ACTA MED PORT, Suppl 1: 147, 1980

HOMOGRAFT VALVES: IS DEGENERATION INEVITABLE?

Endre Bodnar, William H Wain, Donald N Ross

Department of Surgery. Cardiothoracic Institute. London and Homograft Department. National Heart Hospital. London.

Since the first successful sub-coronary insertion (Ross 1962), the homograft aortic valve has been the favourite amongst many types of mechanical or biological cardiac valve replacements at the National Heart Hospital. Recent studies on long term patient survival after homograft insertion have revealed excellent results (Bodnar et al 1979), surpassed only by the autotransplanted pulmonary valves. (Ross 1967; Ross et al 1979).

It is generally accepted that homograft valves inserted into the aortic position have two major advantages (Ross 1962), they are non-thrombogenic, and (Bodnar et al 1979) their haemodynamic performance is identical to that of a normal aortic valve. However, two major disadvantages are often reported as well (Ross 1962): difficulties in the collection, preparation and storage of these valves, and (Bodnar et al 1979) the rapid degeneration which affects the function of the homograft (Stinson et al 1977; Anderson and Hancock 1976; Lefrak and Starr 1979).

An analysis of the overall performance of the homograft valve in the aortic position has show satisfactory long term results (Bodnar et al 1979). The present work focuses attention on the degeneration of homograft valves in terms of incidence, onset and pattern.

MATERIALS AND METHODS

Surgical patients who underwent isolated aortic valve replacement with homografts between 1964 and 1978 have been selected for the study. The valves have been inserted with standard cardiopulmonary bypass operation and with a standard surgical technique (Ross et al 1979). No anticoagulants were administered in the entire series.

The homografts have been collected from mortuaries under nonsterile conditions and within 48 hours of death. Antibiotics, or ethylene oxide or gamma irradiation were used to sterilise the valves and freeze drying, flash freezing or a nutrient solution were applied for preservation (Table 1). Details of these current methods have been reported recently (Wain et al 1977).

Follow up data has been obtained at Outpatient Clinics or at reoperation at the National Heart Hospital, and in some cases from information supplied by other centres or by the patient's family doctor.

Degeneration was defined as calcific or non-calcific tissue decay or shrinkage in the inserted valve causing stenosis and/or incompetence.

Technical failure was assessed as valve malfunction due to improper surgical technique and without concomitant degeneration.

Table 1
Aortic valve replacement with homograft and autograft valves

Preservation	Period	Number
Freeze Dried Homografts	1964-1967	145
Frozen Homografts	1968-1970	89
Fresh Homografts	1971-1979	202
Total		436

The diagnosis of infection on the valve was generally based on positive bacteriological reports, and in some cases the negative bacteriology was overruled by the macroscopic appearance of the valve.

Thromboembolism was defined as either thrombotic apposition on the valve with or without systemic embolisation, or systemic embolism with or without thrombotic apposition on the valve.

Valve-related death was defined as death either caused by or only accompanied by any of the above mentioned malfunctions.

The actuarial survival curve and the individual event-free proportions were assessed according to Anderson et al (1974). The instantaneous rate of events as well as significance levels were calculated as decribed previously (Bodnar et al 1979).

RESULTS

The incidence and the onset of the possible valve related complications is demonstrated by the individual event-free curves (Fig. 1). There was only one minor embolism resulting in 99.7±% free of embolism, whereas 90% was found free of infection (Fig. 2) and 90% free of technical problems after 14 years (Fig. 3). The probability of degeneration barely exceeded 40% during this 14 years period giving a 59% proportion free of degeneration (Fig. 4).

The probability of freedom from reoperation was 55% over 14 years (Fig. 4), and the indication for the vast majority of these reoperation was degenerative failure of the valves.

The incidence of reoperation was not reflected in survival figures, 85% survival after 14 years, as the probability of valve related death and that of the reoperation was found to be significantly different, $P+< 0.05$.

The changes in the intensity of the risk factors were assessed by calculating the instantaneous rate of the reoperation (Fig. 5 and 6). The increase in risk is certainly time-dependent during the first decade of the follow up period, but after this period no further acceleration was found. In fact, the risk of the valve failure seemed to be decreasing once the first ten years were over.

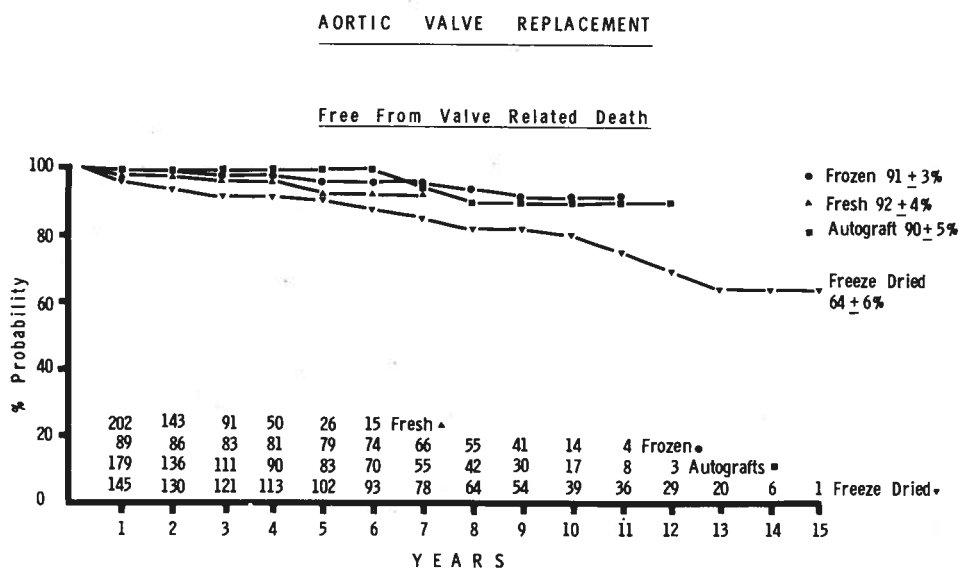

Fig. 1 — *Incidence and onset of the possible valve related complications demonstrated by the individual event-fore curves.*

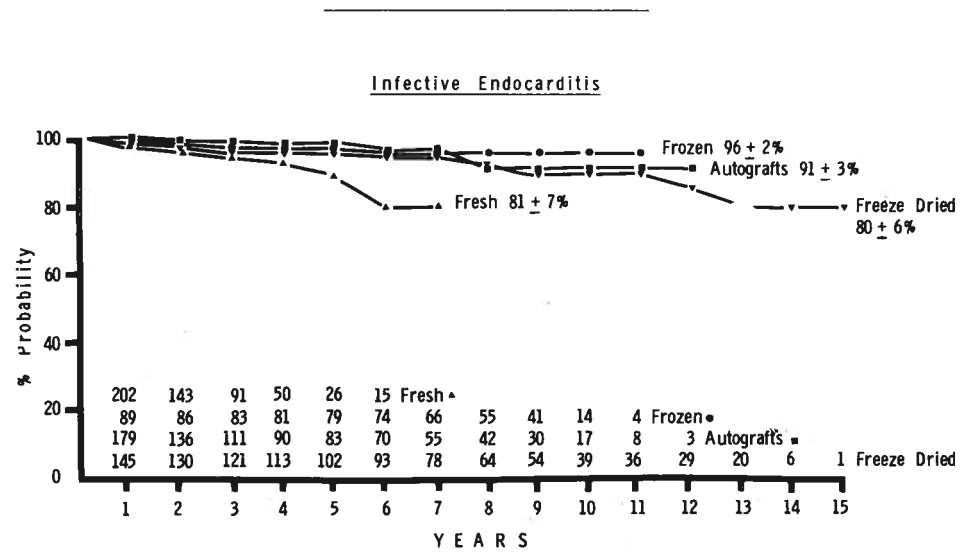

Fig. 2 — *Probability of freedom from infective endocarditis related with time after aortic valve replacement.*

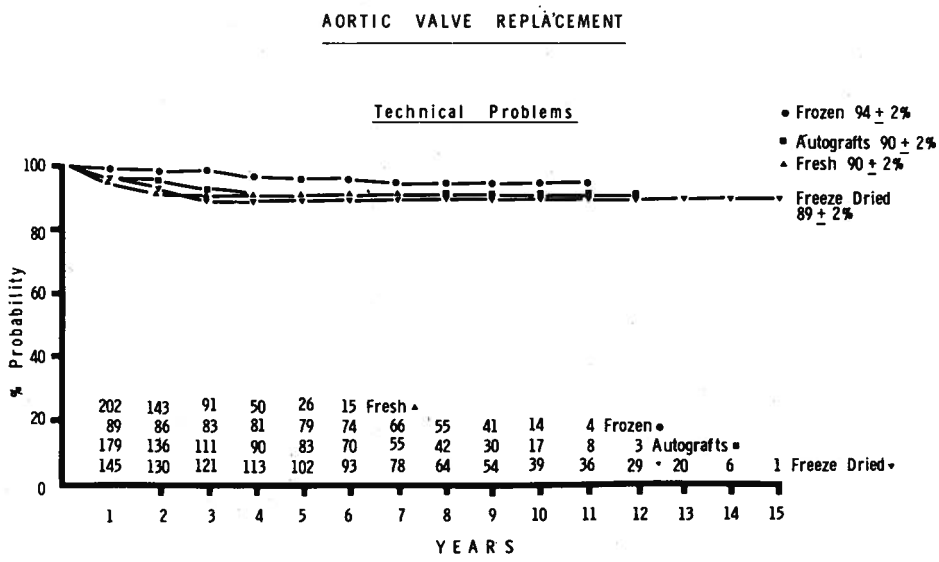

Fig. 3 — *Probability of freedom from technical problems related with time after aortic valve replacement.*

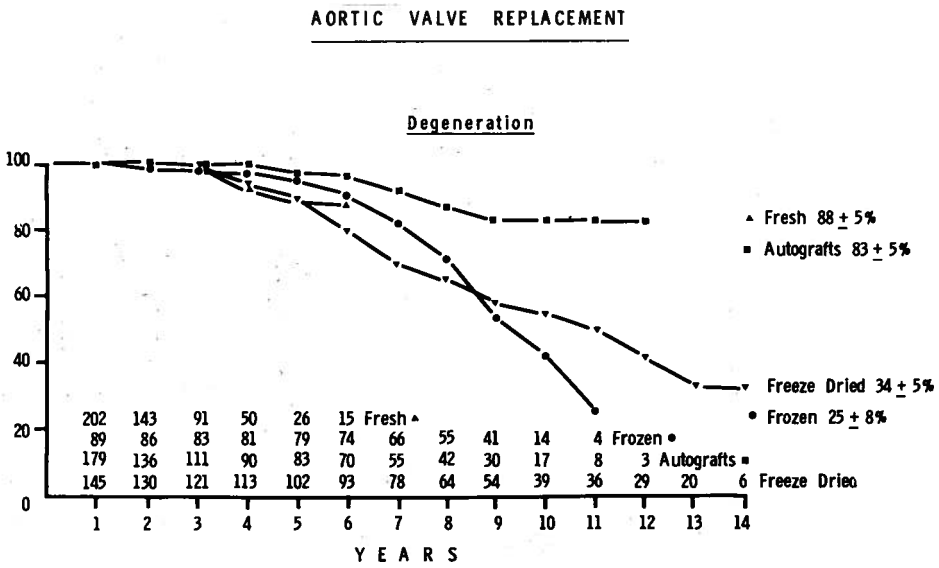

Fig. 4 — *Probability of freedom from degeneration related with tisue after aortic valve replacement.*

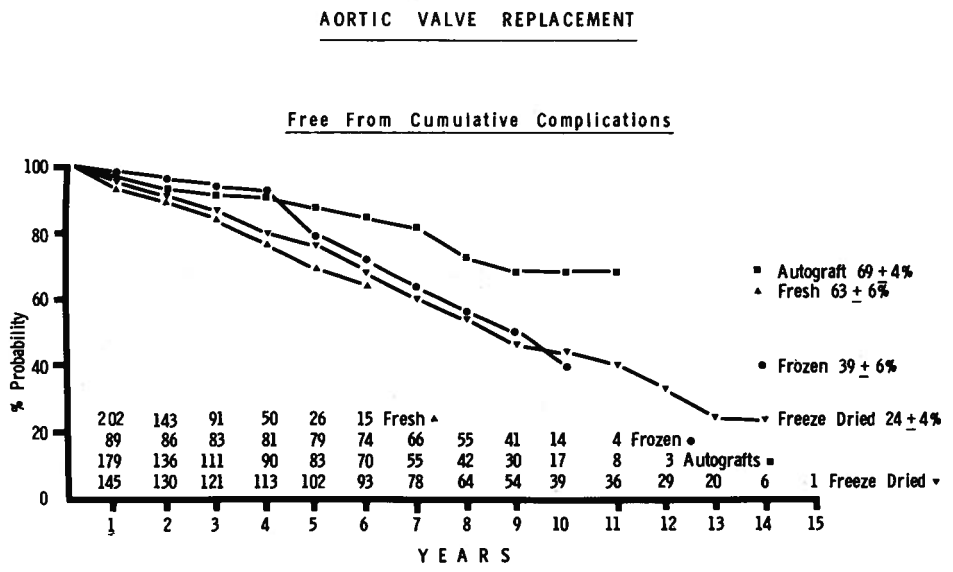

Fig. 5 — *Probability of freedom from complications related with time after aortic valve replacement.*

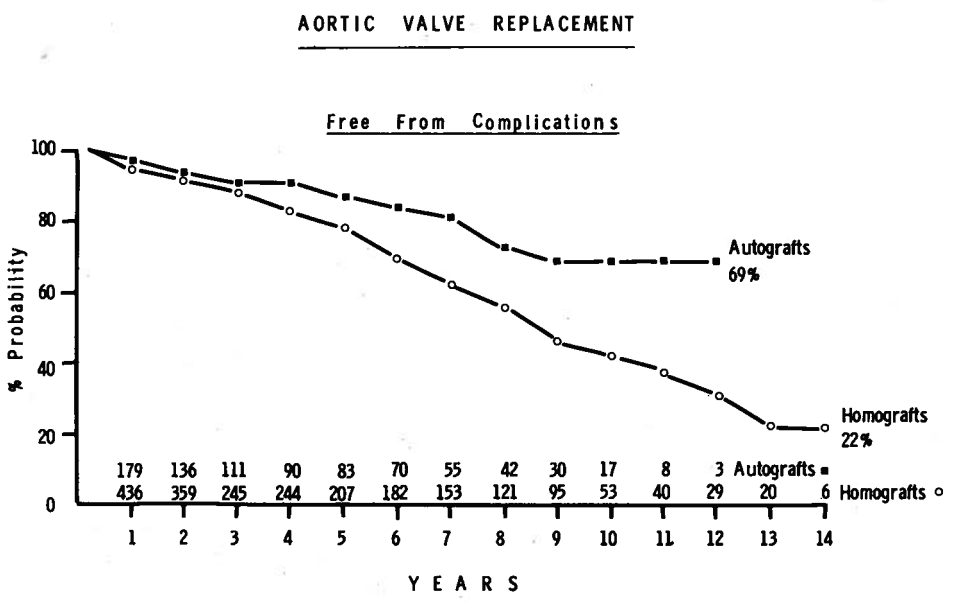

Fig. 6 — Probability of freedom from cumulative complications related with time after aortic valve replacement.

DISCUSSION

The study concentrated on the complications following homograft insertion. Theoretically, two further complications would have been assessed, the haemolysis caused by the valve and the pathological bleeding caused by the anticoagulant treatment due to a given valve. In fact, anticoagulant treatment is unnecessary, thus never administered after homograft insertion, and haemolysis is unknown as a complication of homograft valves so far.

It is obvious from the results, that degeneration is the major single factor responsible for homograft failure. Nevertheless, it is not inevitable during the first 14 years of post-operation survival, as approximately 60% of the patients were found to be free from degenerative processes. In this respect results can be looked at more optimistically than has been suggested by other reports based partly on theoretical considerations and partly on selected publications in the field (Lefrak and Starr 1979) who had no personal experience with homografts.

The instantaneous rate of reoperation gave very important information on the long term dynamism of events. In a shorter follow up study Stinson et al (1977) found the pattern of reoperations were randomly dispersed and for this reason he proposed an exponential model and projected a 3.3% annual reoperation rate. The present study could not confirm his findings and projections. The calculated rate of reoperation would be 37% in 14 years according to Stinson's 3.3% annual reoperation, in fact we found a rate of 45% after 14 yers. The difference between the calculated and observed percentages cannot be incidental since the instantaneous rate of reoperation shows a progressive deviation from a simple exponential scheme during the first ten years of the study and semed to be declining only during the last four years (Fig. 4).

The striking difference between the probability of reoperation and that of the valve related death reflects the benign nature of the homograft degeneration which is a slow process, identical, or very similar to the natural history of aortic valve disease. Consequently, reoperation for homograft failure is always elective with its timing dependent on the clinical symptoms of the patient. Beside the good quality of life without anticoagulants and without restrictions, this benign mode of failure is a third major advantage of homografts when compared to any other type of prosthetic valve.

In conclusion, the statistical assessment of 14 years' experience with homograft valves suggests that degeneration is not inevitable during this period. These encouraging long term results support the continued use of these valves.

RESUMO

HOMOENXERTOS VALVULARES: SERÁ INEVITÁVEL A DEGENERESCÊNCIA?

Para poder concluir da eficácia a longo prazo, os autores analisam os resultados de 14 anos de experiência na aplicação de homoenxertos valvulares na posição aórtica. Dum modo geral, aceitam-se como vantagens as suas qualidades não trombogénicas e o seu funcionamento hemodinâmico idêntico aos das primitivas válvulas, e como inconvenientes à dificuldade de obtenção, preparação e armazenamento, e a rápida degenerescência que poderá afectar o funcionamento do homoenxerto. É sobre esta degenerescência possível que incide a análise, pois a sua eficiência global ficou demonstrada em outro trabalho.

Revifica-se que, em 14 anos se registaram apenas 1 embolismo, 90% tiveram infecção e 90% não tiveram consequências resultantes de técnica. A probabilidade de

degenerescência em 14 anos foi de 41%, dando uma proporção de 59% livres de degenerescência. A probabilidade de não reoperação foi de 55 aos 14 anos, e a quase totalidade de reoperações tiveram como base a falência por degenerescência.

Os autores concluem desta análise estatística de 14 anos de experiência que a degenerescência não é obrigatória a longa distância, e que os bons resultados encorajam a continuação do uso de homoenxertos valvulares na posição aórtica.

REFERENCES

ANDERSON RP, BONCHECK LJ, GRUNKEMEIER G, LAMBERT L, STARR A: The analysis and preparation of surgical results by actuarial methods. *J Surg Research* 16: 224, 1974.

ANDERSON ET, HANDCOCK EW: Long term follow up of aortic valve replacement with the fresh aortic homograft. *J Thorac Cardiovasc Surg* 72: 150, 1976.

BODNAR E, HABERMAN S, WAIN WH: A comparative method for the actuarial analysis of cardiac valve replacements. *Br Heart J*, November 1979.

BODNAR E, MARTELLI V, WAIN WH, ROSS DN: Long term surgical results with homografts inserted for aortic valve disease. *IN PRESS: Proceeding of Symposium on Bioprosthetic Cardiac C Valves*, April 1979, Munich.

BODNAR E, WAIN WH, MARTELLI V, ROOS DN: Long term performance of 580 homograft and autograft valves used for aortic valve replacement. ***Thorac Cardiovasc Surgeon*** 27: 31 1979.

LEFRAK EA, STARR A: Cardiac Valve Protheses. *Appleton-Century-Crofts*, New York, 1979, p. 273.

ROSS DN: Homograft replacement of the aortic valve. *Lancet* 2: 487, 1962.

ROSS DN: Replacement of aortic and mitral valve with a pulmonary autograft. *Lancet* 2: 956, 1967.

ROSS DN, MARTELLI V, WAIN WH: Allograft autograft valves used for aortic valve replacement. In: Tissue Heart Valves, *Ed: M.I. Ionesco, Butterworths*, London, 1979.

STINSON EB, GRIEPP RB, BIEBER CP, SHUMWAY NE: Long term results of isolated aortic and mitral valve replacement with fresh aortic allografts. In: Proceedings of 2nd Henry Ford Hospital International Symposium on cardiac surgery, *Ed: J.C. Davila, Appleton-Centry-Crofts*, New York, 1977.

WAIN WH, PEARCE HM, RIDDEL RW, ROSS DN: A re-evaluation of the antibiotic sterilisation of the heart valve allograft, *Thorax* 32: 740, 1977.

Adress for reprints: *Endre Bodnar*
Department of Surgery
Cardiothoracic Institute
2 Beaumont Street
London W1N 2DX
England