

MEDICAL PRACTICE

*Hospital Topics***Cardiac surgery in Wessex**

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Abstract

The results of 3000 consecutive operations using cardiopulmonary bypass show that the overall early mortality was 6.1%, dropping from 8.9% in the first 1000 to 4.4% in the third 1000. Operations for valve disease have been the most common, the early mortality for aortic valve replacement being 3.1% and for mitral valve replacement 2.9%. Combined aortic and mitral valve replacement had an early mortality of 4.4%. The number of patients undergoing isolated coronary artery bypass grafting has increased from 59 in the first 1000 to 292 in the third 1000 operations, with an overall early mortality of 1.3%. Six hundred and ninety seven patients underwent surgery for congenital heart disease with an overall early mortality of 10.9% (7.5% in the last 2000 cases). The patients have been followed up from one to 8.5 years. A high proportion have returned to work and enjoy a normal life. At the time of review, 87% of the 3000 patients were alive. Long waiting times for outpatient and inpatient care indicate underprovision of facilities relative to regional demand.

Introduction

Reports of total experience from units undertaking open heart surgery remain infrequent. This report of 3000 consecutive open heart procedures performed at the Wessex Cardiac and Thoracic Centre in Southampton between September 1972 and April 1981 is a sequel to the first 1000 cases already reported.¹ The first 1000 cases are included in this report and thus may be compared with the second and third cohorts of 1000 patients.

Wessex region and facilities

The community of 2.8 million served by the regional unit remains unchanged and the facilities have remained unaltered since 1976, with one operating room, four intensive care unit beds, and 20 surgical ward beds. A second cardiac catheter room was brought into operation in May 1979. There are two consultant cardiac surgeons, two consultant adult cardiologists, and one consultant paediatric cardiologist (since October 1978). One fully committed and one part time consultant anaesthetist and two radiologists (the second was appointed in June 1976) make up the permanent medical staff. The complement of junior medical staff remains unchanged as does that of nursing and technical staff.

There remain three experienced perfusionists who have overall control of the extracorporeal bypass management. A dedicated 24 hour laboratory service has been maintained with the help of considerable automation, particularly for blood gas analysis. The homograft valve service remains in the care of a single technician and provides material for aortic valve replacement and the repair of complex congenital lesions.

Because of the increased capacity for investigation, the number of patients undergoing cardiac catheterisation rose from 618 in 1976 to 957 in 1981. As a result despite a 25% increase in the number of operations from 1976 to 1980, the waiting time for surgery has risen from six weeks in 1976 to at least six

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months for non-urgent cases in 1981. This does not show the full extent of the number of patients waiting, as many more are waiting for outpatient assessment and cardiac investigation. This, in turn, is due to a deliberate policy to restrict cardiac investigation and so avoid lengthening the surgical waiting list.

Patients and methods

The patients varied in age from 12 hours to 81 years and in weight from 2.0 kg to 120 kg.

Cardiac catheterisation was omitted in some patients with aortic stenosis in the first 1000 patients but is now carried out in every case of valvular heart disease, with coronary angiography being routinely performed in men over 30, women over 40, and in all who have chest pain regardless of age.

The anaesthetic technique has altered little in the last 2000 cases.

during the same hospital admission as operation. In the last 2000 operations it has been defined as death within 30 days of operation.

All operations for valve replacement or repair are shown in the first two lines of table I, and this includes 318 patients who have had additional procedures such as coronary artery bypass grafting and replacement of the ascending aorta. The number of valve procedures has declined from 577 in the first 1000 to 477 in the third 1000, but the early mortality for valve replacement has stayed fairly constant, 4.7% overall.

All operations for isolated coronary artery bypass grafting are shown on the third line; the number of these procedures rose from 59 in the first 1000, to 191 in the second 1000 and to 292 in the third 1000. The early mortality was 1.3%, and this includes emergency coronary artery bypass grafting for unstable angina and impending infarction.

The miscellaneous group included all operations for acquired heart disease except valve procedures or those for isolated coronary artery bypass grafting. This, therefore, includes operations such as resection of left ventricular aneurysm, with or without coronary artery bypass

TABLE I—Type of operations performed

	1st 1000		2nd 1000		3rd 1000		Total	
	No of patients	% Early mortality	No of patients	% Early mortality	No of patients	% Early mortality	No of patients	% Early mortality
Acquired disease:								
Valve replacement procedures	557	4.8	528	4.6	447	4.7	1532	4.7
Conservative valve procedures	20		41		30	3.3	91	1.1
Isolated coronary artery bypass grafts	59	1.7	190	1.6	292	1.0	541	1.3
Miscellaneous	40	32.5	55	14.5	44	9.1	139	18.0
Congenital disease	324	14.8	186	7.5	187	7.5	697	10.9
Total	1000	8.9	1000	4.9	1000	4.4	3000	6.1

TABLE II—Isolated valve replacement procedures. (Early deaths in parentheses)

	1st 1000	2nd 1000	3rd 1000	Total
Single valve replacements:				
Aortic	179 (7)	208 (5)	167 (5)	554 (3.1%)
Mitral	178 (7)	129 (1)	106 (4)	413 (2.9%)
Tricuspid	5	5	4	14
Total	362 (3.9%)	342 (1.8%)	277 (3.3%)	981 (3%)
Multiple valve replacements:				
Aortic and mitral	95 (4)	51 (4)	34	180 (4.4%)
Aortic and tricuspid	1	1	—	2
Aortic and pulmonary	—	2	—	2
Mitral and tricuspid	11	—	—	11
Tricuspid and pulmonary	—	1	—	1
Aortic, mitral, and tricuspid	23 (2)	5 (1)	11 (2)	39 (12.8%)
Total	130 (4.6%)	60 (8.3%)	45 (4.4%)	235 (5.5%)

It consists essentially of induction with phenoperidine and minimal thiopentone, muscle relaxation with pancuronium, and is maintained with nitrous oxide supplemented with additional phenoperidine.²

Until the beginning of 1978 (just after the start of the third 1000) conventional normothermic perfusion was used in adults, using disposable bubble oxygenators with a Ringer's lactate prime and flow rate of 2.4 l/m². Since 1978, moderate hypothermia to 30°C and myocardial preservation with cold cardioplegic solution³ has been used. In infants deep hypothermia with circulatory arrest has been used,⁴ again with the addition of cardioplegia, since 1978.

There has been a trend away from routine mechanical ventilation overnight of patients so that most patients are now extubated within six hours of return to the intensive care unit. Most children and infants have been extubated within four hours of return to the intensive care unit, although this depends on factors such as the age of the child, clinical state, and the time of day.⁴ Most of the last 2000 patients returned to the general ward within 24 hours.

There has always been excellent liaison between cardiologists and surgeons so that emergency cardiac catheterisation of a patient likely to require immediate surgery may be planned to allow appropriate timing of the operation.

Results

Table I shows the 3000 operations broken down into three groups of 1000. In the first 1000 operations early death was defined as death

grafting, repair of acquired ventricular septal defect, resection of aortic aneurysm, and rarities such as the removal of atrial myxomas. This has been a fairly constant small group with a diminishing early mortality.

The number of operations for congenital heart disease was higher in the first 1000 cases owing to a backlog of cases that has since, been worked off. The figures for the last two cohorts of 1000 are remarkably constant although, year by year, there has been a slight increase since the appointment of a paediatric cardiologist (BRK) in 1978.

ACQUIRED HEART DISEASE

Valve disease

Table II shows all isolated valve replacement procedures. The early mortality for 554 patients undergoing isolated aortic valve replacement was 3.1%, and this includes 163 patients who received antibiotic sterilised homografts with three early and six late deaths. The early mortality for 413 patients undergoing mitral valve replacement was 2.9%. The number of isolated mitral valve replacement operations has fallen from 178 in the first 1000 to 129 in the second and then to 106 operations in the third.

The commonest multiple valve procedure was aortic and mitral replacement, with an early mortality of 4.4%. The overall early

mortality for the 235 patients undergoing replacement of more than one valve was 5.5%.

Table III shows the additional procedures performed in patients undergoing single valve replacement. The commonest of these was coronary artery bypass grafting, which has increased in frequency in the three groups as operative mortality has fallen. Concurrent valve repair was also common, 32 patients undergoing aortic valve replacement also having mitral valve repair (early mortality of 3.1%) and 44 patients undergoing mitral valve replacement also had tricuspid annuloplasty performed, with an early mortality of 11.4%. Of the patients undergoing aortic valve replacement, 43 also had replacement of the ascending aorta, with a 12% early mortality.

Some 41 patients had multiple valve replacements with additional procedures, with an early mortality of 20%.

Coronary artery disease

Table IV shows that not only has the frequency with which coronary artery bypass grafting is performed increased, but that there is an increasing tendency to perform more grafts per patient. In the first 1000 patients no patient had more than three grafts, but

20 in the second 1000 and 98 in the third 1000 had more than three grafts.

In 193 operations an additional procedure was performed with coronary artery bypass grafting. The 153 operations in which a valve was also replaced have already been shown in table III. Twenty five of the remaining 40 operations were for left ventricular aneurysmectomy together with coronary artery bypass grafting, with one death.

Patients over 65

The number of patients operated on over the age of 65 has increased from 102 (with 10.8% early deaths) in the first 1000 patients to 162 (with 4.9% early deaths) in the third 1000. The oldest patient, who was 80, underwent successful mitral valve replacement in 1980 and is still enjoying an independent existence.

CONGENITAL HEART DISEASE

Table V lists the 697 operations for congenital heart disease classified into infants and those aged over 1 year. Despite a steady

TABLE III—Additional procedures performed in patients undergoing single valve replacement. (Early deaths in parentheses)

	1st 1000	2nd 1000	3rd 1000	Total
Patients undergoing aortic valve replacement:				
Coronary vein graft	7 (1)	33 (1)	43 (1)	83 (3.6%)
Ascending aortic replacement	17 (1)	12 (2)	14 (2)	43 (12%)
Mitral valve repair	5	14	13 (1)	32 (3.1%)
Mitral valve repair and tricuspid valve repair	—	3	—	3
Mitral valve repair and coronary vein graft	—	1	1	2
Ventricular septal defect	—	2	3	5
Patients undergoing mitral valve replacement:				
Coronary vein graft	5	13 (3)	25 (2)	43 (12%)
Ascending aortic replacement	2 (2)	—	—	2 (100%)
Descending aortic replacement	1	—	—	1
Tricuspid annuloplasty	11 (2)	22 (3)	11	44 (11.4%)
Resection of left ventricular aneurysm	5	2	—	7
Resection of left ventricular aneurysm and coronary vein graft	3	2 (1)	—	5 (20%)
Atrial septal defect	—	2	—	2
Removal of left atrial myxoma	—	—	1	1
Patients undergoing tricuspid valve replacement:				
Coronary vein graft	—	—	1	1
Mitral valve repair	—	—	1	1
Total	56 (11%)	106 (9.4%)	113 (5.3%)	275 (8%)

TABLE IV—Operations for isolated coronary artery bypass grafting. (Early deaths in parentheses)

	1st 1000	2nd 1000	3rd 1000	Total
Coronary artery bypass graft × 1	22	40 (1)	42 (1)	104 (1.9%)
Coronary artery bypass graft × 2	27	62	70	159
Coronary artery bypass graft × 3	10 (1)	68 (1)	82	160 (1.3%)
Coronary artery bypass graft × 4	—	17 (1)	73 (1)	90 (2.2%)
Coronary artery bypass graft × 5	—	2	22 (1)	24 (4.2%)
Coronary artery bypass graft × 6	—	1	3	4
Total	59 (1.7%)	190 (1.6%)	292 (1%)	541 (1.3%)

TABLE V—Operations for congenital heart disease. (Early deaths in parentheses)

	1st 1000		2nd 1000		3rd 1000		Total		Grand total
	< 1 year	> 1 year	< 1 year	> 1 year	< 1 year	> 1 year	< 1 year	> 1 year	
ASD (secundum or sinus venosus)	—	110	1 (1)	42	1	35	2 (1)	187	189 (0.5%)
ASD (ostium primum)	3 (2)	12	—	6	—	—	3 (2)	18	21 (9.5%)
Common atrium	—	5	1	2	—	—	1	7	8
Ventricular septal defect	6 (1)	36 (2)	19 (2)	14	21	13	46 (3)	63 (2)	109 (4.6%)
Ventricular septal defect and PS	—	18	—	8	2	3	2	29	31
Fallot's tetralogy	6 (4)	36 (6)	7	20 (1)	12 (1)	14	25 (5)	70 (7)	95 (12.6%)
Pulmonary valvotomy	1 (1)	30 (1)	4	14 (1)	3	12	8 (1)	56 (2)	64 (4.7%)
Aortic valve stenosis	7 (6)	12 (1)	—	2	3	9	10 (6)	23 (1)	33 (21%)
TGA (simple)	2 (2)	3	6 (1)	1	12	1	20 (3)	5	25 (12%)
TGA (complex)	2 (1)	1 (1)	1	—	4 (1)	—	7 (2)	1 (1)	8 (38%)
Double outlet right ventricle	1 (1)	4 (1)	3 (1)	2 (1)	1	1	5 (2)	7 (2)	12 (33%)
Truncus arteriosus	1	1 (1)	4 (1)	—	2 (1)	—	7 (2)	1	8 (38%)
TAPVD	4 (3)	1	1	—	5	—	10 (3)	1	11 (27%)
Total atrioventricular canal	—	3 (2)	—	3	4 (2)	2	4 (2)	8 (2)	12 (33%)
Fontan for tricuspid atresia	—	2 (1)	—	4	—	3 (1)	—	9 (2)	9 (22%)
Miscellaneous	4 (4)	13 (7)	8 (4)	13 (1)	11 (5)	13 (3)	23 (13)	39 (11)	62 (39%)
Total	37 (25)	287 (23)	55 (10)	131 (4)	81 (10)	106 (4)	173 (45)	524 (31)	697 (10.9%)

ASD = Atrial septal defect. PS = Pulmonary stenosis. TGA = Transposition of the great arteries. TAPVD = Total anomalous pulmonary venous drainage.

increase in the proportion of infants, the operative mortality in this challenging group has fallen to 12% in the last 1000 cases. The largest subgroup was closure of secundum or sinus venosus atrial septal defect, the only early death among the 189 patients being in a moribund 6 month old baby. In the first 1000 cases 14 of the children having isolated ventricular septal defect closure were infants, in the second 1000 the figure had risen to 58, and in the third 1000 to 62. The overall mortality for these closures was 4.6%. Ninety five cases of Fallot's tetralogy were corrected, 53 of them in the last 2000 patients, with two deaths. There were 25 operations for simple transposition of the great arteries, and the three deaths were all in babies under 3 days old.

The miscellaneous group, which comprised a mixed and formidable collection of cases, includes a group of six patients who underwent correction of the interrupted aortic arch complex with one early death.

Two infants under 24 hours old had corrective surgery and both survived; one had pulmonary atresia with intact ventricular septum and the other obstructed total anomalous pulmonary venous drainage.

Intra-aortic balloon pump

Since the acquisition in 1976 of an intra-aortic balloon pump it has been used in 53 patients who could not be weaned from the cardiopulmonary bypass machine, and 36 of these patients left hospital. Five of them had the pump inserted just before cardiac catheterisation.

Late mortality

Most of the 215 notified late deaths occurred in the first 1000. If early and late deaths are added together 87% of all patients are still alive at the time of writing.

Discussion

One of the purposes of a report such as this is to note the changing pattern in demand as reflected in the practice of the unit concerned. In Wessex the increase in coronary artery surgery from 6% to 30% of all open heart procedures has been the most striking trend, and this continues. At the same time, there has been a modest decrease in the amount of valve surgery, notably for mitral valve disease, which is presumably related to the lessening incidence of rheumatic heart disease nationally. Nevertheless, there continues to be a sustained demand for surgery for degenerative valve disease, notably for the calcified aortic valve and for degenerative mitral regurgitation with or without chordal rupture, and there are still many patients with rheumatic disease coming forward for surgery. The demand for surgery for congenital heart disease has remained remarkably constant, but the trend towards corrective surgery in infancy is clearly shown in table II.

Another obvious factor for analysis is that of surgical risk. The overall hospital mortality in the third 1000 was less than half that in the first 1000 cases (table I) and may now be compared favourably with the risk attached to any other form of major surgery. The improved safety for the patient may be ascribed to several factors set against a background of increasing experience affecting the whole team. Specifically, we would cite the introduction of cold cardioplegia for myocardial protection in late 1977 as a most important safety factor, being particularly valuable in the difficult case and when operations are carried out by surgeons in training. The intra-aortic balloon pump, as the only available mechanical means of circulatory support, has proved life saving on 37 occasions after cardiopulmonary bypass and, when used judiciously before operation, has resulted in critically ill patients reaching the operating room with improved chance of survival. New antiarrhythmic drugs and inotropic agents have helped considerably in improving postoperative care.

Surgical risk in relation to advanced age has not shown an appreciable correlation. The proportion of patients over 65 has slowly increased to 16% of all adults operated on in the third

1000, yet the early mortality in this group was not appreciably different from that in younger patients.

The connection between surgical risk and the presentation of the patient has, as might be expected, proved to be extremely important. Thirty per cent of those who presented as emergencies (defined as those whose operation took place out of normal working hours or who displaced another from the day's planned list) were early deaths in the first 1000. Although the proportion of emergency operations for all age groups has steadily increased from 11% to 14%, the early mortality has now fallen to 15%.

The risk in individual categories of valve disease shows an early mortality of 3.1% for isolated aortic and 2.9% for isolated mitral valve replacements, and the risk for multiple valve replacement is also acceptably low in this series, with an early mortality rate of 4.4% for combined aortic and mitral valve replacement. The mortality figures for both single and multiple valve replacement throw doubt on those quoted by Oakley.⁵

The most important change in surgical practice in treating valve disease has resulted from identifying associated coronary artery disease. This is treated by coronary artery bypass grafting with the same angiographic criteria for grafting as are used when treating patients with isolated symptomatic ischaemic heart disease. This, in turn, results from routine coronary angiography in all patients being investigated for valve disease. This policy, which was in use for much but not all of the time covered by this report, has not resulted in an appreciable increase in early mortality and will, we hope, improve long term survival.

The steady increase in coronary artery surgery and in the number of grafts per patient has already been commented on, and the safety of coronary artery bypass grafting is reflected in the early mortality figure of 1.3%. The need for reoperation, both for progressive disease and graft occlusion has, so far, been a minor problem, with only 19 reoperations in this series. Of much greater concern is the scale of demand for coronary artery surgery and the need we are now experiencing to ration the service we can offer our regional population.

While cardiac surgery in adults has been consolidated in recent years, as is borne out by the consistency of our figures, surgery for congenital heart disease and, in particular, the correction of complex lesions in infants and neonates, has been a genuinely developing specialty. The determination to correct rather than palliate life threatening lesions in infancy whenever practicable has resulted in a steady reduction in early mortality in this difficult area and, we believe, has been beneficial to the families concerned. With growing experience in this highly specialised surgery have come considerable gains in the understanding of each abnormality and its variants, in the knowledge of what is possible and what is not, and in the management of the small patient at every stage. The results reported here compare favourably with those coming from larger centres specialising in paediatric care. Nevertheless, if the results of surgery in infants are to be improved throughout the United Kingdom, this specialised surgery should be concentrated in fewer, more experienced units.⁶

Conclusion

In conclusion, we have reported the performance of a regional cardiac surgical unit drawing on a population of 2.8 million people over a period of 8.5 years. This has been achieved with one operating room and four intensive care beds.

Although valve surgery has been the largest category in this review, and the early results and long term follow up show clearly the benefits of this type of surgery to the community, the problem of providing a service to the large number of sufferers from coronary artery disease, also a demonstrably cost effective undertaking, remains our outstanding challenge.

The absolute number of patients treated for congenital heart disease is relatively small, reflecting the yield from our regional population size, but the quality of result achieved compares favourably with other reports.

We believe that in presenting our experience in Wessex we are adding to the sum of hard data for contemporary clinicians and administrators alike, thereby giving useful evidence for future development in our speciality.

We would like to express our sincere thanks to the junior medical staff, nurses, technicians, laboratory staff, and many others who have contributed so much to our work and who have made this report possible. We would also particularly like to thank Mrs Anne Longhurst for the painstaking retrieval of the information regarding this large number of patients and Mrs Julie Mintram for her secretarial help.

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Clinical Topics

Identification of adverse reactions to new drugs. II (continued): How were 18 important adverse reactions discovered and with what delays?

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In the first half of part II (published last week, p 289) I described how the first 13 out of 18 important adverse reactions to new drugs had been discovered and in each case tried to identify features affecting the initial reports and subsequent verification of causality. I now continue with the remaining five adverse reactions identified and conclude part II by assessing the "avoidable delays" in recognising the major adverse reactions.

Results (continued)

The table published in the first half of part II lists the 18 important adverse reactions selected for review of the discovery process.

(14) PSEUDOMEMBRANOUS COLITIS DUE TO TETRACYCLINES—DRUGS MARKETING 1949; NO REGULATORY WARNING IN UK

Alerting—Pseudomembranous colitis was reported by Reiner *et al*¹ three years after tetracyclines had been introduced.

Verification—Klotz *et al*² reported another series of cases in which one patient showed a clear relation of symptoms to repeated re-challenge. Taken in conjunction with characteristic biopsy appearances of a relatively unusual nature causality was established beyond reasonable doubt, but the reaction was extremely rare.

Comment—The incidence is of the order of 1 in a million prescriptions. A cohort approach would have been of no value.

(15) PSEUDOMEMBRANOUS COLITIS DUE TO LINCOMYCIN—DRUG MARKETING 1964; UK REGULATORY WARNINGS 1976 AND 1979

Alerting—After four years a clinical trial by Price *et al*³ showed that diarrhoea occurred in 35 out of 71 patients receiving lincomycin, which was significantly more than the 8% and 13% of patients taking phenoxymethylpenicillin and phenethicillin. Against the previous background of colitis with tetracyclines the report of three cases by Benner and Tellman⁴ six years after marketing provided prima facie evidence.

Verification—Three years later Scott *et al*⁵ reported that of seven consecutive cases of pseudomembranous colitis seen in a six month period six patients had received lincomycin, and the antibiotic history of the seventh was obscure. Review of necropsy records at the two hospitals where the authors worked yielded only one additional case over a two year period, also in a patient who had been given lincomycin.

Comment—The long delay before alerting cannot be explained. The incidence is not known; it is not possible to say what sample size would have been needed for a recorded-release cohort study.

(16) PSEUDOMEMBRANOUS COLITIS DUE TO CLINDAMYCIN—DRUG MARKETING 1968; UK REGULATORY WARNINGS 1976 AND 1979

Alerting—Clindamycin was developed as an "improvement" on lincomycin and has a similar range of antibacterial activity. In a randomised comparative study with lincomycin in 12 volunteers⁶ diarrhoea occurred after 10 out of 24 single doses of 500 mg clindamycin, compared with eight out of 24 after 500 mg lincomycin. In the first clinical trial, however,⁷ it was thought that diarrhoea was less frequent at a dose of 300 mg six-hourly but no comparative study was performed. The first three cases were reported five years after marketing.⁸

Verification—Confirmatory reports the same year^{9 10} with x ray and biopsy findings made a causal relation almost certain. After an overall delay of 15 years an analysis of adverse reactions notified to the Committee on the Safety of Medicines¹¹ showed a great excess of

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