Brief Communications

Clinical Course of Myocardial Infarction Among Diabetic Patients

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The clinical course of myocardial infarction (MI) was compared between 154 known diabetic (Ds) and nondiabetic (NDs) MI patients matched for age, sex, and hospital ward. In both groups similar numbers of cases with cardiac rupture, shock, pulmonary edema, and clinically observed arrhythmias were found. In contrast, Ds patients had significantly more frequent A-V and intraventricular conduction disorders than NDs ($P < 0.02$). Ds also died twice more often from MI (36%) than matched controls (18%). The excess case fatality rates from MI among Ds were limited to the period between the second and seventh day of hospitalization. The excessive fatality of Ds from MI resulted mainly from the high liability of insulin-dependent diabetic patients (IDDs), with the relative risk of over 4 in relation to NDs. Ds with arrhythmias and/or conduction disorders had a particularly poor prognosis for surviving, the relative risk exceeding 3. No ready explanation of this phenomenon is presently available. DIABETES CARE 3: 526–529, JULY–AUGUST 1980.

Epidemiologic studies have shown that diabetes increases the risk of coronary death.[1,2] The excess mortality is probably the sum of higher coronary morbidity[1] and higher case fatality rates from myocardial infarction (MI) among diabetic as compared with persons with normal carbohydrate tolerance.[3–7,9]

The earlier study carried out in Warsaw pointed to the close similarities in prehospital MI case fatality rates in diabetic and nondiabetic patients.[8] However, hospital deaths from this condition among diabetic patients were twice as frequent as in the control group.[8] In the present study the attempt was made to compare the clinical course of MI in diabetic and nondiabetic patients to find the poor predictors of the higher hospital mortality due to infarction among diabetic patients.

MATERIALS AND METHODS

Three hundred and eighteen cases with MI and diabetes mellitus as a main comorbidity were found on statistical forms filled in for each patient hospitalized in Warsaw during 1972 and 1973. These cases constituted about 6% of all patients hospitalized due to MI in internal wards of 13 hospitals. In that period all patients with MI, as a rule, were treated in district hospitals, and 50% of those patients had been hospitalized within 3 h of the onset of MI.[10] In 1972 and 1973 no agreed upon policy regarding the treatment of MI diabetic patients was implemented in Warsaw hospitals and only a few of the wards had Coronary Care Units for management of MI patients.

Each patient with MI and diabetes was matched with a control MI patient without diabetes of the same sex and approximately the same age. To exclude the bias connected with different policies in the management of MI in particular hospitals, the control MI patients were randomly chosen from all MI patients hospitalized in the same hospital ward as MI diabetic patients during 1972 and 1973.

Hospital records formed the basis for the evaluation of the clinical course of MI and diabetes mellitus. Of 318 MI diabetic patients, 51 were excluded because their records were unavailable and 83 were excluded because diabetes mellitus had been diagnosed just before or during hospitalization due to MI (10 and 8 deaths were recorded in the two groups, respectively). The remaining 184 persons with diabetes mellitus diagnosed at least 6 mo before hospitalization plus their control cases of MI formed the study groups.

Using the criteria applied in the Myocardial Infarction Registration in some European countries,[10] MI was confirmed in 154 pairs. For those patients, information about complications of MI, such as hypotension (systolic blood pressure below 90 mm Hg), pulmonary edema, arrhythmias, A-V and intraventricular conduction disorders, as well as the

onset of MI, duration of hospitalization, and previous medical history was also gathered. In the diabetic group the hypoglycemic treatment before and after MI was also determined, which was treated as an indication of severity of diabetes mellitus. The relative mortality risk for the diabetic subjects was calculated by dividing case fatality rate in the study group by the rate in the control group.[11] The significance of the differences between both groups was tested using the chi-square statistic.

RESULTS

The groups under study included 93 pairs of men and 61 pairs of women. Since the clinical course of MI in men and women was similar, it seemed justified to carry out further comparisons of both sexes jointly.

Table 1 shows that the highest mortality in the diabetic group compared with the control group was among the youngest diabetic patients and that the difference decreased with increasing age. In total, there were nearly twice as many deaths in the diabetic compared with the control group. No relation between duration of disease and mortality rates was observed.

Regarding mortality in relation to the date of onset of MI, the number of deaths on the first day of hospitalization was similar (Table 2). However, in the diabetic group deaths between days 2 and 7 were 3.2 times more frequent than in the control group, and between days 8 and 28, 1.7 times as frequent. There were few deaths in both groups after 4 wk of hospitalization.

Autopsies were performed in almost the same proportion of death cases in both groups (in the diabetic group 75% and in the control group 79% of deaths). In the diabetic group 2 of 42 autopsies showed, in addition to MI, embolism of the pulmonary artery and in another two cases cardiac rupture. Similarly, in the control group there were two cases of cardiac rupture and one of pulmonary embolism.

TABLE 1
Structure of the groups under study according to age and case fatality experienced during hospitalization

Age (yr)	Number of diabetic subjects	Duration of diabetes mellitus (yr) ($\bar{X}$ ± SD)	Case fatality rates from MI: Among diabetic subjects, Percent	(N)*	Among matched nondiabetic subjects, Percent	(N)*
30–45	7	5.5 ± 5	42.8	(3)	—	
45–54	22	6.8 ± 6	31.8	(7)	9.1	(2)
55–64	46	7.5 ± 7	26.1	(12)	8.7	(4)
65–74	67	8.2 ± 6	40.3	(27)	26.7	(18)
75 and over	12	14.9 ± 12	58.3	(7)	41.7	(5)
Total	154	6.9 ± 8	36.4	(56)†	18.8	(29)†

* Number of deaths shown in parentheses.
† $X^2 = 11.84$; df = 1; P = 0.0005.

TABLE 2
Case fatality rates according to the day of hospitalization following MI*

Day of hospitalization	Case fatality rates: Among diabetic subjects, Percent	(N)†	Among nondiabetic subjects, Percent	(N)†
1st	7.8	(12)	5.8	(9)
2nd–7th	14.3	(22)	4.5	(7)
8th–28th	11.0	(17)	6.5	(10)
29th and later	3.2	(5)	1.9	(3)
Total	36.4	(56)	18.8	(29)

* In the diabetic group 75% and in the control group 78% of persons who survived MI were hospitalized longer than 28 days.
† Number of deaths shown in parentheses.

Both groups were characterized by a similar number of previous MIs (28.6% of the diabetic group and 22.0% of the nondiabetic group) and by the same proportion of patients with a history of hypertension (28.6% among diabetic and 27.3% among control groups). Diabetic patients, however, were treated more frequently with digoxin before hospitalization than the control group (17.8% of the diabetic and 10.1% of the control groups), but this difference was not significant. On admission, in both groups, the frequency of patients who reported chest pain was similar (53.9% and 54.9%, respectively, among diabetic and control groups).

Frequency of MI complications was examined by analyzing separately the occurrence of each complication. The results are shown in Table 3. The diabetic group showed significantly more frequent A-V and intraventricular conduction disorders, when analyzed jointly, than the control group. With preinfarction documentation lacking, the conduction disorders include both patients suffering from such disorders due to MI as well as patients who had suffered from them before MI; the same holds true for arrhythmias.

To ascertain which MI features were especially poor predictors among diabetic patients, the mortality in both groups, depending on the occurrence of each MI complication, was analyzed (Table 4). A difference in mortality was observed between the diabetic and nondiabetic groups with arrhythmias and/or disorders of conduction (I° A-V block and right-bundle branch block were not taken into analysis). It should be stressed that diabetic patients with arrhythmias or with disorders of conduction had a worse prognosis than the controls, irrespective of appearance or absence of hemodynamic complications; that comparison was therefore carried out after combining these subgroups into larger groups. The prognosis for diabetic patients having the above complications was 3.0 times worse compared with the nondiabetic group. This difference was highly significant. In the diabetic group 42.2% did not show any of the earlier mentioned complications, and among the nondiabetic group there were 44.8% such persons. In these two subgroups the difference in mortality was not statistically significant.

TABLE 3
Frequency of MI complications observed during hospitalization

Complications of MI	Diabetic subjects (N = 154)		Matched nondiabetic subjects (N = 154)	
	Percent	(N)*	Percent	(N)*
1. Hypotension and/or pulmonary edema	27.9	(43)	25.3	(39)
2. Arrhythmias				
a. Ventricular†	13.6	(21)	13.6	(21)
b. Supraventricular only‡	17.5	(27)	22.1	(34)
3. Conduction disorders				
a. A-V block I°	3.9	(6)	0.7	(1)
b. A-V block II° or III°§	3.9	(6)	1.3	(2)
c. Left bundle branch block	16.9	(26)	10.4	(16)
d. Right bundle branch block	3.2	(5)	5.2	(8)
4. Severe pain in chest once again	15.6	(25)	11.3	(17)
5. Deaths	36.4	(56)¶	18.8	(29)¶

* Number of patients with complications of MI shown in parentheses.
† In available ECG records, ventricular premature beats of 6/min or more and/or ventricular tachycardia were found.
‡ In available ECG records, supraventricular premature beats of 6/min or more, or atrial fibrillation, or paroxysmal tachycardia without ventricular arrhythmias were found.
§ Patients were not digitalized before and after MI.
‖ $X^2 = 4.73$; df = 1; P = 0.02.
¶ See Table 1.

Further analysis considered the relationship between hypoglycemic therapy applied during the first week following MI and mortality during the course of MI. The greatest and highly significant difference was observed between insulin-dependent diabetic patients and its matched control subgroup; the relative death risk for diabetic patients was 4.0. The difference in mortality between diabetic patients treated with oral drugs and a corresponding control subgroup bordered on statistical significance; the risk of death for diabetic patients was 1.5. Due to the very limited number of patients treated with diet alone, this group was not analyzed. The hypoglycemic therapy applied during the first week following MI was taken into account because it yielded more contrasted values of the relative risk of death than the hypoglycemic therapy applied before MI.

TABLE 4
Case fatality rates from MI according to complications observed during hospitalization

Complications observed during hospitalization	Diabetic subjects			Nondiabetic subjects		
	Number with complications	Case fatality rate		Number with complications	Case fatality rate	
		Percent	(N)*		Percent	(N)*
Hypotension and/or pulmonary edema only	17	76.5	(13)	21	71.4	(15)
Arrhythmias and/or conduction disorders‡	72	47.2	(34)†	64	15.6	(10)†
Without above complications	65	13.8	(9)	69	5.8	(4)
Total	154	36.4	(56)	154	18.8	(29)

* Number of deaths shown in parentheses.
† $X^2 = 13.805$; df = 1; P = 0.0001.
‡ This group consists of patients with arrhythmias and/or with conduction disorders (II° or III° A-V block or left-bundle branch block) only, or together with hypotension and/or with pulmonary edema.

DISCUSSION

In this study, as in several others,[3–5,7–9] the case fatality rate from myocardial infarction among diabetic subjects was twice that of the control group. Unlike the close agreement between the estimates of relative risk, the absolute levels of mortality from MI among diabetic patients vary widely among different studies. These contrasts may result from selection arising from the differences in the rates of hospitalization, its urgency, or even the age of the patients hospitalized for MI in various localities.

In the present study the frequencies of clinically observed MI complications were similar in both groups as also reported by others.[4,5] However, MI diabetic patients with arrhythmias and/or conduction disorders had a worse prognosis for survival than the nondiabetic group with the same complications. This suggests that the excess mortality among MI diabetic patients may be caused by the more frequent occurrence and/or irreversibility of ventricular fibrillation among diabetic compared with nondiabetic patients. Other authors did not find more frequent ventricular fibrillation among diabetic compared with nondiabetic subjects,[5,7,9] but this may result from different methods of analysis.

Management with insulin following MI for insulin-dependent patients or a higher blood glucose level was the other predictor of excess deaths among diabetic subjects. This observation agrees with other studies.[1,7] It is too early to explain exactly the poor prognosis for survival of these diabetic subjects, but it may be related to the metabolic consequences of deficiency of endogenous insulin, i.e., a high level of free fatty acids and their harmful effect on the heart.[12,13]

The present findings do not confirm the hypothesis of a more frequent occurrence of a painless course of MI in diabetic patients.[14] However, this may be the consequence of selection of MI patients for hospitalization, because severe pain due to infarction is among the main symptoms qualifying for hospital admission in our study. Furthermore, the disagreement in findings may be due to different methods of data collection in both studies.

In the present study, disorders of A-V and intraventricular conduction were significantly more frequent among diabetic subjects with MI than among nondiabetic subjects. This corresponds to the findings of the other part of this study, which dealt with patients in whom diabetes was diagnosed during hospitalization following MI (unpublished data). Other authors also observed that MI diabetic patients compared with

the MI control group more often suffered from conduction disorders[4,9] and that patients with inexplicable conduction disorders had impairment of carbohydrate tolerance significantly more often than control groups.[15,16] In attempting to explain the mechanisms of this pathology, the changes in the nervous structures or small vessels of the conduction system specific for diabetes should be considered. In addition, the specific metabolism of the muscle fibers of the conducting tissue (i.e., its greater glucose dependence) should be taken into account.[17]

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