	92	110/70
6	18 F	0.62	80	110/60
7	20 F	0.31	96	130/80
8	50 F	0.62	92	150/90
9	28 F	0.31	78	130/70
10	21 F	0.62	76	120/80
11	45 F	0.62	80	110/70
12	35 F	0.31	80	130/70
13	34 F	0.92	82	110/60
14	21 F	0.62	76	110/70
15	19 F	0.32	72	110/60
16	31 M	0.31	66	130/80
17	28 M	0.62	80	120/85
18	21 M	0.62	60	130/70
19	34 M	0.92	62	130/80
20	13 M	0.92	60	110/60
21	33 M	0.92	90	120/90
22	25 M	0.92	75	110/70
23	21 M	0.62	66	130/60
24	26 M	0.31	62	130/80
25	27 M	0.62	100	120/75
26	32 M	0.31	76	130/90
27	30 M	0.92	76	120/70
28	22 M	0.92	76	120/70
29	25 M	0.32	78	110/80
30	29 M	0.62	86	130/70
Mean	27.4	0.60	78.5	
S D	7.7	0.30	11.2	

DISCUSSION

There are basically three methods of assaying plasma norepinephrine - radioimmunoassay, chromatography and fluorimetry. The normal plasma norepinephrine varies in accordance with the method used as mentioned under introduction.(10,12,13).

In this study a fluorimetric method is used. Using this method the normal plasma norepinephrine on average in normal men and women is found to be 0.59 nanogrammes per millilitre. The value for a normal female tend to be on the lower side overaging 0.49 nanogrammes per millilitre and that of normal males averages 0.65 nanogrammes per millilitre. The range for the 30 normal men and women seen in this study was 0.31 - 0.92 ng/ml. This agrees with a fluorimetric method described by Weil-maherbe (13). The other two methods appear to give results that are about one half of those obtained by fluorimetric methods. Certain agents do affect the amount of norepinephrine detected by fluorometric method and those include septicaemia, trauma, drugs - methyldopa, halothane, reserpine, chlorpramazine, and nicotine (13).
As far as possible it was made sure that patients were not on the drugs mentioned and in fact patients with hypertensive heart failure were omitted from

the study because often the patients use a host of drugs whose nature they do not know.

Emotion leading to autonomic nervous discharge may contribute to release of norepinephrine from the nerve ending but this unfortunately is a difficult factor to eliminate. Both patients and controls were reassured before blood was taken and this was at the end of the history taking and physical examination. This may have helped to diminish nervousness. It is also unlikely that the significant difference observed between controls and patients and the difference between various functional grades can be accounted for purely by emotional differences.

Heart failure in this country is mainly due to valvular damage resulting from rheumatic heart disease whereas the Western world and Europe it is due to coronary heart disease.

Etiological differences in the syndrome of heart failure do not seem to play a part in the way the autonomic nervous system responds since the elevated norepinephrine evident in this study has been documented elsewhere (5).

However one observation that is striking is the fact that for patients in functional grade III, prognosis for them in much better than those in grade IV. The implication here would be that the ability of the heart in grade III is better than in grade IV and perhaps those in grade II are better off than those in grade III. This observation is supported by the fact that the mortality increases from grade II to grade IV. Since norepinephrine is a positive ionotropic agent, one possible explanation that can be drawn here is that when one looks at functional classes one is also looking at the residual functional ability of the heart as a pump so that those in class IV will not benefit from norepinephrine however high it rises. Or is it that the norepinephrine is toxic to the myocardium ? (36). A combination of the two may also have a role - i.e., pump failure and toxicity of norepinephrine on the myocardium.

This observation is an important one in treatment of congestive heart failure because it implies that those patients that are severely affected may not derive much benefit from ionotropic agents but may benefit more from other methods of treatment. It has in fact been demonstrated that patients on the long term do better functionally, when they are treated with agents that inhibit norepinephrine e.g. captopril (21).

The cardiothoracic ratio also brings out the fact that there is progressive reduction in the ability of the heart to rid itself of the blood contained therein as it increases significantly as one moves from grade II to IV.

CONCLUSION

Using a routine laboratory method as opposed to special and expensive methods, it has been possible to demonstrate high levels of plasma norepinephrine in congestive heart failure and its probable relationship with mortality. For patients in a functional class it has been demonstrated that the higher the class the higher the norepinephrine and also that the greater the risk of death. This may not necessarily be so for an individual in any given class but high plasma norepinephrine does seem to portend a bad prognosis.

RECOMMENDATIONS

It would be recommended as evidence by the study that patients functionally in class III and IV be treated with agents that inhibit noradrenaline and less of ionotropic agents.

It would also be recommended that patients treated with noradrenaline inhibitors be studied prospectively and be compared with patients treated otherwise. A comparative study using other assay methods be carried out in order to compare the results.

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APPENDIX II

Functional cardiac status as described by New York Heart Association Creteria Committee (Ref 15).

CLASS I: No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation dyspnoea or anginal pain.

CLASS II: Slight limitation of physical activity comfortable at rest but ordinary physical activity results in fatigue, palpitation, dyspnoea, or anginal pain.

CLASS III: Marked limitation of physical activity. Comfortable at rest but less than ordinary physical activity causes fatigue, palpitation dyspnoea, or anginal pain.

CLASS IV: Unable to carry out physical activity without discomfort, Symptoms of cardiac insufficiency or of anginal syndrome may be present even at rest. If any physical activity is undertaken discomfort is increased.

APPENDIX I:

A measured quantity of plasma was added 10 cc of 0.4 perchloric acid. Contents were then centrifuged at 30,000 x g for ten minutes. The volume of the clear supernatant was then adjusted to 25 ml with 0.4 N perchloric acid in a beaker containing 400 mg of aluminium oxide, 200 mg of EDTA and 10 mg of sodium metabisulphite. The contents were then mixed vigorously on a rotamixer and pH adjusted to 8.00 with 10 N sodium hydroxide. The aluminium oxide was allowed to sediment and supernatant discarded. The aluminium oxide was washed several times (at least thrice) with distilled water and finally the catecholamines were eluted with 3 cc of 0.05 N perchloric acid (by shaking for at least 15 minutes). The contents were spun at 30,000 x g for 10 minutes and supernatant retained for analysis.

An aliquot of 0.4 cc. of perchloric acid eluted was taken into a microcuvette to this 0.2 cc of phosphate buffer 0.2 M (pH 7.0) was added followed by 40 microlitre of 0.25% potassium ferricyanide and contents shaken vigorously. After exactly a minute 0.4 cc of distilled water was added and the fluorescence read using vivatron modular photometer system. The activation wave length was 405 nm and

emission was 420 nm at pH 7.0. A blank without potassium ferricyarride was similarly run. standards in the range 10 - 100 nanogrammes were similarly treated.

Note The water used for dissolving the chemicals and for other procedures in the analysis was double distilled.

The main drugs interferring with this fluorometric method include nicotine, methyldopa ampicillin, promethazine, sulphonanudes, vitamin B complex. It was ensured as far as possible that the patient was not on these drugs.

APPENDIX III: NAME AGE SEX IP NO.

HISTORY.

Presence or absence of	Ordinary	Less than ordinary	At rest
Dyspnoea ±			
Palpitation ±			
Anginal pain ±			
Fafigure ±			

NYHA GRADE Admission + = Presence of
Discharge - = Absence of

EVIDENCE OF CONGESTIVE HEART FAILURE

A. 1. Ventricular third heart sound in absence of mitral stenosis.
2. Elevated jugularvenous pressure
3. Edema
4. Lung basal crepitations
5. Blood pressure
6. Heart rate
7. Radial pulse rate.

B 8 Chest Xray CTR Evidence of edema Congestion Effusion

C. ECG findings

D. ECHO (M-mode) findings
Laboratory norepinephrine Admission
Discharge