

ABO Blood Type and Arteriosclerosis Obliterans

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ABO blood type is associated with several conditions whose pathogenesis at some stage involves the coagulation of blood. The prevalence of type O blood has been demonstrated to be higher in patients with bleeding peptic ulcer than in either ulcer patients without bleeding or healthy controls [1-3]. By contrast, in venous thromboembolism a deficit of type O cases has been found [4]. Although there is conflicting evidence on the frequency of ABO types in patients with myocardial infarction, most studies have found a smaller proportion of type O cases than would have been expected; this area has recently been reviewed [5].

SUBJECTS AND METHODS

Cases with arteriosclerosis obliterans were selected by methods detailed elsewhere [6]. Male cases were chosen from one Boston vascular surgeon's records for the years 1964-1969; female cases were chosen from his and three other surgeons' records for the years 1945-1969. The ABO type was available only for the hospitalized patients, comprising 50%-60% of all cases of arteriosclerosis obliterans seen by these surgeons. Most subjects resided in eastern Massachusetts, although there were many from elsewhere in New England and some from other sections of the country. The small number of nonwhite patients seen were not included.

RESULTS

The ABO type was ascertained in 149 male and 353 female nondiabetic cases, representing 92% and 94%, respectively, of the surgeons' hospitalized cases. The large majority of cases had not previously been seen by a vascular specialist. The distribution of ABO types in those 16 male and 24 female cases who had had arteriography or surgery prior to visiting one of the surgeons was compared with that of the other cases; no significant difference was found, and all are included in the subsequent analysis.

The distribution of ABO type among the cases, by sex, is given in table 1. To obtain the expected distribution, ABO frequencies among 2,583 controls collected in Boston in a previously published study [4] (pooled Boston control series)

Received May 20, 1971; revised July 23, 1971.

This study was aided by U.S. Public Health Service grant T01 GM00007 from the National Institute of General Medical Sciences, National Institutes of Health.

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TABLE 1

DISTRIBUTION OF CASES OF ARTERIOSCLEROSIS OBLITERANS AND
POOLED BOSTON CONTROL SERIES BY ABO TYPE

ABO Type	Female Cases	Male Cases	Control Series
A	164 (47)*	69 (46)	952 (37)
B	40 (11)	20 (13)	303 (12)
AB	14 (4)	3 (2)	98 (4)
O	135 (38)	57 (38)	1,230 (47)
Total	353 (100)	149 (99)	2,583 (100)
χ^2 (1 df): †			
A + B + AB:O	10.5 ($P < .01$)	4.2 ($P < .05$)	...
A:O	12.9 ($P < .001$)	5.6 ($P < .02$)	...
Relative risk: †			
A + B + AB:O	1.4	1.4	...
A:O	1.6	1.6	...

* Percentage in parentheses.

† Cases versus control series.

were used. The comparison of observed and expected frequencies showed in each sex a significant excess of blood type A and a deficit of blood type O among the cases of arteriosclerosis obliterans.

There are several circumstances in which an association between ABO type and arteriosclerosis obliterans would be observed when in fact no such association existed. Within the scope of the data available in this study, three of these could be examined:

1. Was an ethnic group with a low prevalence of blood type O present in greater numbers among cases than controls? It is known [7, 8] that the proportion of persons with blood type O is lower among Jews than among non-Jews. Thus, if the cases of arteriosclerosis obliterans included a higher proportion of Jews than the control population, the deficit of type O among cases could be attributable to this difference in ethnic composition. In this study, ethnic group was recorded for female cases only, and analysis controlling for ethnicity was confined to that sex. Since the pooled Boston control series did not specify ethnic composition, additional data were required for comparison. In order to reduce the probability of obtaining expected ABO frequencies that were not representative of the population, two independent sets of estimates were used:

Estimate A: The expected values for Jews were provided by the pooled results of surveys of ABO type in 1,140 Jews living in New York City, Brooklyn, and Ohio [7]. The expected values for non-Jews were based on the pooled Boston control series, which should provide a conservative estimate (i.e., a low blood type O frequency), since there no doubt were some Jews in the control sample chosen.

Estimate B: The expected values for Jews and non-Jews came from a survey of ABO type in 923 Brooklyn blood donors [8], who had been classified by surname as "definitely Jewish" or "definitely not Jewish."

The comparison of observed and expected distributions (table 2) showed a

TABLE 2
OBSERVED AND EXPECTED ABO FREQUENCIES IN JEWISH AND NON-JEWISH FEMALE CASES

CONTROL POPULATION AND ABO TYPE	Non-Jews				Jews			
	Cases Observed	Cases Expected	$\chi^2(1 \text{ df})$	Relative Risk	Cases Observed	Cases Expected	$\chi^2(1 \text{ df})$	Relative Risk
Population A:								
A + B + AB	166	149.0	3.9*	1.3	42	33.8	4.7*	2.1
O	115	132.0			12	20.2		
Total	281	281.0	54	54.0
Population B:								
A + B + AB	166	136.8	11.7**	1.5	42	33.5	5.0*	2.1
O	115	144.2			12	20.5		
Total	281	281.0	54	54.0

NOTE.—See text for explanation of populations A and B. Ethnic group was not available for 18 cases.

* $P < .05$.

** $P < .001$.

significant deficit of type O blood among cases of arteriosclerosis obliterans both for Jews and for non-Jews and for both sets of expected values.

2. Did patients who came to the four surgeons for care tend to belong to a particular segment of the population with a low frequency of blood type O? To investigate this possibility, ABO type was obtained from the charts of patients hospitalized with abdominal aortic aneurysm who had been chosen from the records of the two surgeons who provided the majority of the cases of arteriosclerosis obliterans. The distribution of ABO type among these patients with aneurysm was no different from that expected from the distribution in the pooled Boston control series (table 3).

TABLE 3
OBSERVED AND EXPECTED ABO TYPE OF PATIENTS WITH ABDOMINAL
AORTIC ANEURYSM (BOTH SEXES)

ABO Type	Cases Observed	Cases Expected*	$\chi^2(1 \text{ df})$
A + B + AB	77	80.0	Not significant 0.2
O	74	71.0	
Total	151	151.0	...

* Based on ABO frequencies in pooled Boston control series.

3. Although the association of ABO type and arteriosclerosis obliterans is significant, its strength is not great; the risk of the disease for persons who are not type O is about 1.4 times that for those who are type O. Could this association, then, be secondary to a factor which is more strongly associated with arteriosclerosis obliterans than ABO type and which is more prevalent in non-type O than in type O persons? The only known factors with sufficiently strong associations with arteriosclerosis obliterans would be cigarette smoking and hypertension [6, 9]. However, since neither smoking nor blood pressure data were available for the control populations used in assessing the ABO type association, it could not be directly determined if either was playing a confounding role. Nonetheless, among the cases of arteriosclerosis obliterans, the percentage of current cigarette smokers did not differ significantly among persons of each ABO type (75% in types A + B + AB and 73% in type O), nor did the percentage of hypertensive cases differ (52% in types A + B + AB and 50% in type O). Thus, in order for cigarette smoking or hypertension to affect the results for ABO type, one or both must be associated with ABO type in the population as a whole, and this to date has not been demonstrated.

There is some evidence to suggest that the prevalence of blood type O increases with increasing age, the opposite being true for blood type A [10]. In the present study, although no data on the age distribution of control subjects were available, the cases (all older than 35) almost certainly had a higher mean age. Thus, the

cases may be slightly overrepresented by type O persons, and the risk estimates presented may be slight underestimates of the actual risk to type A persons.

In contrast to the findings relating age and cigarette smoking to the site of disease [6, 11], there was no significant difference between ABO distributions of cases with aortoiliac and cases with femoropopliteal occlusions.

Although a group of diabetic cases had been selected, ABO type was not available in sufficient numbers to permit any conclusions to be drawn.

DISCUSSION

In a given population, ABO blood group frequencies may vary substantially with ethnic group and national origin [7]. If such characteristics are ignored in the selection of controls and if the resulting composition of cases and controls is not similar, any association observed between ABO type and the disease under study could be attributable to other characteristics of the ethnic group which predominated among cases. If, on the other hand, ethnic characteristics other than ABO type are *not* playing a role but if ethnicity is nonetheless taken into account in the analysis, then the ABO distributions of cases and controls will have been made unnecessarily more similar and a larger sample size will be necessary to demonstrate the presence of an association. Since it is not known what effects other ethnic characteristics have on the development of arteriosclerosis obliterans, the safest policy would seem to be to study the relationship of ABO type and arteriosclerosis obliterans with and without taking ethnicity into account. This was done in the present study and a deficiency of type O cases was found in each instance.

Information on ABO type was available only for hospitalized cases, and consequently it is not possible from the data in this study to decide whether the association of ABO type and arteriosclerosis obliterans holds for all cases in the population or only for those relatively severe cases that require hospitalization for surgical evaluation.

Of the two pathologic processes involved in the development of arteriosclerosis obliterans—atherosclerosis and thrombosis—it seems likely that whatever role ABO type plays is at the level of thrombosis. As previously noted, ABO type is known to be associated with venous thromboembolism, a condition involving thrombosis but not atherosclerosis. A recently published study of arteriosclerosis obliterans [12] compared the ABO blood type of men with various arteriographic patterns of disease. Blood type A was particularly common in cases with single occlusive lesions with minimal arterial irregularity, but not in cases where irregularity was the predominant pathology. Here, occlusion presumably signified thrombus formation, and irregularity, atheromata. Then, too, the present study has shown that abdominal aortic aneurysm, an atherosclerotic condition in which thrombosis is not thought to play a pathogenetic role and which has some other etiologies in common with arteriosclerosis obliterans (e.g., smoking [6, 13]), does not share the association with ABO type. An explanation for these findings may lie in the fact that plasma antihemophilic globulin levels tend to be higher in type

A persons than in type O persons [14]. The relevance of this to clinical thrombosis, however, has not yet been demonstrated.

SUMMARY

A study was made of the distribution of ABO blood type among 502 hospitalized cases of arteriosclerosis obliterans obtained from the records of four Boston vascular surgeons. Compared with the ABO blood type distribution in a control population, the cases had a higher proportion of type A and lower proportion of type O blood, the differences persisting when ethnicity was taken into account. The ABO distribution in patients with abdominal aortic aneurysm did not differ from that of the control population.

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