

Thrombophilia in Diabetes: Thrombelastographic Investigations

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Clinical evidence supports the existence of a thrombophilic tendency in diabetes. Experimental investigations have defined these alterations through analysis of the coagulation factors in diabetes, and with respect to its treatment. This was accomplished, so far, by studying the prothrombin time and whole blood-clotting time. Several data indicate the presence of a significant increase of prothrombin activity in diabetes, which is more pronounced in severe and improperly treated cases. In a number of cases also a shortening of the whole blood-clotting time is produced.^{1, 2, 7, 8}

Recent observations have pointed out that a thrombophilic tendency can be detected by means of thrombelastography.^{3, 4} This technic consists in measuring the variations of the clot elasticity during its formation. The results obtained appear to be more closely correlated with the hemostatic function of the clot than the usual coagulation tests. This should be particularly true in the presence of hemorrhagic or thrombotic alterations.

The thrombelastographic signs of a thrombophilic tendency are characterized by: a) a shortening of the reaction time (r); b) a shortening of the clot formation time (k); and c) an increase of the maximal amplitude (ma).

The application of this method to the study of the thrombophilic tendency in diabetes made it possible to detect significant variations of the thrombelastographic patterns, as observed in thrombophilic diseases. No correlations could be detected between such findings and the other clinical data.

MATERIAL AND METHODS

1. *Material.* Forty-one consecutive diabetic patients were included in this study. They were grouped in connection with the following patterns: a) severity of the disease, according to the clinical data and the amount of insulin necessary for proper treatment; b) somatic type of the patient, by considering obese, normal and thin diabetics; c) presence of diabetic retinopathy; d) duration of the disease; e) duration of insulin treat-

ment; f) age of the patient.

2. *Thrombelastographic determinations.* The thrombelastographic determinations, as described elsewhere,³ were carried out in oxalated plasma. The reaction time r , the clot formation time k , and the maximal amplitude ma were evaluated in all cases.

3. *Correlations between the clinical and thrombelastographic data.* The results obtained are presented in a group of graphs, by taking into consideration the clinical data, as indicated above, and by particularly correlating the thrombelastographic variations of the maximal amplitude with the age of the patients and the duration of the disease, when these data were available.

RESULTS

1. *Reaction time (r) of the thrombelastogram.* In normal cases the reaction time (r) of the thrombelastogram varies between 5 and 10 mm. corresponding to 2.5-3.0 minutes. In the diabetic patients, a number of values were below the normal range or at the lower limit of the normal values (figure 1).

2. *Clot formation time (k).* These values presented more marked modifications than the reaction time. Most of the values were grouped between 2 and 4 mm., with a maximum at 2 mm. The normal values vary between 4 and 10 mm. No particular distribution of the values

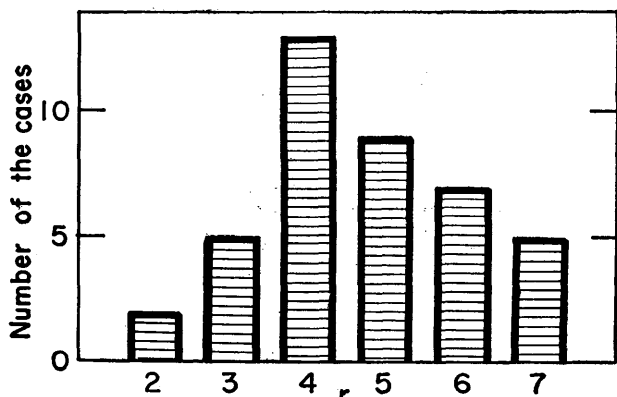


FIG. 1. Reaction time (r) of the thrombelastogram in a group of diabetics. A number of values are below the normal range (between 5 and 10 mm.), or at the lower limit of the normal values.

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with respect to the severity of the cases (light, medium and severe diabetes), or the somatic type of the patients was to be found (figure 2).

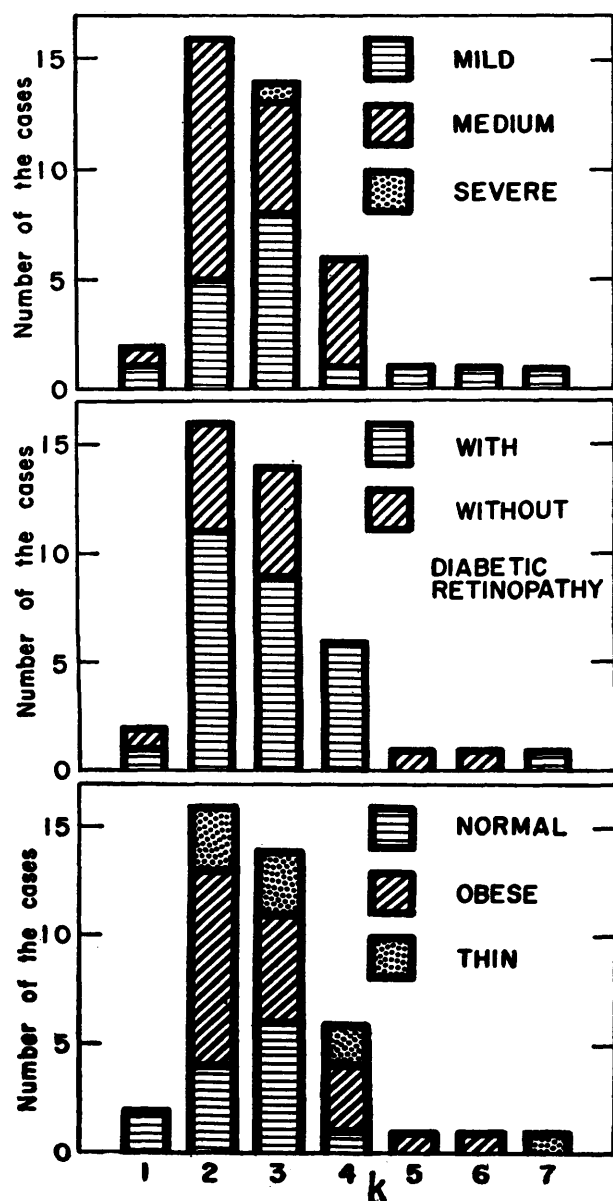


FIG. 2. Reduction of the clot formation time (k) of the thrombelastogram (normal values: 4 to 10 mm.) in a group of diabetics. No particular distribution of the values with respect to the severity of the cases, the somatic type of the patients and the presence of retinopathy.

3. *Maximal amplitude (ma)*. The most significant data have been obtained by analyzing the maximal amplitude of the thrombelastogram (ma). Normal values are included between 50 and 60 mm. In diabetic patients, almost all values were above 60 mm., some of them reaching 75 mm. and more. Maximum values have

been observed around 65 and 71 mm. No particular distribution could be detected with respect to the clinical data considered (severity of the diabetes, somatic type of the patients, presence of retinopathy) (figure 3).

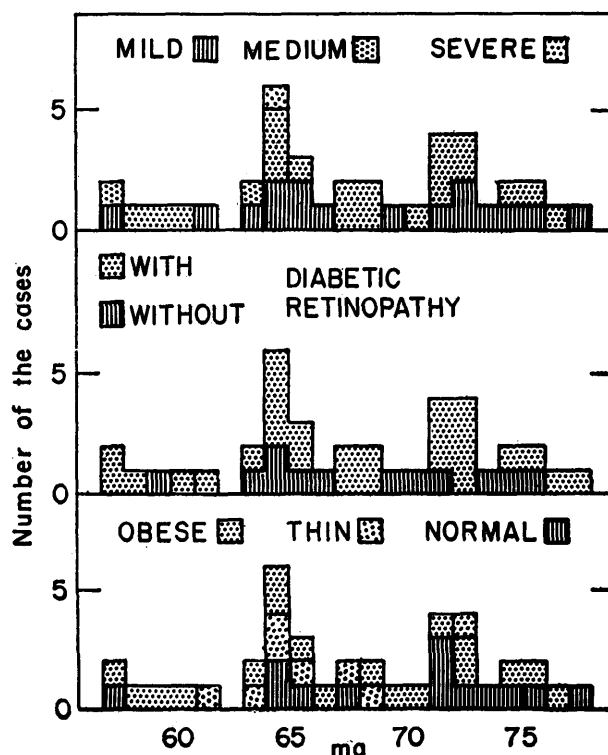


FIG. 3. Increase of the maximal amplitude (ma) of the thrombelastogram in a group of diabetics (normal values: 50 to 60 mm.). No particular distribution with respect to the clinical data.

4. *Correlation between the increase of ma and the age of the patients*. By comparing the ma-values with the age of the patients, it could be observed that the maximal increases of ma were detected practically at all ages. No correlation could be, therefore, evidenced, between these two data (figure 4).

5. *Correlation between the increase of ma and the duration of the disease*. The same is also true for this kind of correlation, which could not be found, comparing the duration of the disease with the increase of ma (figure 4).

DISCUSSION

The pathogenesis of thrombophilic conditions can be related to a number of humoral, vascular and hemodynamic factors. The humoral factors include chiefly the increased activity of the coagulation factors. The diagnostic efforts for the clinical identification of such patterns were not always successful, insofar as several tests did not present the expected specificity. Some useful

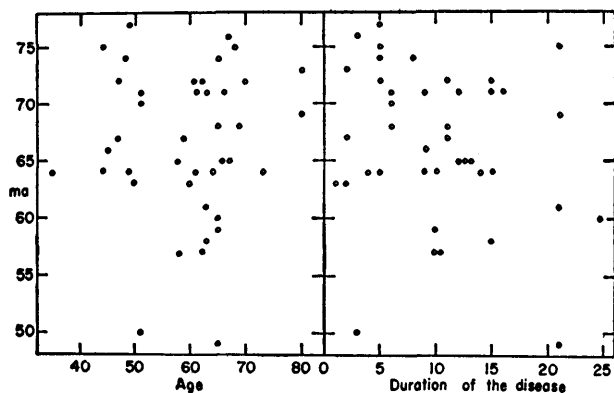


FIG. 4. No correlations of the increase of *ma*, the age of the patient and the duration of the disease.

hints were obtained by determining the whole blood-clotting time in silicone tubes, the factor VII activity, the prothrombin time in diluted plasma, etc.

Thrombelastographic researches have shown, both experimentally and clinically, that a large number of thrombophilic conditions can be detected by using this new technic.⁵ Typical thrombophilic patterns were observed by adding in vitro an excess of isolated, concentrated platelets to a platelet-free plasma. Similar results were obtained through animal experiment by binding the femoral vein, and studying the thrombelastographic modification in the venous blood of the opposite limb. Clinically, the thrombelastographic alterations, assumed to be consistent with the presence of a thrombophilic condition, were detected in the majority of cases which are usually accompanied by this tendency, i.e., thrombosis, thrombophlebitis, hypertension, etc.⁵ Also after administration of cortisone to normal subjects, typical thrombophilic patterns have been observed.⁵ These results coincide with the observations of thrombotic complications in subjects treated with cortisone for therapeutic purposes, and are accompanied by thrombelastographic signs of thrombophilia.

On the basis of these observations the results obtained in diabetic patients suggest the possibility of detecting a thrombophilic tendency in these patients also by means of thrombelastography. The most significant pattern for diagnostic purposes is represented by a reduction of the clot formation time and the increase of the maximal amplitude. These alterations do not appear to be correlated with other clinical data of the diabetic disease, such as the age of the patient, the duration of the disease, the somatic type of the patient, the presence of retinopathy, and the severity of the disease.

The connections of the thrombelastographic alterations

with the diabetes cannot be easily explained. Tentatively, it might be suggested that the balance between sympathetic and parasympathetic hormones could influence the tendency for an increased or decreased activity of coagulation factors. In fact, it is known that adrenalin may produce a tendency for hypercoagulability, while insulin is supposed to induce the opposite situation.⁶ Such speculations ought to be confirmed by further experiments. There is sufficient evidence that the finding of a thrombophilic tendency by means of thrombelastography in diabetes might be of diagnostic importance.

SUMMARY

Thrombelastographic determinations have been carried out on a group of forty-one cases of diabetes. In the majority of these cases a reduction of the clot formation time and an increase of the maximal amplitude in the thrombelastogram have been found. No correlation could be established between these findings and the age and somatic type of the patient, the duration and severity of the disease and the presence of retinopathy.

SUMMARIO IN INTERLINGUA

Thrombophilia in Diabete

Determinaciones thrombelastographic esseva effectuate in quaranta-un patientes con diabete. In le majoritate de iste patientes, un reduction se notava in le tempore del formation del coagulo insimul con un augmentation del amplitude maximal in le thrombelastogramma. Nulle correlation poteva esser establite inter iste constatationes e le etate o le typo somatic del patiente, le duration e le grado de severitate del morbo, e le presentia o absentia de retinopathia.

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