

Effect of Diabetic Control on Retinopathy

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SUMMARY

This paper presents an analysis of the literature regarding the effect of control of diabetes on retinopathy. In diabetics with age of onset before forty years of age and with a duration greater than fifteen years, there is a significantly higher incidence of retinopathy in those judged to have been under poor control than in those with better control. Those patients with poor control had a significantly higher incidence of the more severe forms of diabetic retinopathy. While this association does not necessarily imply a cause and effect relationship, it is not compatible with a point of view which accepts poor control as of little consequence in diabetes. *DIABETES* 15:497-99, July, 1966.

A recent critical review¹ has indicated that there is a higher incidence of retinopathy in diabetic patients who have been judged to be under poor control than in those maintained in good control. A key summary from this review which illustrates this point is shown in table 1. In the present paper, analysis is confined to retinopathy and is extended to include: (a) data corrected for duration of diabetes and (b) information on the relationship between different stages of diabetic retinopathy and good or bad control.

Duration of diabetes

Two studies^{2,3} have indicated the importance of including duration of diabetes in an evaluation of the effect of control on retinopathy. In the study of Keiding et al.² it was apparent that the incidence of diabetic retinopathy increased with the duration of the disease whether control was good, fair, or poor. This is brought out in figure 1. Here, studies on more than 2,500 diabetics with onset under the age of forty are combined. Two large individual series^{4,5} are compared with a composite graph combining five other independent series.^{2,3,6-8} In all of these studies the diagnosis of retin-

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TABLE 1

Angiopathy more frequent with poor than with good control of diabetes

| Observer | Year | Number of patients | Incidence of angiopathy* | |
|------------------------------------------|------|--------------------|--------------------------|---------------------------------|
| | | | Good control (per cent) | Fair or poor control (per cent) |
| Spoont, Dyer, Day & Blazer ¹⁴ | 1951 | 50 | 16 | 68 |
| Dunlop ⁹ | 1954 | 167 | 10 | 50 |
| Root, Pote & Frehner ¹⁵ | 1954 | 189 | 10 | 66 |
| Constam ¹⁶ | 1954 | 53 | 47 | 94 |
| Giffin & Cortesi ¹⁰ | 1955 | 46 | 29 | 81 |
| Lambie & MacFarlane ¹⁷ | 1955 | 78 | 20 | 48 |
| Mohnike ¹⁸ | 1957 | | 30 | 70 |
| Buschmann, Fritze & Marsch ¹⁹ | 1958 | 1,547 | 19 | 42 |
| Johnsson ¹¹ | 1960 | 99 | 32 | 54 |

*Retinal, renal and/or vascular disease.

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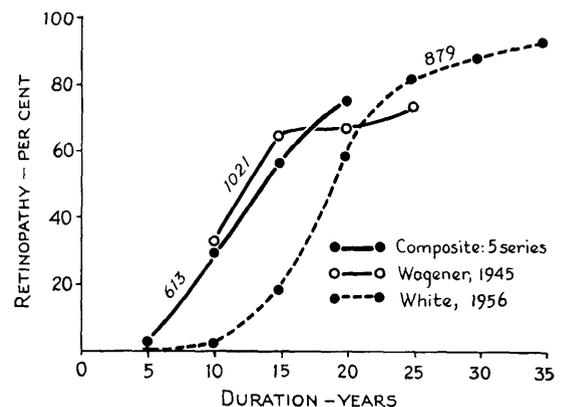


FIG. 1. Incidence of retinopathy as a function of duration of diabetes.

opathy was made during life by accepted ophthalmologic criteria. The shapes of the curves are uniform. It is likely that the curve from White's series is shifted to the right because of an earlier age of diagnosis in this pediatric age group. It is apparent from the shape of these curves that an analysis of the effect of control on the incidence of retinopathy is impossible in diabetics with a duration less than five years. It is also apparent

that analysis between five and fifteen years is complicated by the fact that one is dealing with the steep portion of the curve, and a small error in dating the onset of the disease might lead to an apparently significant difference in the incidence of retinopathy. For diabetes with duration greater than fifteen years, however, accurate figures can be expected. Results from five series which can be analyzed in this fashion^{2,9-12} are shown in figure 2. There is a significantly higher incidence of retinopathy in those diabetics judged to have been under poor control than in those with better control.

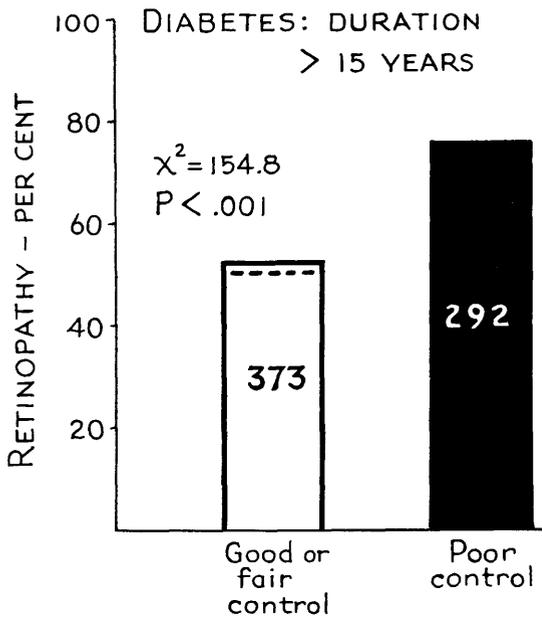


FIG. 2. Effect of control on incidence of retinopathy in diabetics with duration greater than fifteen years. The dotted line indicates data if only those with good control are considered.

The major difficulty in an analysis of this type is variability in criteria for control. For the purposes of this review, "poor" control is characterized particularly by frequent episodes of ketoacidosis. Using this as the major criterion, it is likely that diabetics of this variety are comparable in different series and thereby make up a homogeneous group. In only one large series¹¹ does this method of classification become questionable. This author included only the classes of "good" and "fair" control in his report. In table 2, the latter group was included as "fair" control (line 1) or "poor" control (line 2). The final conclusions are not altered by the shift.

Stages of retinopathy

Variations in classification of retinopathy complicate

TABLE 2

Retinopathy in diabetes of duration greater than fifteen years: Chi square analysis of effect of control

| Control | χ^2 | P |
|---------------------------|----------|------|
| (1) Good & fair vs. poor | 154.8 | .001 |
| (2) Good & fair vs. poor* | 20.6 | .001 |
| (3) Good vs. fair & poor | 9.1 | .01 |

*See text for explanation.

consideration of the problem. Depending upon the observer, there can be from three to nine different stages of diabetic retinopathy. For purposes of simplicity, only three stages are recognized in this review: Stage I—microaneurysms; Stage II—microaneurysms and hemorrhages and/or exudates; Stage III—retinitis proliferans. Results from four series^{2,10-12} can be analyzed in this fashion (figure 3). Those patients with poor control had a significantly higher incidence of Stage II and III retinopathy than did those with good or fair control. This did not apply to Stage I retinopathy.

DIABETES: DURATION > 15 YEARS

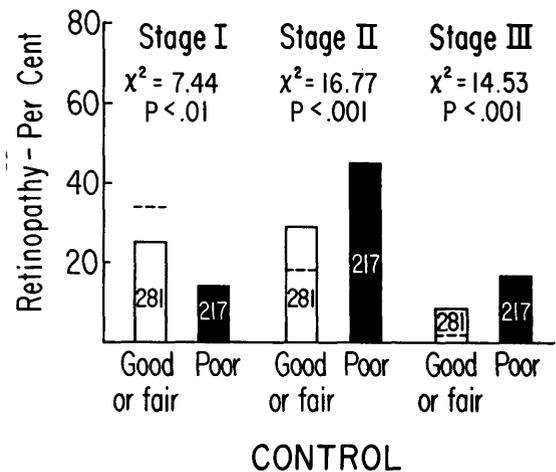


FIG. 3. Data which suggest that good control does not delay or prevent the development of retinal microaneurysms (Stage I) but that poor control may be decisive in hastening or causing hemorrhages and exudates (Stage II) and proliferative retinopathy (Stage III). The horizontal broken lines indicate data if only those cases with good control are considered.

DISCUSSION

There appears to be a positive correlation between effective treatment of diabetes mellitus and prevention or delay in appearance of its retinal vascular lesions, particularly the more severe forms of retinopathy. Such an

association, however, does not necessarily mean a *cause and effect* relationship. Rapidly progressive vascular disease could just as well cause diabetes that is difficult to control; or some common cause could be the cause of both the poorly controlled diabetes and the more serious forms of diabetic retinopathy. In spite of these reservations about a cause and effect relationship, the published data are hardly in accord with a point of view which accepts poor control as of *little consequence* in diabetes. Finally, it is tempting to speculate that Stage I retinopathy is part of the natural progression of the diabetic state and that efforts at good control of diabetes are particularly effective in forestalling or preventing more serious lesions.¹³

ACKNOWLEDGMENT

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