Chapter 3

Methods

Patients

Consecutive B-thal/HbE or suspected thalassemic patients attending the hematologic clinic of Chulalongkorn hospital or admitted into the ward during June 1, 1987 to September 30, 1987 were screened. Eligible patients gave a consent and enrolled in the study. Patients were excluded if hemoglobin electrophoresis were not "hemoglobin EF" or had one or more exclusion criteria. Target B-thal/HbE sample was determined to be 35 patients.

Acute problems such as infection and/or acute hemolysis were managed accordingly until patients were in stable stage, then enrollment began. So, out patients were usually enrolled on that particular follow up days and in-patients on the last few days before discharge.

Inclusion criteria

Thalassemic patients, age $\geq$ 14 year, and hemoglobin electrophoresis were "EF".

Exclusion criteria

hemoglobin electrophoresis not "EF", congenital heart disease, pregnancy, iron deficient anemia (documented from iron study subsequently), other systemic illness (diabetes mellitus, hypertension, pulmonary tuberculosis), on any cardiotonic or any antiarrhythmic drugs.

History taking, physical examination and blood test

All pertinent data were recorded in the designed sheets, taken

on the same day as echocardiogram, blood test, chest x-ray and electrocardiogram. Number of blood transfusion and hemoglobin levels were obtained from the medical records.

Echocardiogram

Two dimensional echocardiogram ("Aloka" Sect-Scan SSD-720, ultrasound recorder SSZ-93) was used to determine cardiac chamber sizes, cardiac contractility and function. Recordings were made with the patient in a semisupine anteroposterior or a 20 degree left anterior oblique position. The left ventricular (LV) and right ventricular (RV) dimensions were recorded with the echobeam in a standard plane to guard against forshortening of the measured diameter of the LV (minor axis). The transducer was positioned in the left sternal border and directed posteriorly to define the endocardial surfaces of the interventricular septum (IVS) and LV posterior wall (LVPW) at the level of the tips of the mitral valves. The interspace selected was that in which the mitral valve could be recorded with the transducer perpendicular to the chest wall(30). The echo beam was then directed to record the other intracardiac structures and chambers.

Critique of methods Echocardiographic measurements of LV function are widely used but the data must be analysed critically. The single plane echocardiogram measures the minor diameter of the left ventricle: in normal patients the LV is symmetrical and the echo measurements represent over-all LV size and function,but this is not necessarily so in patients with cardiac disease and ventricular dilatation(31). Nonetheless ,stroke volume and cardiac output were calculated for comparison with measurements in the literature.

Chest x-ray and electrocardiogram (ECG)

Chest roentgenogram in the standard 6-ft posteroanterior view, upright position was taken and interpreted by a radiologist. Twelve-leads electrocardiogram was read by a cardiologist. Both physicians had not seen the patients.

Roentgenographic criteria of chamber hypertrophy and/or enlargement (32)

Left ventricle: cardiothoracic ratio exceeds 50% and the apex lies below the diaphragmatic curve

Right ventricle: cardiothoracic ratio exceeds 50% and the apex lies above the diaphragmatic curve

Biventricular prominence: cardiothoracic ratio exceeds 50% and the apex lies about the diaphragmatic curve

Roentgenographic criteria of pulmonary hypertension

The heart is seen to be slightly to moderately enlarged.

The enlargement is mainly due to increase in the size of the right ventricle.

The right atrium may also dilate.

The main pulmonary artery and its right and left branches may be considerably enlarged, but this enlargement is rapidly terminated lateral to the hilus, and the peripheral lung fields are ischemic.

Electrocardiographic criteria for chamber hypertrophy and/or enlargement

ECG criteria for infancy and childhood (33)

Right Ventricular Hypertrophy

1. Voltage of R in V_1 greater than maximum for age (Table 2)
2. Voltage of S in V_6 greater than maximum for age (Table 2)
3. R/S ratio in V_1 greater than maximum normal for age (Table 2)
4. Positive T in V_1 after third day of life when R/S ratio greater than 1
5. qR pattern in right precordial lead V_1

Left Ventricular Hypertrophy

1. Voltage of R in V_6 greater than maximum normal for age (Table 3)
2. Voltage of S in V_1 greater than maximum normal for age (Table 3)
3. Secondary T wave inversion in V_5 and/or V_6

4. Deep Q wave, $\geq$ 4 mm, over the left precordium

Combined Ventricular Hypertrophy

1. Direct signs of right plus left ventricular hypertrophy (as above)
2. Direct signs of right ventricular hypertrophy with the following signs in left chest leads:
   a: q wave (2 mm or more)
   b: sizable R (voltage not necessarily abnormal) with tall, positive T in V_6
   c: T inversion, after a positive T in right chest leads
3. Direct signs of left ventricular hypertrophy with:
   a: sizable R or R' in right chest leads (voltage not necessarily abnormal) or R/S ratio greater than 1
   b: marked clockwise rotation of QRS vector
4. Apparently normal electrocardiogram in the presence of marked true cardiac enlargement

Table 2 Criteria for right ventricular hypertrophy
maximal measurements for age 3 months-16 years (precordial leads)

wave		measurement (mm)
R in V_1		19 or more
S in V_6		5 or more
R/S in V_1	3-6 months	4.0
	6 mo - 3 yr	2.4
	3-5 years	1.6
	6-15 years	0.8 or more

Table 3 Criteria for left ventricular hypertrophy

maximal measurements by age groups (precordial leads)

wave	age	measurements (mm)
S in V_1	0-1 day	28
	1 day -1 yr	19
	1 yr -16 yr	25 or more
R in V_5	0-3 years	30
	3-15 years	35 or more
R in V_6	0-6 months	16
	6-12 months	19
	1-16 years	21 or more

ST segment depressed in V_5 or V_6

T waves inverted in left precordium may be found in severe LVH

ECG criteria for adults (more than 16 years)

Left Ventricular Hypertrophy by Estes' point system (34)

	points
# R or S in limb leads $\geq$ 20 mm	3
S in V_1 or V_2 $\geq$ 30 mm.	
R in V_5 or V_6 $\geq$ 30 mm.	
# Negative ST- wave (without digitalis).	3
# Negative terminal P in V_1 $\geq$ 0.04 sec.	3
# Left axis deviation; -30 degrees or more.	2
# Repolarization abnormality (with digitalis).	1
# QRS $\geq$ 0.09 sec.	1
# Intrinsicoid deflection > 0.05 sec. in V_5 or V_6.	1
Total	13

Definite LVH = 5 points.

Probable LVH = 4 points.

Right Ventricular Hypertrophy Criteria (34)

Right axis deviation of more than +110 degrees

R wave or R' in V_1 of 5 mm or more

R wave in lead AVR of more than 5 mm or more

R/S ratio- lead V_1 greater than 1 and V_6 less than 1

QRS complex may be slightly prolonged but less than 0.12 sec

S_1 ,S_2 ,S_3 pattern may be present

ST segment depression, upward convexity, and inverted T wave in leads V_1 and V_2

Delayed intrinsicoid deflection in lead V_1 (0.035 to 0.055 second)

Prominent P wave in lead II

Biventricular Hypertrophy Criteria (34)

right axis deviation of more than + 90 degrees

voltage criteria for left ventricular hypertrophy

Normal control

Twelve volunteers, all of whom were hospital employees, were evaluated exactly as the B-thal/HbE patients. These served as a quality control of the study.

Statistical analysis

Student unpaired T-Test, Chisquare test, and analysis of variance were used when appropriate.