Heart rate and ectopic prematurity in relation to sustained ventricular arrhythmias

SALIM YUSUF, ROBERTO LOPEZ, PETER SLEIGHT

From the Department of Cardiovascular Medicine, University of Oxford, John Radcliffe Hospital, Headington, Oxford

SUMMARY Forty-four patients with acute myocardial infarction were studied using 24-hour electrocardiographic monitoring. A linear correlation has been shown to exist between heart rate preceding accelerated idioventricular rhythm and ventricular tachycardia and the rates of these. The prematurity index was found to be inversely related to the preceding heart rate and also to the rate of accelerated idioventricular rhythm or ventricular tachycardia. Faster heart rates preceded extrasystoles with shorter prematurity indices and a significant inverse correlation was observed between preceding heart rate and prematurity index. Patients developing ventricular tachycardia had more frequent isolated ventricular extrasystoles and faster heart rates preceding the episode as compared with patients not showing ventricular tachycardia. No association was observed between ventricular tachycardia and accelerated idioventricular rhythm. All four patients developing ventricular fibrillation showed preceding ventricular tachycardia, with three of these patients demonstrating faster rates of ventricular tachycardia (>170/min) and shorter prematurity indices (<0.80) than patients without ventricular fibrillation.

Heart rate may influence the severity of ventricular arrhythmia; the prematurity of an extrasystole is of importance in patients developing accelerated idioventricular rhythm or ventricular tachycardia.

In an attempt to define rhythms predictive of ventricular fibrillation and ventricular tachycardia, several workers have identified "warning arrhythmias". The early ventricular extrasystole interrupting the T wave has long been considered to be hazardous and a precursor of ventricular fibrillation. Patients with acute myocardial infarction, antiarrhythmic therapy has been instituted when R on T extrasystoles have been identified. However, recent reports have challenged this view. Other reports suggest that faster heart rates, frequent isolated ventricular extrasystoles, and couplets predispose to ventricular tachycardia and ventricular fibrillation. However, the relation of the preceding heart rate to the prematurity of an extrasystole (prematurity index = coupling interval between preceding sinus complex and the first extrasystole/QT interval of the preceding sinus complex); and the relation of the prematurity index to the rate of the following ventricular arrhythmia has not been studied in patients with myocardial infarction.

The purpose of this study was to investigate the following:

(i) The relation of the mean heart rate and the heart rate preceding a run of ventricular arrhythmia to the incidence and the rate of the ventricular arrhythmia and to the prematurity of the extrasystole starting the ventricular arrhythmia.

(ii) The relation between the prematurity index and the rate and incidence of ventricular tachycardia and accelerated idioventricular rhythm.

(iii) The association of a particular ventricular arrhythmia to other types of arrhythmia.

Methods

Forty-four patients admitted to the coronary care unit of the Radcliffe Infirmary with both electrocardiographic (recent ST segment elevation and Q wave development) and enzyme evidence (at least twice normal values of creatine kinase) of acute myocardial infarction were studied at a mean time of six hours after the onset of chest pain. Thirty patients were studied within six hours, 11 between six and 12 hours, and three between 12 and 18 hours after the onset of chest pain. Twenty-four of these
patients had anterior infarction and 20 had inferior infarction. The routine management was unaltered by the study procedure; diuretics, digoxin, and antiarrhythmic drugs were administered as indicated. A total of eight patients received lignocaine (100 mg as a bolus followed by an infusion of 4 mg/min for the first two hours, 3 mg/min for the next two hours, and then 2 mg/min for a period of 20 hours) as antiarrhythmic therapy when ventricular fibrillation or frequent runs of ventricular tachycardia were observed by the nursing staff. Five patients at entry were already on beta-adrenergic blocking drugs for treatment of angina pectoris or hypertension. Nine patients received oral atenolol 100 mg once daily as they were part of a prospective trial of beta-adrenergic blockade. No patient received beta-adrenergic blockers as antiarrhythmic therapy. Of the eight patients on lignocaine, five were also on beta-blockers so that 17/44 were on lignocaine or beta-blockers.

All patients had normal serum levels of potassium and calcium throughout the entire study period.

DETECTION OF VENTRICULAR ARHYTHMIAS
In all patients we made continuous recordings of the electrocardiogram on the Oxford Instruments Medilog tape-recorder for the first 48 hours after admission. The records were then analysed on an Oxford Instruments Medilog electrocardiograph analysis system at 60 times real time. An observer always checked that the signals counted by the analysis system were accurate. In addition, the tape was then reanalysed by visual counting by the observer. Hourly counts of heart rate, isolated ventricular extrasystoles, couplets (two consecutive ventricular extrasystoles), triplets (three consecutive ventricular extrasystoles), episodes of accelerated idioventricular rhythm (> 3 consecutive ventricular extrasystoles at a rate less than 120 beats/min), and ventricular tachycardia (> 3 consecutive ventricular complexes at a rate > 120/min) were recorded. Ventricular fibrillation occurred in only four of the 44 patients.

In most patients all isolated ventricular extrasystoles were recorded on paper. In a few patients with hourly rates of ventricular extrasystoles > 50/hour, sample recordings of ventricular extrasystoles during this period were obtained. In addition, all couplets, triplets, episodes of accelerated idioventricular rhythm, ventricular tachycardia, and ventricular fibrillation were recorded on paper. In cases of sustained accelerated idioventricular rhythm or ventricular tachycardia, the beginning and the end of the arrhythmia were recorded. These recordings were then analysed to ascertain:

(1) The prematurity index of the ventricular extrasystoles, couplets, triplets, accelerated idioventricular rhythm, ventricular tachycardia, and ventricular fibrillation.

(2) The heart rate preceding runs of accelerated idioventricular rhythm, ventricular tachycardia, and ventricular fibrillation from five consecutive sinus complexes.

(3) Rates of accelerated idioventricular rhythm and ventricular tachycardia.

STATISTICAL METHODS
Standard methods of correlation and regression, and paired and unpaired t tests were used. All data are expressed as mean ±1 standard deviation.

Results

(A) HEART RATE

(i) Variation over 24 hours (Fig. 1)
A significant positive correlation was observed between the standard deviation and the mean of the individual hourly heart rates over the first 24 hours (r = 0.507; p < 0.001) indicating greater variability in patients with higher heart rates.

(ii) Comparison between anterior and inferior infarcts
Although the mean heart rate in patients with anterior infarction tended to be higher (73.89 ± 18.94) as compared with 67.58 ± 13.36 in patients with inferior infarction, this did not reach statistical significance (p > 0.05).

(iii) Relation of mean heart rate to ventricular arrhythmias
The mean heart rate averaged over 24 hours in

![Graph illustrating the relation of mean heart rate to the variation in heart rate.](http://heart.bmj.com/)

*Fig. 1 Relation of the mean heart rate to the variation in heart rate.*
patients with ventricular tachycardia was not significantly different from those without ventricular tachycardia. Mean heart rate in patients with only accelerated idioventricular rate was 63 ±11·36 as compared with 69 ±12·70 in patients with accelerated idioventricular rate and ventricular tachycardia and 82·83 ±33·15 in patients showing ventricular tachycardia alone. This trend, however, did not reach statistical significance.

(iv) Relation of preceding heart rate to rate of ventricular arrhythmias
A significant positive correlation between preceding heart rate and the rate of the accelerated idioventricular rate or ventricular tachycardia was observed when compared as continuous variables (r=0·491; p <0·001). This relation was even more significant when accelerated idioventricular rate was considered separately (r=0·696; p <0·001; n=52) (Fig. 2). In contrast, no significant relation between preceding sinus rate and the rate of ventricular tachycardia was observed (r=0·295, n=34) (Fig. 3). However, the heart rate preceding ventricular tachycardia was faster (78·92 ±21·83) compared with the heart rate preceding accelerated idioventricular rate (67·79 ±18·01) (2p <0·02; unpaired "t" test; Fig. 4).

(v) Relation of preceding heart rate to prematurity index (Fig. 5)
A significant inverse correlation between the heart rate preceding accelerated idioventricular rate and ventricular tachycardia and the prematurity index of the first ventricular extrasystole was observed (r =-0·525; p <0·001, n =70).

(B) PREMATURITY INDEX
(i) Prematurity index and rate of ventricular arrhythmia
A significant inverse correlation between the prematurity index and the rate of the following accelerated idioventricular rate or ventricular tachycardia was observed (r =-0·506; p <0·001) (Fig. 6). In addition, the prematurity index preceding accelerated idioventricular rate was significantly longer than the prematurity index preceding ventricular tachycardia (1·89 ±0·53 and 1·32 ±0·48, respectively) (2p <0·001) (Fig. 4).

(ii) Prematurity index in patients with and without ventricular tachycardia
There was no significant difference when the prematurity index of both isolated ventricular extrasystoles and repetitive ventricular arrhythmia were compared in patients with and without ventricular tachycardia (1·31 ±0·38 in patients with ventricular tachycardia and 1·45 ±0·52 in those without it).

(C) ISOLATED VENTRICULARExtrasystoles
Forty-three of the 44 patients studied had ventricular arrhythmias during the 24-hour period.

(i) Incidence of ventricular extrasystoles related to time after chest pain
The number of isolated ventricular extrasystoles decreased significantly from 75·68 ±122·6 in the
first 24 hours to 40.98 ± 87.25 in the second 24 hours (paired “t” test 2p < 0.05).

(ii) Relation to incidence of accelerated idioventricular rate and ventricular tachycardia
Because the frequency of isolated ventricular extrasystole is not normally distributed, the data were expressed as logarithms before applying Student’s “t” test. In patients showing ventricular tachycardia, the log$_{10}$ ventricular extrasystole was 1.75 ± 0.45 as compared with 1.11 ± 0.87 in patients without ventricular tachycardia (2p < 0.01) (Fig. 4). In addition patients showing ventricular tachycardia and accelerated idioventricular rate had a significantly greater frequency of isolated ventricular extrasystoles as compared with patients showing neither rhythm (1.71 ± 0.70 in patients with tachycardia and/or accelerated rhythm and 0.83 ± 0.66 in patients without either) (2p < 0.001). This suggests that patients with repetitive ventricular rhythms have more frequent isolated ventricular extrasystoles. This is even more pronounced in patients with ventricular tachycardia.

(D) COUPLETS AND TRIPLETS
The incidence of couplets and triplets was 55 per cent and 34 per cent, respectively. Though both tended to be higher in patients with ventricular tachycardia (75% and 50%, respectively) as compared with patients without ventricular tachycardia (43% and 25%), this was not statistically significant.

(e) ASSOCIATION OF VENTRICULAR TACHYCARDIA AND ACCELERATED IDIOVENTRICULAR RHYTHM
We did not see any particular tendency for accelerated idioventricular rhythm and ventricular tachycardia to coexist in eight patients having both, eight with ventricular tachycardia only, and nine with accelerated idioventricular rhythm only.

(f) ANALYSIS OF DATA WITH RELATION TO TIME
The relation of preceding heart rate to the prematurity index and to the rate of accelerated idioventricular rhythm or ventricular tachycardia was similar in the first and second 12 hours of recording, and in patients presenting within or after six hours of pain. Similarly, the relation between the prematurity index and the rate of
accelerated idioventricular rhythm or ventricular tachycardia was independent of time.

(G) InFLUENCE OF DRUGS ON RELATION BETWEEN PRECEDING HEART RATE, PREMATURETY INDEX, AND RATE OF ACCELERATED IDIOVENTRICULAR RHYTHM AND VENTRICULAR TACHYCARDIA

Fourteen patients were on beta-blocking drugs during the period of tape-recording. The correlations between (1) preceding heart rate and prematurity index; (2) preceding heart rate and the rate of accelerated idioventricular rhythm and ventricular tachycardia; and (3) prematurity index and the rate of accelerated idioventricular rhythm and ventricular tachycardia were calculated in patients with and without beta-blocker treatment (Table). Similar correlations were found in all instances except one in the beta-blocker group, where no significant relation between preceding heart rate and the rate of accelerated idioventricular rhythm and ventricular tachycardia was observed. This suggests that the change in the prematurity index occurring at different heart rates is independent of any direct pharmacological action of beta-blockers and is probably related to heart rate changes per se.

Lignocaine was used in six patients within an hour of admission: four after ventricular fibrillation; and two for frequent ventricular tachycardia. In two other patients lignocaine was given after frequent runs of ventricular tachycardia were observed by the coronary care unit nurses approximately two hours after admission. This was continued for 24 hours as a continuous infusion and produced almost complete suppression of any ventricular tachycardia or accelerated idioventricular rhythm in these patients. It was therefore not possible to assess if the relation between preceding heart rate, prematurity index, and rate of sustained ventricular arrhythmia was altered by lignocaine.

(H) CHARACTERISTICS OF PATIENTS WITH VENTRICULAR FIBRILLATION

Four patients developed ventricular fibrillation within an hour of admission and all four showed separate runs of ventricular tachycardia two to 30 minutes before the episode of ventricular fibrillation compared with only one of four patients showing accelerated idioventricular rhythm. Three patients had preceding ventricular tachycardia with rates 170, 178, and 178/min. In one of these, an episode of ventricular tachycardia at 178/min deteriorated into ventricular fibrillation. The fourth patient had ventricular tachycardia at a rate of 138/min. In comparison only two out of the 40 patients without ventricular fibrillation had ventricular tachycardia at rates exceeding 170/min. In the first three patients the fibrillation was initiated by R on T ventricular extrasystoles (prematurity index = 0.62, 0.62, and 0.80, respectively). The fourth episode of ventricular fibrillation was initiated by an extrasystole falling at the end of the descending limb of the T wave (prematurity index = 0.90). In comparison, no patient without fibrillation showed a prematurity index less than 0.80. Two patients without fibrillation showed R on T extrasystoles (prematurity index = 0.82 and 0.84) one of whom also showed a run of ventricular tachycardia (170/min). Therefore patients with ventricular fibrillation showed faster ventricular tachycardia rates and earlier extrasystoles before the episode.

Discussion

Lown et al.4 defined a series of types of ventricular arrhythmia which were thought to be associated with an increased risk of ventricular fibrillation. Other workers have supported this original concept.5-11 Recent reports, however, do not support this and ventricular fibrillation has been reported to occur without warning arrhythmias.12,13 In addition warning arrhythmias have been found to be equally common in patients with and without ventricular fibrillation.5,14 Since the incidence of ventricular fibrillation is relatively low in patients in hospital because of the delay in admission (20 out of 850 admissions in one series),15 many investigators6,8,10 have looked at the precursors of ventricular tachycardia which are known to be associated with a high mortality. In our own study all four patients with ventricular fibrillation demonstrated ventricular tachycardia, with three having ventricular rates of 170/min or more before the episode. We have therefore studied "warning arrhythmias" before ventricular tachycardia occurs.

Like previous authors,5,10 we have observed a
higher incidence of isolated ventricular extrasystoles in patients with ventricular tachycardia. Though
couplets and triplets were more frequent in patients
with ventricular tachycardia as compared with those
without ventricular tachycardia, this difference did
not reach statistical significance. We have also
shown a significant decrease in the incidence of
ventricular extrasystoles with increasing time from
onset of chest pain, as the delay in the onset of tape-
recording would affect the probability of detecting
warning arrhythmia.16 Further, Lie et al.7 have
suggested that time after onset of chest pain should
be an important criterion for the institution of anti-
arrhythmic therapy.

In this study we have chosen a new and quantita-
tive approach to study the relation between
preceding heart rate, prematurity index, and the
rate of accelerated idioventricular rhythm and
ventricular tachycardia. To use sharp distinctions
of R on T and non-R on T is not wholly accurate
as there can be ventricular extrasystoles with
widely differing prematurity indices in each
category. Similarly the rate of ventricular tachycar-
dia or accelerated idioventricular rhythm is
more accurate than arbitrary definitions (about
which there is no unanimity)17 as the rates may
vary within each category. We have, therefore,
chosen to measure the individual prematurity index
and relate it to the rate of the accompanying
ventricular arrhythmia.

We have demonstrated a significant inverse
correlation between the prematurity index and the
rate of ventricular arrhythmia. However, Fig. 6
shows considerable scatter and it is evident that in
some individual instances short prematurity index
did not always lead to ventricular tachycardia. We
have also shown that ventricular tachycardia is
preceded by extrasystoles with a prematurity index
significantly shorter than those preceding acceler-
ated idioventricular rhythm. However, when we
compared the prematurity index in patients with
and without ventricular tachycardia, no significant
difference was obtained, consistent with the observa-
tions of De Soyza et al.5 and Chou and
Wenzke.6 The possible reasons for this apparent
discrepancy should be considered. The early studies
of Smirk1 and Bleifer et al.,3 though stressing that
the R on T ventricular extrasystole was associated
with a higher incidence of ventricular fibrillation
and tachycardia, also showed that this did not
always happen. It was Bleifer et al.2 who demon-
strated that R on T extrasystoles alone did not
carry a serious prognosis but that when seen in
combination with repetitive ventricular arrhythmia
they were dangerous. In fact, the majority of
Smirk's patients showed both the R on T
phenomenon and couplets, though this was not
discussed in his paper. Further, Dolara18 has shown
that the QT interval may be prolonged and when
associated with a slightly premature extrasystole
this gives the appearance of an R on T; this may
have a different significance. Recently Greene
et al.19 have reported that artificial cardiac
stimulation leading to repetitive ventricular activity
in patients after myocardial infarction could
identify patients prone to ventricular tachycardia
and sudden death. It is possible that only in such
patients whose ventricles are "vulnerable" to
ventricular tachycardia is the R on T extrasystole
of importance. In other patients it may not have
the same significance.

Reports that late ventricular ectopic beats may
initiate ventricular fibrillation and tachycardia do
not necessarily contradict the role of the R on T
extrasystole in their causation. Firstly, several
factors (for example critical mass of myocardium
available for re-entry, critical relation between
conduction velocity and refractory period in certain
parts of the myocardium, local myocardial electro-
lyte changes, disturbances of nervous regulation,
etc.) other than an extrasystole falling in the
"vulnerable period" may affect the response of the
ventricle regarding the development of ventricular
tachycardia and fibrillation.20 Secondly, Waldo and
Kaiser21 have shown, using epicardial recordings,
that localised fibrillation occurring in the infarct
zone continues after the T wave of the surface
electrocardiogram and that this was often associated
with the development of ventricular tachycardia
and fibrillation. It may therefore be possible that
ventricular extrasystoles occurring apparently after
the T wave on surface recordings may be occurring
during the period of fragmented electrical activity
when the ventricle may be "vulnerable".

We have shown a significant relation between
preceding heart rate and the rate of sustained
ventricular arrhythmia. This relation appears to
be mainly for accelerated idioventricular rhythm
and not for ventricular tachycardia. This observation
supports the possibility that accelerated idioven-
tricular rhythm is usually an escape rhythm.17
However, the heart rate preceding runs of ventricu-
lar tachycardia was significantly higher than that
preceding accelerated idioventricular rhythm. Lie
et al.7 have reported a higher incidence of sinus
tachycardia immediately preceding ventricular
fibrillation. Recent experimental work22 has shown
that a rapid heart rate may increase ventricular
extrasystoles, non-homogeneity of refractory periods
in contiguous areas of the myocardium, and
vulnerability to ventricular fibrillation. In addition
slow heart rates caused by vagal stimulation per se
also increased ventricular fibrillation threshold. These considerations support our observations of a direct relation between heart rate and the rate of ventricular arrhythmia.

A significant inverse correlation between preceding heart rate and the prematureity of the ventricular ectopic has been shown. This may indicate that increasing heart rates may lead to ventricular ectopic beats with shorter prematureity index. The possibility that this may be an artefact must be considered. It is possible that as heart rate increases, and the RR interval decreases, the coupling interval of a manifest ventricular extrasystole may shorten correspondingly. However the QT interval also shortens with increasing heart rate and therefore any shortening of the prematureity index at fast heart rates is likely to be real and not artefact. However, the underlying mechanism for this relation is unclear and we are not aware of any work relating heart rates to the prematureity index.

We have shown that faster heart rates are associated with ventricular ectopic beats with shorter prematureity, which may in turn lead to faster ventricular arrhythmia in “susceptible” patients. This relation, however, may not exist in patients not susceptible to repetitive ventricular arrhythmias.

References


Requests for reprints to Dr S Yusuf, Department of Cardiovascular Medicine, John Radcliffe Hospital, Headington, Oxford OX3 9DU.