Blood group as a prognostic indicator in breast cancer

P J HOLDSWORTH,   J THOROGOOD,   E A BENSON,   A D CLAYDEN

Abstract

A retrospective analysis of 1001 patients with invasive breast cancer showed a difference in survival between patients with different blood groups. Analysis of time from operation to local recurrence and to general recurrence reinforced this finding. The difference between blood groups became increasingly significant after accepted prognostic factors were allowed for. Patients at particularly high risk of early death or general recurrence were those with blood groups B and AB, those with group AB having a greater relative local recurrence rate.

Introduction

Several factors are known to influence survival of women with breast cancer,[1] but little is known of the prognostic influence of different blood groups. In a series of 1323 radical mastectomies for cancer carried out from 1940 to 1965 Donegan associated 10 year survival with various constitutional, clinical, and pathological factors, and analysis of the blood groups of 986 patients showed that a good survival was associated with blood group AB (10 year relative survival 66·2%) and a poor survival with blood group B (10 year relative survival 27%).[2] We present a similar sized series and compare the results.

Patients and methods

Between 1976 and 1981 in a study of prognostic factors in breast cancer the Yorkshire Breast Cancer Group collected 1186 cases of operable, invasive breast cancer (T_0-T_3, N_0-N_{1B}, M_0); information about blood groups was available for 1001 of these. The remaining
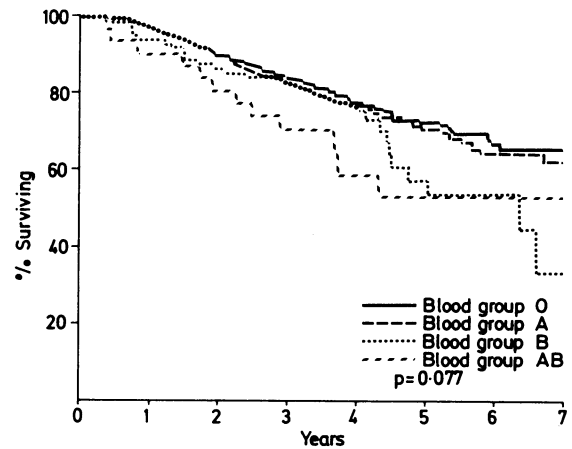

FIG 1—Survival of patients with breast cancer according to blood group.

TABLE I—Distribution of blood groups

	Blood group				Total
	O	A	B	AB	
Women with operable breast cancer (%)	485 (48·4)	403 (40·3)	82 (8·2)	31 (3·1)	1001
Women in Yorkshire Region* (%)	462·82 (46·2)	419·73 (41·9)	85·65 (8·6)	32·80 (3·3)	1001

*Figures from Blood Transfusion Service (n = 30 473) scaled down to proportions out of 1001.

TABLE II—Log rank survival analysis of patients with breast cancer

Blood group	No of patients	No of deaths observed	No of deaths expected	Relative death rate	Relative general recurrence rate	Relative local recurrence rate
O	485	120	130·69	0·92	0·93	0·87
A	403	106	107·29	0·99	0·98	1·05
B	82	27	19·97	1·35	1·27	1·14
AB	31	12	7·05	1·70	1·80	2·10
Total	1001	265				
p				0·077	0·077	0·038

General Infirmary at Leeds, Leeds LS1 3EX

P J HOLDSWORTH, FRCSED, surgical registrar, department of urology

E A BENSON, MA, FRCS, consultant surgeon

Yorkshire Regional Cancer Organisation, Cookridge Hospital, Leeds LS16 6QB

J THOROGOOD, BSC, data processor

Department of Community Medicine, University of Leeds, Leeds LS2 9JT

A D CLAYDEN, PHD, senior lecturer in medical statistics

Correspondence to: Mr P J Holdsworth.

185 cases were not included because certain data were missing. The numbers of patients available for analysis at the time of operation and one, two, and five years later were 1001, 966, 883, and 259, respectively. These were not survival figures but reflect the fact that only a proportion of the patients had undergone the follow up at five years. The standard treatment used was simple mastectomy and usually radiotherapy if axillary nodes were affected.

Results

The distribution of particular blood groups in the population of women presenting with operable breast cancer was not significantly different from that of women in the areas of Yorkshire covered by the contributing surgeons ($\chi^2 = 1·98$; p = 0·57) (table I).[3]

Log rank analysis[4] showed a difference in survival between patients with different blood groups. Patients with blood groups B and AB had higher relative rates of death and general recurrence than those with groups O and A when analysed as four separate groups (table II, figs 1 and 2), but the differences just failed to reach significance (p = 0·077). A significant result was, however, observed when the time to local recurrence was analysed (p = 0·038) (fig 3), and in this case patients with group AB alone had a high relative local recurrence rate. When the high risk groups, B and AB, were combined and compared with the combined low risk groups, O and A, a significant difference in survival (p = 0·015) and general recurrence (p = 0·023) was seen (figs 4 and 5). This combination of groups increased the
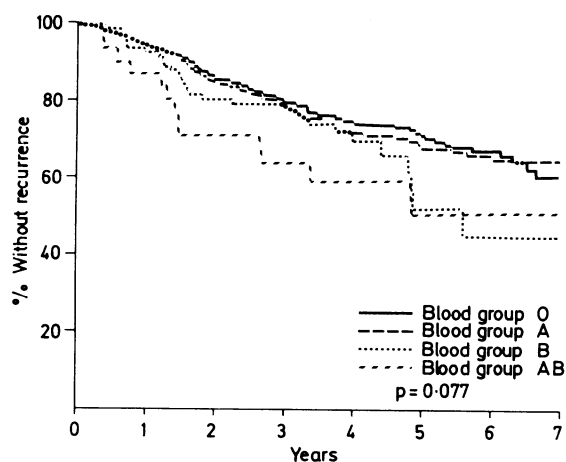
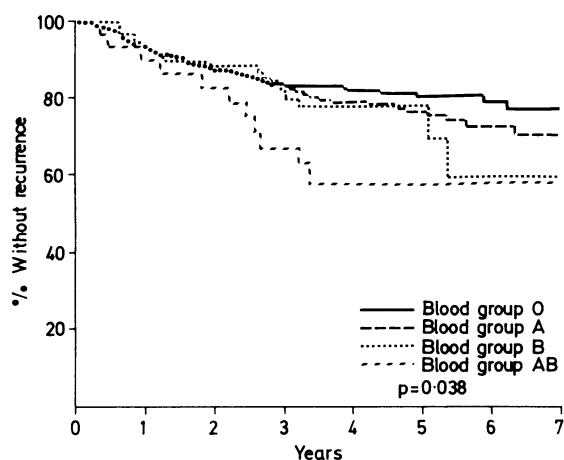FIG 2—Rate of general recurrence of breast cancer according to blood group.

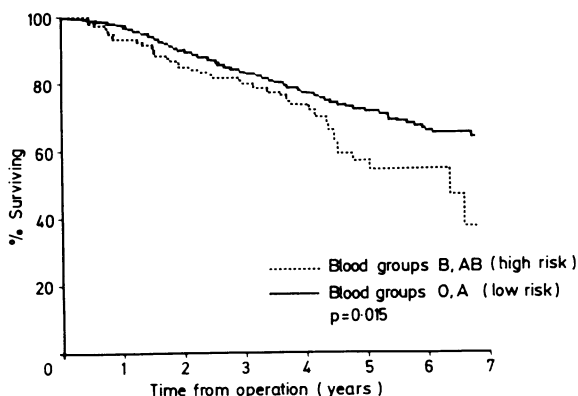FIG 3—Survival without local recurrence in patients with breast cancer according to blood group.

FIG 4—Survival of patients with breast cancer with high risk and low risk blood groups.

remained significant, and most increased in significance, when these prognostic factors were allowed for individually. The relative risk[5] of patients having B or AB blood group in all cases lay between 1·5:1 and 1·8:1.

To examine the influence of more than two prognostic factors simultaneously we used Cox's regression model[5] on the established key prognostic factors, T stage, M stage, clinical stage, pathological grade, and pathological nodal invasion. This tested whether blood group could make any useful contribution to a model of survival, and a stepwise analysis was used to identify a set of independent variables that were significantly related to survival. T stage, N stage, and blood group were found to enter the model, and the contribution of blood group was significant (p = 0·013) with a relative risk of 1·57 (95% confidence interval 1·12-2·21. The pathological factors grade and nodal invasion, together with blood group, all entered the model, and blood group again made a significant contribution (p = 0·025)
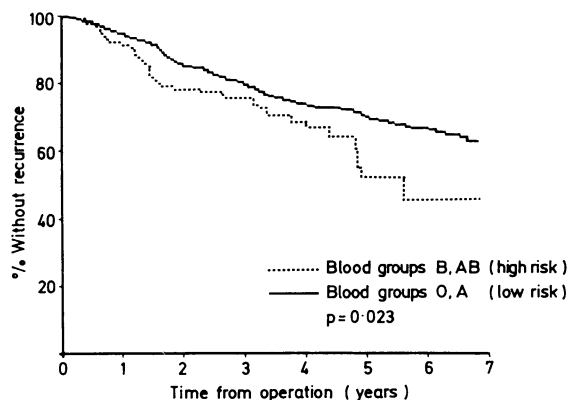
FIG 5—Survival without general recurrence in patients with breast cancer with high risk and low risk blood groups.

FIG 6—Survival without local recurrence in patients with breast cancer with high risk and low risk blood groups.

p value for the analysis of time to local recurrence to 0·063 (fig 6). Thus the type of blood group may have a different effect in an analysis of time to local recurrence (in which patients with group AB were at particularly high risk) than in an analysis of time to general recurrence or death (in which those with groups B and AB had high relative rates of death and general recurrence). To see whether established prognostic factors[1] accounted for the difference in survival we analysed the results allowing for individual factors such as TNM stage, clinical stage, etc (table III). Rhesus factor was also included because of its relation to blood groups. By taking these factors into account we ensured that the overall difference between blood groups was not biased by the presence of a particular factor. All results

TABLE III—Results of analysis controlling for effect of blood group and other prognostic factors on relative risk of death of patients with breast cancer

Factor allowed for	Relative risk (95% confidence limits)	p Value
Blood group	1·52 (1·08-2·14)	0·015
Blood group and:		
Palpable axillary nodes	1·51 (1·08-2·12)	0·016
Cancerous axillary nodes	1·60 (1·13-2·28)	0·008
T stage	1·64 (1·17-2·31)	0·004
N stage	1·51 (1·08-2·12)	0·017
Clinical stage	1·63 (1·16-2·30)	0·004
Pathological size of lump	1·62 (1·14-2·31)	0·007
First grade	1·51 (1·06-2·15)	0·022
Grade assessed at one centre	1·64 (1·16-2·33)	0·005
Tubules	1·67 (1·13-2·46)	0·010
Pleomorphism	1·79 (1·21-2·65)	0·003
Mitotic activity	1·72 (1·16-2·55)	0·006
Nodes invaded	1·47 (1·02-2·10)	0·036
T stage and M stage	1·57 (1·12-2·21)	0·013
Grade and nodes invaded	1·56 (1·08-2·27)	0·025
Clinical stage and grade and nodes invaded	1·69 (1·17-2·46)	0·009
Rhesus factor	1·51 (1·08-2·12)	0·017