CARDIOGENIC SHOCK FOLLOWING ACUTE MYOCARDIAL INFARCTION AND THE ROLE OF ETHYL ADRIANOL IN ITS TREATMENT

By Chin Hock Lim and Charles C. S. Toh

SYNOPSIS

Cardiogenic shock occurred in 12.4% of patients with acute myocardial infarction and carried with it a mortality rate of 84.3%.

The mean age of shock patients was 56 years and the peak incidence was in the 50-59 age group.

The male to female ratio was 6:1, and both males and females were equally subject to cardiogenic shock.

Diabetes mellitus and/or hypertension were important predisposing factors.

Ethyl Adrianol was used in 40 patients and a positive pressor response was seen in 13 patients, of whom 6 survived.

INTRODUCTION

The intensive management of patients with acute myocardial infarction in Coronary Care Units has led to an improvement in survival rates from 25%-30% to 15%-20%, due mainly to the effective prevention and aggressive treatment of arrhythmias and cardiac failure. Further improvement in survival rates can only come about if there is a satisfactory solution to the problem of cardiogenic shock, which occurs in 10%-20% of patients with acute myocardial infarction (Shubin and Weil, 1970; Toh *et al*, 1970; Scheidt *et al*, 1971). It claims a mortality rate of 80%-100% (Toh *et al*, 1970; Scheidt *et al*, 1971). The high mortality rate and the current controversy over the use of alpha-stimulating or beta-stimulating agents in the treatment of shock (Block *et al*, 1966) reflects the unsatisfactory therapy of cardiogenic shock. To date, artificial mechanical circulatory support is of only temporary value and drug therapy remains the only available mode of treatment of shock.

The aim of this paper is to review our experience of cardiogenic shock and the use of Ethyl Adrianol (Effortil) in its treatment.

MATERIAL AND METHODS

From January 1969 to March 1971, 409 patients with definite acute myocardial infarction were monitored in the Coronary Care Unit, Department of Medicine (Medical Unit II), Singapore, fulfilling at least 2 out of 3 criteria, viz.:

1. Typical clinical history.
2. Electrocardiographic changes showing Q waves or evolution of ST segment and T wave abnormalities.
3. Characteristic increase in S.G.O.T., S.C.P.K. or S.L.D.H.

Cardiogenic shock was diagnosed if the systolic arterial pressure was less than 90 mm. Hg., and there were signs of peripheral vasoconstriction, such as cold skin, reduced urine flow, mental confusion, restlessness or apathy. Patients with hypotension lasting less than half an hour or vasovagal in origin were excluded. The parameters recorded were blood pressure, mental state, urine flow, cyanosis, state of the extremities and blood gases where possible. Metabolic acidosis or any arrhythmias which arose were documented and treated accordingly. Ethyl Adrianol, isoprenaline, metaraminol, sodium bicarbonate and oxygen were given accordingly, and pain was relieved with either omnopon or pentazocine.

Pharmacology of Ethyl Adrianol—Effortil (Boehringer Ingelheim)

Ethyl Adrianol—1-(3 hydroxyphenyl)-1-hydroxy-2-ethylamino-ethane hydrochloride, has a positive inotropic effect on the heart and it reduces peripheral vascular resistance but increases renal blood flow. It is less potent than isoprenaline but it does not stimulate ectopic pacemakers (Abstract from Boehringer Ingelheim, Renna, 1965).

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It is administered intravenously; 10 mgm. is given as a bolus dose, while 50 mgm. is diluted in one pint of 5% dextrose solution and infused rapidly, the rate regulated according to response and the height of the central venous pressure.

RESULTS

The overall hospital mortality rate for patients monitored in the Coronary Care Unit from April 1967 to December 1969 was 19·5% (Wan *et al*, 1970). Fifty-one (12·4%) of the 409 patients developed cardiogenic shock; 43 of these patients died—a mortality rate of 84·3%.

Predisposing Factors

Toh (1970) found the mean ages of the male and female patients with definite infarction, monitored in the Coronary Care Unit to be 53·7 and 58·9, years respectively. The mean age of the patients with cardiogenic shock was 56 years which is not significantly different from the population at risk. The survivors had a mean age of 57 years while those who succumbed had a mean age of 56 years. There were 7 females (13·7%), and 44 males; a female:male ratio of 1:6. Fig. 1 shows the highest incidence of shock in the oldest age group of 70 years or more.

Sixteen patients (31%) had diabetes mellitus, this incidence was twice as common as the population at risk. Toh (1969) found the incidence of diabetes, hypertension and diabetes plus hypertension in patients with infarction to be 18·2%, 33% and 6·1% respectively. In this series, known past hypertension was present in 15 patients (29%) and both diabetes and hypertension in 6 patients (12%) (Fig. 2). Diabetes mellitus and a combination of both diabetes and hypertension appear to be significant risk factors as their incidence in shock patients were significantly higher (Tables I to III) ($p<0·01$).

Thirteen patients (25%) had one or more previous infarcts while 8 (15%) had preceding angina but no infarction. There was a greater incidence of previous infarction or angina among those who died (59%), than in those who survived (25%) (Fig. 3) ($p<0·01$).

Anterior infarction was seen in 26 patients (51%) while 19 patients (37%) had inferior infarction. Only 4 patients (8%) had both anterior and inferior infarction, and 1 (2%) had sub-endocardial infarction (Table IV).

In a number of patients, it was difficult to determine the onset of shock as they presented with shock on admission, and the duration of shock was therefore uncertain. Forty-three percent of patients developed shock within 24 hours (Fig. 4). Nine patients developed shock more than 48 hours after the onset of pain. Clinical evidence of left ventricular failure was not present in 4 patients. The majority of patients died within 24 hours (90%), while 37 patients (70%) died within 6 hours of onset of shock (Table V). The mean survival time was 16·5 hours.

Of the 11 patients with supraventricular arrhythmias 4 had atrial fibrillation, while 1 had atrial flutter. Paroxysmal atrial tachycardia was seen in 2 patients. There was a high incidence of heart block; 13 patients (25%) had complete heart block, and 9 of these were paced. Three patients had ventricular ectopics while 2 developed ventricular fibrillation. Right bundle branch block was seen in 12 patients (23·5%); 6 of these had concomitant left posterior hemiblock (Table VI).

The central venous pressure varied from −5 cm. of H20 to +19 cm. of H20, while the majority of patients (10 out of 13) had blood pH values below 7·3.

Response to Ethyl Adrianol

There were 40 patients treated with intravenous Ethyl Adrianol, 1 with metaraminol and 10 with isoprenaline. One patient (A.M.) had 13 episodes of ventricular fibrillation while on intravenous isoprenaline for cardiogenic shock. He responded to cardioversion on 13 occasions and was finally stabilised while on Ethyl Adrianol. However, he subsequently developed complete heart block, and was temporarily paced, but he died 2 weeks later from recurrent cardiogenic shock.

Twenty-seven patients showed no response at all to Ethyl Adrianol, while 13 had a marked vasopressor response (Tables VII and VIII). Patient L.A.H.—a 48 year old male, had an unrecordable blood pressure on admission but rose to 90 mm.Hg. systolic 10 minutes after Ethyl Adrianol was given, while another patient, S.D. had an unrecordable blood pressure initially but rose to 200/90, 10 minutes after a bolus dose of Ethyl Adrianol. Of the 10 patients treated with isoprenaline only 2 patients showed a rise in blood pressure but no amelioration of the clinical signs. The vasopressor response cannot be entirely attributed to the drug per se as there was rapid fluid infusion and correction of metabolic acidosis concurrently. Of the 13 patients with vasopressor response to Ethyl Adrianol (Figs. 5 and 6), 6 had clinical improvement, that is, the extremities became warm and conscious level improved. Seven patients can be regarded as having secondary cardiogenic shock; 6 of these had concomitant complete heart block and shock, they improved with pacing or reversion

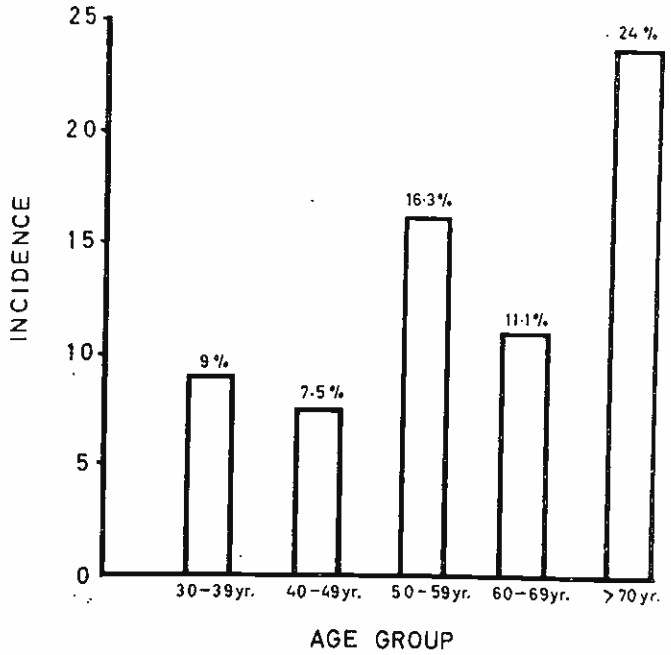

Fig. 1. Incidence of cardiogenic shock according to age group.

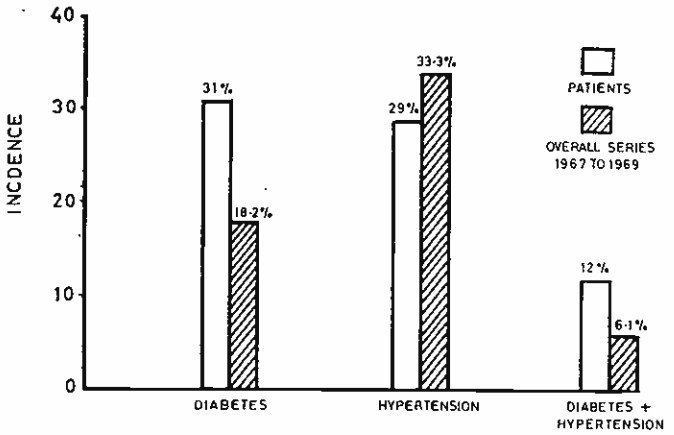

Fig. 2. Incidence of diabetes, hypertension, diabetes and hypertension in shock patients and in overall series.

TABLE I

THE RELATIONSHIP BETWEEN DIABETES MELLITUS AND CARDIOGENIC SHOCK AMONG PATIENTS WITH CARDIOGENIC SHOCK

	Patients with Diabetes Alone	Patients without Diabetes or Hypertension	Total
Shock patients	16	14	30
Non-shock patients	33	213	246
TOTAL	49	227	276

$p<0.01$

TABLE II

THE RELATIONSHIP BETWEEN HYPERTENSION AND CARDIOGENIC SHOCK AMONG PATIENTS WITH MYOCARDIAL INFARCT

	Patients with Previous Hypertension Alone	Patients without Hypertension or Diabetes
Shock patients	15	14
Non-shock patients	80	213
TOTAL	95	227

$p<0.001$

TABLE III

THE RELATIONSHIP BETWEEN THE COMBINED PRESENCE OF DIABETES AND HYPERTENSION AMONG PATIENTS WITH INFARCTION

	Patients with Diabetes and Hypertension	Patients without Diabetes or Hypertension
Shock patients	6	14
Non-shock patients	26	213
TOTAL	32	227

$p<0.01$

TABLE IV

COMPARISON OF THE SITE OF INFARCTION IN THE SHOCK GROUP AND THE OVERALL SERIES

Site of Infarction	Cardiogenic Shock	Overall Series (1967 to 1969)
Anterior	26 patients (51%)	56·5%
Inferior	19 patients (37%)	28·9%
Anterior and Inferior	4 patients (8%)	9·8%
Sub-endocardial	1 patient (2%)	10·0%
Undetermined	1 patient (2%)	—

TABLE V

THE TIME INTERVAL OF ONSET OF PAIN TO SHOCK AND THE DURATION OF SHOCK

Time Interval	Onset of Pain to Shock	Duration of Shock
0 - 6 hours	22	37
7 - 12 hours	12	8
13 - 24 hours	6	2
25 - 48 hours	2	2
>48 hours	9	3

TABLE VI

THE INCIDENCE OF ARRHYTHMIAS DURING CARDIOGENIC SHOCK

Arrhythmia	No. of Patients	Incidence
Atrial fibrillation	4	7·8%
Atrial flutter	1	1·4%
P.A.T.	2	3·4%
Junctional rhythm	4	7·8%
1° Heart block	1	1·4%
2° Heart block	2	3·4%
3° Heart block	13	25·0%
Ventricular ectopics	3	5·8%
Ventricular fibrillation	2	3·4%
Rt. B.B.B.	12	23·0%
Rt. B.B.B. with L.A.H.	6	11·0%
Rt. B.B.B. with L.P.H.	6	11·0%

L.A.H. denotes left anterior hemiblock.
L.P.H. denotes left posterior hemiblock.

TABLE VII

THE RESPONSE TO VARIOUS DRUGS IN CARDIOGENIC SHOCK

Drug	Negative Response	Vasopressor Response	Clinical Response
Ethyl Adrianol	27	13	6
Isoprenaline	8	2	0
Metaraminol	1	1	0

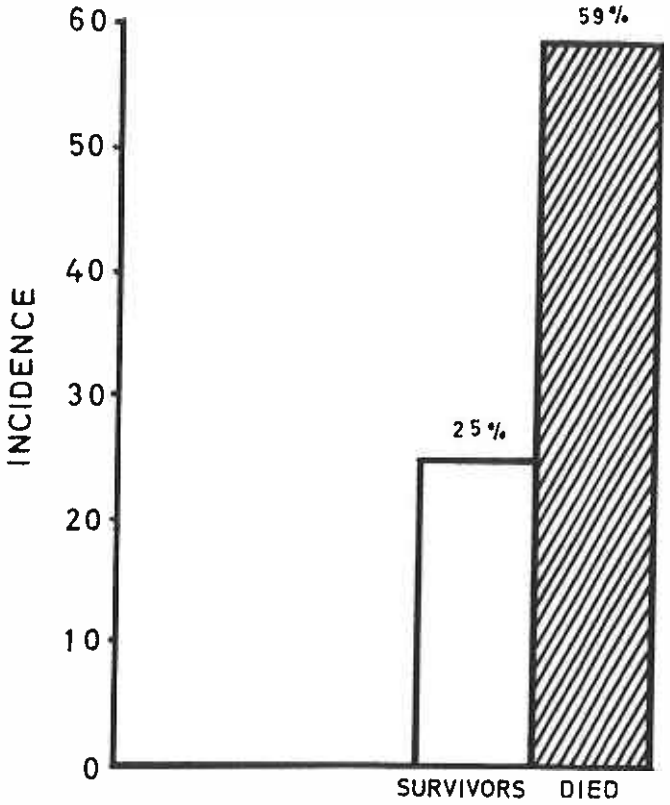

Fig. 3. Incidence of previous infarction or angina in those who survived or died.

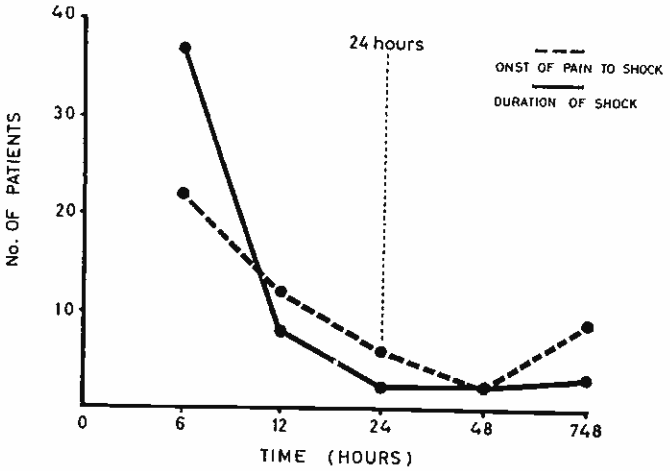

Fig. 4. Graph showing onset of shock and the duration of shock.

to sinus rhythm, and one patient (A.K.) developed shock following the use of both chlorpromazine and pethidine.

DISCUSSION

The mean age of shock patients in this series was similar to the mean ages of male and female patients with acute myocardial infarction as described by Toh *et al* (1970). The peak incidence of shock occurred in the older age group—more than 70 years, this was similar to Scheidt's experience (Scheidt *et al*, 1970). No marked difference was found in the mean ages of survivors and those who succumbed which were 57 and 56 years respectively.

Scheidt *et al* (1970) described a greater incidence of cardiogenic shock in females—37%, while the proportion of females in the population at risk was 25%. In this series, the incidence of shock (13%) in women was similar to the female incidence of infarction which was 13% (Tan *et al*, 1969).

Diabetes mellitus, hypertension occurring together and diabetes itself were important risk factors (Tables I-III). Diabetes mellitus was more common in the group with shock (31%) while its incidence in Tan's series which included shock and non-shock patients was 18·2%. The development of shock is related to the extent of myocardial damage and not to the site of infarction as 25% of the survivors and 59% of those who succumbed had previous infarction and/or angina.

Shock occurred soon after the clinical onset of infarction; 43% developed it within 6 hours while 78% developed it within 24 hours. Eleven patients (21·5%) developed shock 24 hours after the onset of infarction, this may be due to asynergy or progressive myocardial damage after the onset of infarction.

Shock was ameliorated in 5 patients after pacing was instituted. Trifascicular block was seen in 12 patients (23%); 6 had right bundle branch block with left posterior hemiblock while the remaining 6 patients had right bundle branch block with left anterior hemiblock.

Controversy still rages over the choice of pharmacologic agents in the treatment of cardiogenic shock. Shubin and Weil (1967) offered a suggestion that a combination of alpha and beta adrenergic agents be used. In Scheidt's series, the use of either norepinephrine or metaraminol did not influence the survival rate.

Vasopressor response was seen in 13 of the 40 patients treated with Ethyl Adrianol, and 7 of these 13 patients died—a mortality rate of 53% of those who responded. However, 4 of the 6 patients

TABLE VIII

SIXTEEN PATIENTS WITH POSITIVE VASOPRESSOR RESPONSE

Name	Blood Pressure Before Treatment	Blood Pressure 10 Minutes After Bolus Dose	Heart Block	Result Alive/ Died	Drug
L.A.H.	Unrecordable	90/?	—	Died	E.A.
C.K.	90/?	120/90	C.H.B.	Died	E.A.
G.S.H.	70/?	90/70	—	Died	E.A.
W.H.C.	80/60	210/140	C.H.B.	Alive	E.A.
L.S.K.	60/?	70/50	—	Died	E.A.
A.K.	80/60	110/70	—	Alive	E.A.
T.K.S.	80/60	110/70	—	Died	E.A.
M.S.N.	60/?	90/50	C.H.B.	Died	E.A.
K.S.	50/?	110/80	—	Alive	E.A.
K.N.	80/60	110/60	—	Died	E.A.
O.J.C.	70/60	100/80	C.H.B.	Alive	E.A.
S.D.	Unrecordable	200/90	C.H.B.	Alive	E.A.
C.C.S.	75/50	90/52	C.H.B.	Alive	E.A.
M.S.	Unrecordable	110/70	—	Died	I.
M.A.B.	70/?	110/100	—	Died	I.
C.S.	50/?	90/60	—	Died	M.

C.H.B. = Complete heart block.
E.A. = Ethyl Adrianol.
I. = Isoprenaline.
M. = Metaraminol.

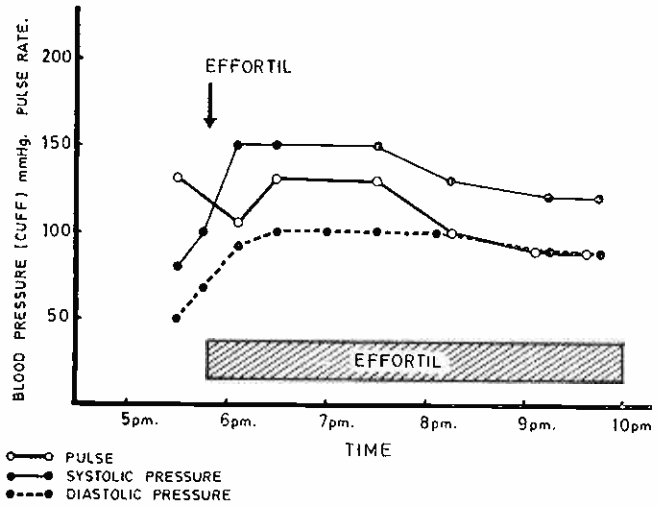

Fig. 5. T.K.S. M.52 Years.

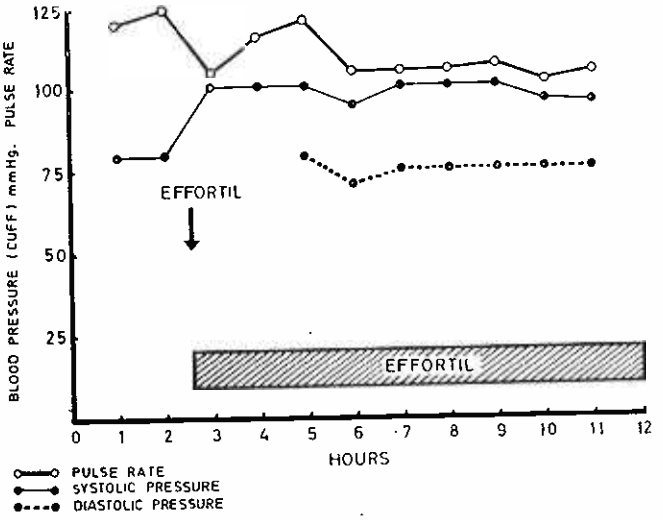

Fig. 6. W.A.S. M.52 Years.

who survived had concomitant complete heart block and in these patients, the shock was probably secondary to the slow ventricular rate and loss of atrial transport. It is more difficult to titrate the dose of isoprenaline because of its potency, and dilution is more difficult when compared to Ethyl Adrianol. This is illustrated by the patient, A.M., who developed 13 episodes of ventricular fibrillation while on intravenous isoprenaline for cardiogenic shock, but was stabilised while on intravenous Ethyl Adrianol. Moreover by increasing the work load on the heart, isoprenaline may have a deleterious effect on the sick myocardium. Maroko *et al* (1971) have shown that in experimental infarction the infarct size is increased by the prior administration of isoproterenol.

Pharmacological agents continue to play a useful though limited role in the treatment of shock, and the answer in the future may lie in mechanical circulatory assistance (Debakey, 1971) with infarctectomy (Heimbecker, 1969) or emergency vein graft bypass.

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REFERENCES

1. Bloch, J.H., Pierce, C.H. and Lillihei, R.C.: "Adrenergic blocking agents in the treatment of shock." Annual Review of Medicine, 17, 483, 1966.
2. Debakey, M.E.: "Mechanical circulatory support: Current Status." American Journal of Cardiology, 27, 1, 1971.
3. Heimbecker, E.: "Surgery for massive myocardial infarction." Progress in Cardiovascular Diseases, 11, 338, 1969.
4. Maroko, P.R., Kjekshus, J.K., Sobel, B.E., Watanabe, T., Covell, J.W., Ross, J. and Braunwald, E.: "Factors influencing infarct size following experimental coronary artery occlussion." Circulation, Vol. XLIII, 67, 1971.
5. Renner, E., Edel, H.H. and Garland, H.J.: "Vergleichende Untersuchungen iiber die Wirkung von Athyladrianol und Nor-Adrenalinauf die Nierenhamodynamik des Jesunden." Medizinishe Klinik, 14, 546, 1965.
6. Sheidt, S., Ascheim, R. and Killip, T.: "Shock after acute myocardial infarction: A clinical and haemodynamic profile." American Journal of Cardiology, 26, 556, 1970.
7. Shubin, H. and Weil, M.H.: "The treatment of shock complicating acute myocardial infarction." Progress in Cardiovascular Diseases, 10, 30, 1967.
8. Tan, Y.T., Toh, C.C.S. and Low, L.P.: "Diabetes Mellitus in Patients with Acute Myocardial Infarction." Proceedings of the 4th Singapore-Malaysia Congress of Medicine, 1969.
9. Toh, C.C.S., Low, L.P. and Tan, Y.T.: "Some Aspects of the Epidemiology of Cardiovascular Diseases in Singapore." Cardiology, Current Topics and Progress, Academic Press, New York/London, 1970.
10. Toh, C.C.S., Low, L.P. and Tan, Y.T.: "Intensive care of acute myocardial infarction in a coronary care unit." Sing. Med. Jour., 11, 38, 1970.
11. Wan, S.H., Toh, C.C.S., Lim, C.H. and Low, L.P.: "Admission and Mortality Patterns in A Coronary Care Unit." Proceedings of the Vth Singapore-Malaysia Congress of Medicine, 1970.