Etiology, Warning Signs and Therapy of Torsade de Pointes
A Study of 10 Patients

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SUMMARY  Torsade de pointes, also called atypical ventricular tachycardia (AVT), was diagnosed in 10 patients, nine on antiarrhythmic therapy and one with acute central nervous system damage. Four patients received quinidine and five disopyramide, either alone or in combination with amiodarone. AVT was dose-dependent in some, but in others, it started shortly after initiation of drug therapy (idiosyncrasy). All patients had QT prolongation longer than 0.60 second immediately before the onset of AVT. This measurement appeared to be a more sensitive predictor of the development of AVT than QTc prolongation or QRS widening. All patients also showed bradycardia before AVT onset. After therapy, the QT immediately decreased, while QTc and QRS remained prolonged for longer periods. Isoproterenol was effective in five of seven patients, but was contraindicated in two others. Ventricular pacing was used in four patients, including the two who did not respond to isoproterenol, and this abolished AVT promptly. Isoproterenol or pacing appear to be the therapy of choice for AVT, while the conventional drugs used to treat the usual form of ventricular tachycardia are not only ineffective, but even contraindicated.

References

a period of 1 year. The ECG warning signs that preceded the AVT in these patients, especially the QRS width, the QT and the Qtc intervals, are analyzed. The therapeutic approaches we and others have used are detailed.

Methods

AVT was diagnosed during a 12-month period in 10 patients, nine females and one male, ages 44–84 years, who were hospitalized in our intensive coronary care unit. This unit is equipped with Mennen-Greatbach bedside monitors with a direct-signal system to a central ECG monitoring console with a delay output of 10 seconds. Eight patients had been hospitalized for recurrent atrial fibrillation or tachycardia, one patient for multiple ventricular premature complexes (VPCs) and one for acute myocardial infarction. Routine electrolyte levels were within normal limits. The associated diagnosis and other clinical data are summarized in table 1.

AVT was diagnosed when a series of ectopic ventricular complexes, usually four to 20 beats, with frequently undulating QRS axis and changing QRS configuration occurred. Heart rates were 150–300 beats/min, with marked variability during the episodes. In every case, a VPC with a long coupling interval, ranging from 0.44–0.68 second, initiated AVT. The episodes usually terminated spontaneously, often with a VPC intermediate in form between the QRS of the basic tracing and that seen during the AVT; sometimes, the final beat was identical to the initiating VPC. The longest spontaneously terminating run of AVT lasted 28 seconds. After termination, the episodes tended to recur unless treated with antiarrhythmic drug. The ECGs recorded before and after the AVT were analyzed for basic rhythm, ventricular rate, QRS width, QT and QTC intervals (Bazett formula) and for associated electrical disturbances. The drug therapy given before the AVT and the response to the therapeutic measures were evaluated.

Results

Antiarrhythmic Drugs Given Before AVT (table 1)

Nine patients (cases 1–9) received antiarrhythmic drug therapy before the appearance of AVT. Quinidine sulfate was given to cases 1–4, disopyramide to cases 5–7 and a combination of disopyramide and amiodarone to cases 8 and 9. Case 10 suffered from transient central nervous system damage and had attacks of paroxysmal atrial tachycardia alternating with sinus bradycardia with constantly prolonged QT and QTC intervals; this patient did not receive any antiarrhythmic drug.

The antiarrhythmic drugs were given chronically to three patients. Case 1 received quinidine sulfate, 1.2
Table 1. (Continued)

<table>
<thead>
<tr>
<th>Rhythm</th>
<th>Ventr. rate</th>
<th>QT</th>
<th>QTc</th>
<th>Effective therapy of AVT</th>
<th>Rhythm</th>
<th>Ventr. rate</th>
<th>QT</th>
<th>QTc</th>
</tr>
</thead>
<tbody>
<tr>
<td>SR</td>
<td>100</td>
<td>0.44</td>
<td>0.56</td>
<td>At 1 mg</td>
<td>SR</td>
<td>95</td>
<td>0.52</td>
<td>0.66</td>
</tr>
<tr>
<td>SR</td>
<td>86</td>
<td>0.48</td>
<td>0.57</td>
<td>VP</td>
<td>SR</td>
<td>105</td>
<td>0.56</td>
<td>0.74</td>
</tr>
<tr>
<td>SR, 3° AVB</td>
<td>38</td>
<td>0.64</td>
<td>0.51</td>
<td>VP</td>
<td>SR, 3° AVB</td>
<td>90</td>
<td>0.46</td>
<td>0.56</td>
</tr>
<tr>
<td>SR</td>
<td>40</td>
<td>0.66</td>
<td>0.54</td>
<td>VP</td>
<td>SR</td>
<td>88</td>
<td>0.46</td>
<td>0.56</td>
</tr>
<tr>
<td>SR</td>
<td>115</td>
<td>0.32</td>
<td>0.44</td>
<td>I 2 µg/min</td>
<td>SR</td>
<td>81</td>
<td>0.59</td>
<td>0.68</td>
</tr>
<tr>
<td>SR</td>
<td>84</td>
<td>0.34</td>
<td>0.40</td>
<td>I 2 µg/min</td>
<td>SR</td>
<td>92</td>
<td>0.38</td>
<td>0.47</td>
</tr>
<tr>
<td>SR, 2° AVB</td>
<td>49</td>
<td>0.66</td>
<td>0.59</td>
<td>VP</td>
<td>SR, 2° AVB</td>
<td>100</td>
<td>0.44</td>
<td>0.57</td>
</tr>
<tr>
<td>SR</td>
<td>75</td>
<td>0.48</td>
<td>0.54</td>
<td>I 2 µg/min</td>
<td>SR</td>
<td>100</td>
<td>0.48</td>
<td>0.62</td>
</tr>
<tr>
<td>SR</td>
<td>63</td>
<td>0.56</td>
<td>0.57</td>
<td>I 2 µg/min</td>
<td>SR</td>
<td>70</td>
<td>0.60</td>
<td>0.65</td>
</tr>
<tr>
<td>SR</td>
<td>64</td>
<td>0.64</td>
<td>0.66</td>
<td>I 2 µg/min</td>
<td>SR</td>
<td>75</td>
<td>0.52</td>
<td>0.58</td>
</tr>
<tr>
<td>SR</td>
<td>71.4</td>
<td>0.520</td>
<td>0.538</td>
<td></td>
<td>SR</td>
<td>89.6</td>
<td>0.503</td>
<td>0.609</td>
</tr>
</tbody>
</table>

For several years and cases 5 and 6 received disopyramide, 300 mg/day, for 3 and 6 months, respectively. An increase of the doses of these drugs within the therapeutic range resulted in the appearance of AVT after 24-48 hours. Therefore, in these patients, AVT can be regarded as a dose-dependent phenomenon. In case 1, the quinidine level on the day of the AVT (7.0 µg/ml) was slightly above normal (range of normal 3.0-6.0 µg/ml). In cases 2, 3, 4 and 7, AVT developed 2-24 hours after beginning quinidine or disopyramide therapy and is therefore regarded as an idiosyncratic reaction. In cases 8 and 9, disopyramide, 300 mg/day, was given for a relatively long period (3 months and 6 months, respec-

Figure 1. Case 7 (A) Typical episodes of torsade de pointes in a patient with second-degree atrioventricular block; note the marked QT prolongation (continuous strips). (B) Ventricular pacing at 100 beats/min abolished ventricular ectopic activity. (All tracings in this and subsequent figures are from monitor leads.)
Baseline ECG and ECG Immediately Before AVT (tables 1 and 2)

Nine patients suffered from recurrent supraventricular tachyarrhythmias and one patient had multiple VPCs. Before receiving the antiarrhythmic therapy or the particular dosage that caused AVT, the heart rate ranged from 65–90 beats/min (mean 74 beats/min), the width of the QRS complex ranged from 0.06–0.11 second (mean 0.074 second), the QT interval ranged from 0.30–0.48 second (mean 0.376 second) and the QTc ranged from 0.39–0.51 second (mean 0.450 second). These measurements were performed during periods of regular sinus rhythm.

Immediately before the initial AVT episode, all patients had a slow ventricular rate (40–65 beats/min). Seven patients had sinus bradycardia, one had nodal bradycardia, and two had atrioventricular blocks, third-degree in case 3 and second-degree, Mobitz type II in case 7. All patients had a widening of the QRS and a prolongation of QT interval and QTc. The width of the QRS complex increased by an average of 23%. The widening was 16% or less in cases 1, 4, 5 and 7, 20% in case 2 and 33–43% in cases 3, 6, 8 and 9. Case 10, who suffered from central nervous system damage, had a 14% increase of QRS width in the immediate pre-AVT period. The mean QT interval increased by 73% (range 0.60–0.70 second), whereas the mean QTc increased by 35.5% (range 0.52–0.71 second).

ECG Immediately After Spontaneous Cessation of AVT (table 1)

In six patients, the spontaneous cessation of the AVTs was followed by a transient acceleration of the ventricular rate compared with the pre-AVT period (increase from a mean rate of 54.5 beats/min to 87.1 beats/min) and shortening of the mean QT interval (from 0.67 to 0.43 second). The mean QTc interval was also shortened, from 0.63 to 0.51 second (fig. 2). In cases 3, 4, 7 and 10 in whom third-degree atrioventricular block, sick sinus syndrome, second-degree atrioventricular block and central nervous system damage were found, respectively, there was no increase in the heart rate or decrease in QT or QTc intervals after spontaneous cessation of AVT.

Therapeutic Measures and Responses (tables 1–3)

In six patients, DC shocks were repeatedly applied, but new episodes of AVT recurred in all. The DC shocks were used to stop long AVTs that led to loss of consciousness, or when AVTs deteriorated into uniform ventricular tachycardia (fig. 3) or ventricular fibrillation. Lidocaine was given to cases 1, 2, 3 and 8 through bolus injections of 100 mg and continuous infusions up to 3 mg/min; this drug was ineffective in all instances. Intravenous procainamide was tried in case 2 and was not only ineffective, but the frequency of the AVT episodes seemed to increase.

Atropine, as much as 1.5 mg i.v., was given to four patients but abolished the AVT in only one (case 1). In the three cases in whom atropine was ineffective, sinus node activity did not increase after its administration.

Isoproterenol (2–8 μg/min) was used in seven patients; this drug was effective in five patients in whom immediate disappearance of the AVT was observed, concomitant with a quickening of the heart rate in all five.

Ventricular pacing was applied to cases 2, 3, 4 and 7. In two, the AVTs were refractory to previous isoproterenol and in the other two, pacing was the first attempted mode of therapy, as isoproterenol was regarded hazardous because of recent myocardial infarction in case 7 and excessive hypertension in case 3. In these four patients all ventricular arrhythmias were abolished at a pacing rate of 88–105 beats/min, always using the lowest effective rate for abolishing the AVT. The pacing was continued for as long as 48 hours and the electrode was withdrawn after an additional 24 hours. In two of these patients, atrial pacing was tried, and although it was initially effective, ventricular pacing was preferred because of the unstable electrode position during atrial pacing.

Table 2. Summary of Important ECG Measurements in 10 Patients with Atypical Ventricular Tachycardia

<table>
<thead>
<tr>
<th>Table 2. Summary of Important ECG Measurements in 10 Patients with Atypical Ventricular Tachycardia</th>
<th>In baseline ECG</th>
<th>Immediately before AVT</th>
<th>Change from baseline ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS (sec)</td>
<td>0.06–0.11 (mean 0.074)</td>
<td>0.07–0.12 (mean 0.091)</td>
<td>9–43% (mean 23%)</td>
</tr>
<tr>
<td>QT (sec)</td>
<td>0.30–0.48 (mean 0.376)</td>
<td>0.60–0.70 (mean 0.650)</td>
<td>33–113% (mean 70%)</td>
</tr>
<tr>
<td>QTc (sec)</td>
<td>0.39–0.51 (mean 0.450)</td>
<td>0.52–0.71 (mean 0.603)</td>
<td>4–55% (mean 35.5%)</td>
</tr>
</tbody>
</table>

Immediately after initiation of the effective treatment (pacing, isoproterenol or atropine), the heart rate increased in all 10 patients, from a mean of 52.4 beats/min to a mean of 89.6 beats/min (an average increase of 71%). The QT shortened, from a mean of 0.65 second to a mean of 0.50 second (an average decrease of 23%). Two patients had a shortening of the QTc interval; in four it became longer and in four others, it did not change; the mean QTc was 0.61 second both before and after therapy. The QRS width narrowed in three patients, from a mean of 0.086 second to 0.073 second (a decrease of 15%). In the other five patients (including cases 2 and 4, in whom atrial pacing was applied initially), QRS width did not change, whereas in cases 3 and 7, in whom ventricular pacing was applied as initial therapy, the QRS complexes became broader with ventricular pacing.

In cases 2, 3, 4 and 7, the QT returned to normal within 24 hours after the quinidine or disopyramide treatment was stopped. These were the patients in
whom the prolongation of the QT interval and the AVT appeared shortly after the beginning of the anti-arrhythmic therapy.

In cases 1, 5, and 6, who received quinidine and disopyramide for long periods before the appearance of the AVT, the QT returned to normal values only after 2, 2 and 3 days, respectively, after cessation of drugs. In cases 8 and 9, who received a combination therapy of amiodarone and disopyramide, the prolongation of the QT interval lasted for 5 days after cessation of the drugs. In case 10, the QT interval prolongation persisted for 2 weeks.

After withdrawal of AVT-inducing drugs and cessation of therapeutic measures against the AVT, the initial supraventricular arrhythmias (atrial fibrillation or tachycardia) occurred in seven of nine patients. This occurred only after the QT regained its normal values (0.30–0.44 second) and the QTc decreased to 0.40–0.42 second.

### Table 3. Details on Response to Various Treatments in 10 Patients with Atypical Ventricular Tachycardia

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of patients receiving therapy</th>
<th>No. of patients with favorable response</th>
</tr>
</thead>
<tbody>
<tr>
<td>DC shock</td>
<td>6</td>
<td>Transient effect in all</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Procainamide</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Atropine</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Ventricular pacing</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

**Discussion**

**Etiology and Mechanisms of AVT**

AVT is a life-threatening arrhythmia that usually occurs during quinidine therapy. However, in our study, only four of the 10 patients developed this complication while taking quinidine, whereas disopyramide caused AVT in three cases and a combination of disopyramide and amiodarone caused it in two others. The relatively high incidence of disopyramide-induced AVT is surprising; disopyramide induces AVT only in sporadic instances and is regarded as safe and well-tolerated. Although disopyramide is used much less frequently than quinidine in our service, a similar number of patients developed AVT on each drug during the 12-month period of this series. Amiodarone has been described to induce AVT only when given in association with other QT-prolonging drugs; the addition of this drug to two of our patients who were already treated with disopyramide resulted in AVT. After the cessation of amiodarone, disopyramide alone did not induce AVT in these patients. The only patient who did not receive anti-arrhythmic drugs before AVT was case 10, in whom acute central nervous system damage was followed by attacks of AVT; this occurrence has already been described.

Both idiosyncrasy and dose-dependency are well-recognized causes of AVT and idiosyncrasy has been assumed to be the more frequent. However, AVT occurred as an idiosyncratic reaction in only four of our patients, whereas it was a dose-dependent phenomenon in five, and in two of these it resulted...
from an assumed combined effect of amiodarone and disopyramide.

**Electrocardiographic Features**

Widening of the QRS complex by 25–50% or QRS width reaching 0.16 second are signs of quinidine toxicity that mandate discontinuation of the drug because they indicate a high risk of developing ventricular tachycardia or fibrillation.22–25 Among the nine patients taking antiarrhythmic drugs in our group, five developed AVT despite a QRS complex widening of less than 20%; the widest QRS we observed was 0.12 second.

According to some investigators,22–25 prolongation of the QT interval with quinidine does not necessarily require modification of the therapy. Other authors who reported cases of AVT described prior QT prolongation but did not advocate a specific value beyond which the drug should be withdrawn. In our series, the most striking feature was the marked prolongation of the QT interval, to 0.60 second or greater; this prolongation preceded the AVT in all cases. Sclarovsky and co-workers14 described polymorphous ventricular tachycardia in some patients with QT interval shorter than 0.56 second. However, in their series, not all patients fulfilled the criterion of torsade de pointes, diagnosed only “when an undulatory rhythm with continuous change in direction (in QRS axis) was observed.”14 In our patients, the range of the QT interval before the AVT was relatively narrow (0.60–0.70 second) while the range of the QTc was wider (0.52–0.71 second). Furthermore, in all 10 patients effective therapy was followed by an immediate shortening of the QT but not of the QTc. Thus, the actual QT rather than QTc may be more reliable in heralding AVT and evaluating the efficacy of therapy. We suggest that an uncorrected QT greater than 0.60 second may be an indication that the patient is at increased risk and may warrant withdrawal of the drug used. However, further data are required to confirm this as an absolute proscription.

All of our patients had a slow heart rate before AVT. The prolonged QT with the antiarrhythmic agents reflects a delayed repolarization process, and bradycardia by itself has a similar effect.11, 28 Thus, the combination of bradycardia and prolonged QT appears to produce a particular proneness to AVT. This may explain why none of our patients developed AVT during an attack of ectopic supraventricular tachycardia. Six of our patients had transient acceleration of the ventricular rate immediately after spontaneous cessation of the AVT. This seems to result from an increased intrinsic sympathetic activity secondary to the sudden decrease in the blood pressure during the AVT.34, 35 However, a tachycardic response does not appear to be a prerequisite for spontaneous cessation of AVT episodes, as no increase of the ventricular rate was found after the spontaneous termination of the episodes in four of our patients, those with atrioventricular block, sick sinus syndrome or brain damage.

In case 2, 3, 4 and 7, who developed AVT as an idiosyncratic reaction, the return of the QT interval to normal was faster than in cases 1, 5, 6, 8 and 9, who had a dose-dependent AVT. All patients were free of supraventricular ectopic activity as long as the QT was prolonged; the recurrence of the initial supraventricular-
ular arrhythmia in seven patients occurred only after the return of the QT to normal.

Treatment of AVT

The therapy of AVT is aimed at shortening and
unifying the prolonged and nonuniform repolarization,
which is the basic electrophysiologic disturbance
responsible for this arrhythmia.5, 11 The use of
conventional therapy for suppression of ectopic
ventricular activity is therefore not only ineffective but
may even aggravate the arrhythmia.11, 13 Acceleration
of the heart rate is the simplest and fastest mode for
shortening the QT interval and for abolishing the tem-
poral dispersion of repolarization present during
AVT.6, 11, 34-39 Isoproterenol is the most commonly
used drug for this purpose11, 37-39 and was effective
in five of the seven patients to whom it was given. Partial
success with isoproterenol has been reported.13
Although isoproterenol can be easily and rapidly
applied, it carries certain risk: It markedly increases
myocardial oxygen demand and may cause a variety
of peripheral vascular effects, and therefore should be
avoided in patients with acute myocardial infarction,
angina pectoris or high blood pressure.

Ventricular pacing for the treatment of AVT can be
instituted safely and rapidly in intensive care
units.6, 13, 14, 16, 18, 20 It can be used safely in patients
with active coronary disease, hypertension and atrio-
ventricular block and in all patients in whom isopro-
terenol therapy is ineffective. Pacing also enables one
to determine accurately the minimal rate at which the
recurrence of AVT can be prevented.14, 38 Although
pacing from the atrium may be hemodynamically ad-
vantageous,40 the electrode anchoring in the ventricle
is much more stable. The unsafety of the atrial elec-
trode position for long-term pacing was demonstrated
in our case 2, in whom AVT's immediately recurred during intermittent failures of atrial pacing.

We conclude that disopyramide, either alone or in
combination with other QT-prolonging agents such as
amiodarone, seems to increase the incidence of AVT.
Prolongation of the actual QT above 0.60 second,
rather than QTc or QRS widening, may be an im-
portant warning sign that requires modification of ther-
apy. A combination of prolonged QT and bradycardia
may be especially deleterious. For therapy of
AVT, we suggest early institution of isoproterenol or
ventricular pacing, which are the most effective means
of increasing the heart rate and shortening the QT in-
terval.

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Deputy Head Nurse, and all other nurses and staff of the intensive
coronary care unit for their invaluable assistance. The secretarial
help of Rachel Kosh is greatly appreciated.

References

1. Selzer A, Wray HW: Quinidine syncope, paroxysmal ventricu-
lar fibrillation occurring during treatment of chronic atrial
arrhythmias. Circulation 30: 17, 1964
2. Dessertenne F: La tachycardie ventriculaire à deux foyers op-
3. Dessertenne F: Le complexe electrique ventriculaire à phase
lente prolongée. Semin Hop Paris 43: 539, 1967
ventriculaire à foyer variable et dyskaliemie. Arch Mal Coeur
62: 1578, 1969
5. Motte G, Counel PH, Abitbol G, Dessertenne F, Slama R: La
syndrome QT long et syncope par "torsade de pointes." Arch
Mal Coeur 63: 831, 1970
en torsade de pointes. Actual Cardio-Vasc Med-Chirurg 6: 171,
1972
7. Slama R, Counel P, Motte G, Gourgon R, Waynberge M,
Touche S: TACHYCARDIES VENTRICULAIRES ET TORSADE DE
PONTES. Actual Cardio-VASC Med-Chirurg 6: 171, 1972
8. Rainer-Pope CR, Schrire V, Beck W, Barnard CN: The treat-
ment of quinidine-induced ventricular fibrillation by closed-
skate resuscitation and external defibrillation. Am Heart J 63:
582, 1962
Heart J 2: 517, 1965
10. Gravel J, Slodki S: Recurrent ventricular fibrillation
12. Koster RW, Wellens HJJ: Quinidine induced ventricular flutter
and fibrillation without digitalis therapy. Am J Cardiol 38: 519,
1976
13. Anderson JL, Mason J: Successful treatment by overdrive pac-
ing of recurrent quinidine syncope due to ventricular tachy-
14. Sclorovsky S, Strasberg B, Lewin RF, Agmon J: Polymor-
phous ventricular tachycardia: clinical features and treat-
ment. Am J Cardiol 44: 339, 1979
ventricular tachycardia: manifastation of disopyramide
toxicity. Am J Cardiol 42: 1049, 1979
ramide induced ventricular fibrillation. Am J Cardiol 43: 1053,
1979
17. Schoomaker FW, Oosten RT, Greenfield JC: Thoridizaine
(Mellaril)-induced ventricular tachycardia controlled with an
18. Leob HS, Pletras RJ, Gunnar RM, Tobin JR Jr: Paroxysmal
ventricular fibrillation in two patients with hypomagnesemia.
Treatment by transvenous pacing. Circulation 37: 210, 1968
19. Evans TR, Curry PVL, Fitchett DH, Krieker DM: Torsade de
pointes: initiated by electrical ventricular stimulation. J Elec-
trocardiol 9: 255, 1976
20. Basso JH, Schiendel DF: Congenital complete heart block and
long QT syndrome requiring ventricular pacing for control of
refractory ventricular tachycardia and fibrillation. J Electro-
cardiol 12: 331, 1979
21. Grossman MH: Cardiac arrhythmias in acute central nervous
system disease. Successful management with stellate ganglion
Saunders, 1966, p 554
23. Marriott HJL: Practical Electrocardiography, 6th ed. Balti-
more, Williams & Wilkins, 1973, p 303
Oxford, Blackwell, 1976, p 84
25. Hurst JW, Logue RB, Schlant RC, Wenger NK (eds): The
Heart, Arteries and Veins, 4th ed. New York, McGraw-Hill-
Blakiston Publication, 1978, p 1948
26. Kossman CE: Torsade de pointes: an addition to the nosog-
27. Bazzett HC: An analysis of the time relations of the electro-
cardiogram. Heart 7: 353, 1920
28. Vismara LA, Vera A, Miller RR, Mason DT: Efficacy of di-
opyramide phosphate in the treatment of refractory ventricular
tachycardia. Am J Cardiol 39: 1027, 1977
29. Sloman JG, Hunt D, Vohra J, Dowling J, Duffield A: Oral diso-
pyramide in the management of cardiac arrhythmias. Med J
Intermediate-density Lipoprotein and Cholesterol-rich Very Low Density Lipoprotein in Angiographically Determined Coronary Artery Disease

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SUMMARY The relationship between the concentrations of intermediate-density lipoprotein (IDL) and other lipoproteins and the extent of coronary artery disease (CAD) was studied in 182 consecutive patients evaluated by selective coronary cineangiography. On univariate analysis, the extent of CAD correlated significantly and positively with very low density lipoprotein (VLDL) cholesterol, IDL cholesterol and low-density lipoprotein (LDL) cholesterol, and negatively with high-density lipoprotein (HDL) cholesterol. Analysis of four subgroups divided by IDL cholesterol and LDL cholesterol levels indicated that moderately increased levels of IDL cholesterol were closely associated with a high frequency of CAD. Moreover, multivariate regression analysis demonstrated that IDL cholesterol for men, LDL cholesterol for men and women and HDL cholesterol for men were significant variables of use in the final weighting procedure. IDL cholesterol was closely associated with cholesterol-rich VLDL. This study shows that IDL and cholesterol-rich VLDL combine to contribute to the development of CAD.

PLASMA LIPIDS and lipoproteins have been reported to be closely related to the development of coronary atherosclerosis.1-7 Plasma lipids are carried in the lipoproteins, each of which has a different effect on atherosclerosis.8 Therefore, the levels of individual lipoproteins are better predictors of coronary artery disease (CAD) than those of plasma lipids. Plasma lipoproteins are usually divided into five classes:8 chylomicrons, very low density lipoprotein (VLDL, d < 1.006), intermediate-density lipoprotein (IDL, d 1.006-1.019), low-density lipoprotein (LDL, d 1.019-1.063), and high-density lipoprotein (HDL, d 1.063-1.210). Recent studies emphasize that the concentrations of LDL correlate positively and HDL correlate negatively with CAD.1, 3, 4, 6

The relationship between VLDL and CAD has been less well defined.8-10 In 1956, Gofman et al.11 reported that atherosclerosis, as manifested by definite evidence of CAD, was associated with an antecedent elevation of the serum S, 20-100 and possibly S, 12-20 lipoprotein (IDL). However, there have been few studies on IDL and the extent of CAD. Only case reports12 and few epidemiologic data are available.6 IDL and cholesterol-rich VLDL accumulate in abnormally high concentrations in the plasma of patients with type III hyperlipoproteinemia (broad β disease), which is highly associated with severe and premature atherosclerosis of coronary and peripheral arteries.13 Thus, it is suggested that IDL strikingly accelerates CAD.
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