Lack of effect of bed rest and cigarette smoking on development of deep venous thrombosis after myocardial infarction

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In a prospective study of patients admitted to a coronary care unit, the incidence of isotopically diagnosed deep venous thrombosis was found to be related to the severity of illness rather than to the duration of bed rest. In addition, no negative correlation was found between cigarette smoking and deep venous thrombosis.

Bed rest is considered to be an important predisposing cause of venous thrombosis (Gibbs, 1957). In patients who have had a myocardial infarction, figures for isotopically-diagnosed venous thrombosis have varied widely, with reported frequencies as low as 12 per cent but as high as 38 per cent (Murray *et al.*, 1970; Wray, Maurer, and Shillingford, 1973; Warlow *et al.*, 1973; Simmons, Shepard, and Cox, 1973; Habersberger, Pitt, and Anderson, 1973; Marks and Emerson, 1974). The recommended period of bed rest after a myocardial infarction has also varied widely (Grodin, Allison, and Shaw, 1967; Hayes, Morris, and Hampton, 1974), and it remains unclear whether the risk of venous thrombosis is associated with the severity of the underlying illness or with prolonged immobility and bed rest to which the more seriously ill patient may be subjected.

During a comparative study of patients with uncomplicated myocardial infarction mobilized after 2 or 9 days (Hayes *et al.*, 1974), we used the ¹²⁵I-labelled fibrinogen uptake test to determine the frequency of venous thrombosis. In addition, we studied the frequency of venous thrombosis in patients whose myocardial infarctions were complicated by heart failure, arrhythmia, or persistent chest pain, and the frequency in patients admitted to a coronary care unit because of chest pain but who were eventually found not to have had a myocardial infarct. We have also considered the suggestion that cigarette smokers with myocardial infarction develop venous thrombosis less fre-

quently than non-smokers (Marks and Emerson, 1974; Handley and Teather, 1974).

Patients and methods

For one year, all patients admitted to the coronary care unit (CCU) at Nottingham General Hospital were considered for entry into a mobilization study. All such patients had a history suggestive of myocardial infarction but the diagnosis was only accepted if characteristic electrocardiographic abnormalities occurred or there was a rise in serum enzymes [creatinine kinase (CK), aspartate aminotransferase (AST), lactic dehydrogenase (LD), or hydroxybutyric dehydrogenase (HBD)]. At 48 hours after admission to hospital, patients with a definite myocardial infarction were divided into 'complicated' and 'uncomplicated' groups. Patients with proven myocardial infarction were placed in the 'complicated' group if they had persistent chest pain, heart failure (judged clinically by the presence of breathlessness, a raised jugular venous pressure, triple rhythm, and basal crepitations or by radiological evidence of pulmonary oedema), or a significant arrhythmia. Any arrhythmia requiring treatment at 48 hours, or a sinus tachycardia of greater than 110 beats/minute was considered significant. Patients without complications were randomly allocated to a 2- or 9-day mobilization programme according to a ward rota (Hayes *et al.*, 1974). Accordingly four groups of patients were derived as follows:

Group 1: Complicated myocardial infarction.

Group 2: Uncomplicated myocardial infarction, mobilized after 2 days.

Group 3: Uncomplicated myocardial infarction, mobilized after 9 days.

Group 4: Chest pain not caused by myocardial infarction.

In groups 1 and 4 no specific mobilization programme was followed, but a record was kept of the first day on which the patients were allowed to walk around the ward.

The study consisted of 266 patients, all of whom had given informed consent, who were assessed for the incidence of isotopically diagnosed venous thrombosis.

^{125}I -labelled fibrinogen was obtained from the Radiochemical Centre, Amersham. Each patient received an intravenous injection of 100 μCi of the labelled fibrinogen within 36 hours of admission to hospital, with the exception of 5 patients in whom the injection was delayed until 72 hours. Isotope scanning using a Pitman 235 localization monitor was done daily (excluding weekends) for 10 days, unless death supervened. Legs were scanned at 5 cm intervals from the level of the popliteal fossa to the ankle and a diagnosis of venous thrombosis was made if a difference in uptake of 20 per cent or more was shown between adjacent sites on the calf or a corresponding position on the opposite limb which persisted for at least 24 hours. The day on which a scan became positive was related to the date of admission to hospital and not to the date of isotope injection.

Results

A total of 266 patients with a suspected myocardial infarction were admitted to the CCU during the study period and were scanned. Table 1 compares the four groups of patients at their formation 48 hours after admission to hospital. Patients in group 1 (complicated myocardial infarction) had a significantly greater mean AST level (251 ± 25 IU) than the patients in groups 2 and 3 (151 ± 99 and $146 \pm$

TABLE 2 Incidence of positive ^{125}I -labelled fibrinogen scans

	Group 1	Group 2	Group 3	Group 4
Scan positive	21	15	10	6
Scan negative	42	69	52	51
% positive	33	18	16	11

TABLE 3 Comparison of active cigarette smokers with non-smokers

	Cigarette smokers	Non-smokers
Scan positive	28	14
Scan negative	85	55
% scan positive	25	20

109 IU respectively). There was also a significantly greater number of patients (39%) in group 1 who had sustained an anterior myocardial infarction compared with groups 2 and 3 (29% and 20%, respectively), reflecting the higher incidence of early complications in patients with anterior myocardial infarction.

In group 1, 33 per cent of patients developed isotopic evidence of venous thrombosis compared with 18 per cent and 16 per cent in groups 2 and 3, respectively, and only 11 per cent in group 4 (Table 2). The higher frequency of isotopically diagnosed venous thrombosis in patients with complicated myocardial infarction (group 1) is statistically significant ($\chi^2 = 10.4658$, $P < 0.05$). Within group 1 the mean day of mobilization of all patients was 6.3 days; the mean day of mobilization of the scan positive patients was 6.6 days; and the mean day of mobility of the scan negative patients was 6.1 days. The enhanced risk of venous thrombosis occurring in patients with a complicated myocardial infarction (group 1) was not selectively associated with any individual complication such as heart failure or arrhythmia.

Information on smoking habits was known in 229 patients but was not recorded in 37 (27 from groups 1, 2, and 3, and 10 from group 4). The number of active cigarette smokers in each of the groups of patients who suffered a proven myocardial infarction was similar (group 1 65%, group 2 63%, and group 3 59%), but was lower in the patients with chest pain not caused by myocardial infarction (group 4 45%). Examination of the combined groups of patients with a myocardial infarction failed to reveal a negative association between cigarette smoking and the development of deep venous thrombosis ($\chi^2 = 0.2662$, $P > 0.5$) (Table 3).

TABLE 1 Comparison of groups at 48 hours after admission to hospital

	Group 1	Group 2	Group 3	Group 4
Patients scanned	63	84	62	57
Mean age (y)	59 ± 9	56 ± 9	55 ± 7	56 ± 9
Men:Women	58:5	74:10	53:9	47:10
Mean duration of chest pain (h)	7.0 ± 11.0	7.7 ± 12.3	6.6 ± 10.6	6.9 ± 10.3
Site of infarction				
Anterior	40	29	20	—
Inferior	12	37	28	—
Others	11	18	14	—
Mean max. AST $\pm$ SD	251 ± 25	151 ± 99	146 ± 109	33 ± 29

This was true when cigarette smokers were compared with those people who had never smoked any form of tobacco ($\chi^2=2.4893$, $P>0.1$), or with persons who had previously smoked cigarettes or who were current pipe or cigar smokers ($\chi^2=0.0269$, $P>0.7$). Similarly, cigarette smoking did not protect against venous thrombosis in patients within each group, including group 4.

Discussion

The results of this study indicate that the risk of developing deep venous thrombosis after myocardial infarction is related to the severity of the underlying illness rather than to the period of bed rest to which our patients were subjected. This is suggested by three facts. First there was a similar incidence of venous thrombosis in patients with uncomplicated myocardial infarction whether they were electively mobilized after two (group 2) or nine days (group 3). Second, within the group of patients with complicated myocardial infarction (group 1), the mean day of mobilization was virtually the same in those patients who developed venous thrombosis as in those who did not. Third, there was a higher incidence of venous thrombosis among group 1 patients than among those in group 3; put differently, more severely ill patients mobilized at 6-6 days had a significantly higher incidence of venous thrombosis (33%) than patients with an uncomplicated illness who were mobilized electively three days later (18%). These findings support the view of Nicolaides *et al.* (1971) that patients who are 'severely' ill are the most likely to develop venous thrombosis. However, in their study the duration of bed rest was not taken into account and the description of 'severely' ill was only applied to those patients who had a low output state for at least 24 hours. Many of the patients in our 'complicated' group would not have been classified as 'severely' ill by this criterion, and this probably accounts for the fact that Nicolaides *et al.* found a very high frequency of deep venous thrombosis (62%) in severely ill patients.

We have been unable to confirm that cigarette smokers with heart attacks develop deep venous thrombosis less frequently than non-smokers, and this finding is contrary to the observations of Marks

and Emerson (1974). We were unable to collect information of smoking habits in 27 patients, but even if it were assumed that those with a positive scan (4 patients) were non-smokers and that all those with a negative scan (23 patients) were smokers, there was still no evidence of any protective effect from cigarette smoking.

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