

## Chapter 11: Renal Transplantation

### *Introduction*

A chapter on renal transplantation is provided for the first time.

Information regarding national transplant activity in the UK, together with patient and graft survival data, are provided annually by the United Kingdom Transplant Support Service Authority (UKTSSA) and will not be duplicated here.

The Renal Association Standards document contained standards and recommendations for renal transplantation which were developed in conjunction with the British Transplantation Society. The British Transplantation Society subsequently produced a more detailed standards document in 1998 entitled “Towards standards for organ and tissue transplantation in the United Kingdom”. These documents largely address organisational issues of renal transplantation, and histocompatibility matching and allocation of donor kidneys. The standards for outcome in renal transplantation address the proportion of recipients with immediate graft function together with patient and graft survival. Whilst it is recommended that blood pressure, serum creatinine and cholesterol are monitored, no standards are recommended for these variables.

This first report on renal transplantation from the Renal Registry has attempted to provide data not available from other sources. These include data relating transplant patients to the pool of dialysis patients from which they are drawn. Data on graft renal function and indices of quality of care are reported. Data related to pre-transplant and post-transplant history are also being collected, but data collection on these variables, which may have significant influence on graft outcome, is not sufficiently advanced to enable meaningful analyses to be performed at present.

It is too early to present graft or patient outcome data on the 1998 cohort of patients who received a renal transplant: these will be presented in the next Registry report.

### *Transplants performed 1998*

In 1998, 656 patients under follow up in participating units were transplanted. Details are given in tables 11.1 and 11.2. The intent is to provide data on transplant activity related to the patients on Renal Replacement Therapy in units participating in the Registry. Thus data on patients transferring in from non-registry units specifically for transplantation are excluded, but data on patients from registry units transferring to non-registry units for transplantation are included.

	<b>Median age</b>	<b>Number</b>
E&W (19 renal units)	43.0	524
Scotland (all units)	39.0	132
<b>Total Registry</b>	<b>42.0</b>	<b>656</b>

**Table 11.1** New transplants from the Registry 1998

The sex distribution is slightly different for Scotland but England and Wales are fairly similar. The newly transplanted patients did not differ in gender from the established transplanted patients although there were some possible differences in primary diagnosis (Table 11.2). In the established transplant patients diabetes was less common. This may reflect a relative reluctance to treat diabetic patients in the past, and the shorter prognosis of diabetic patients.

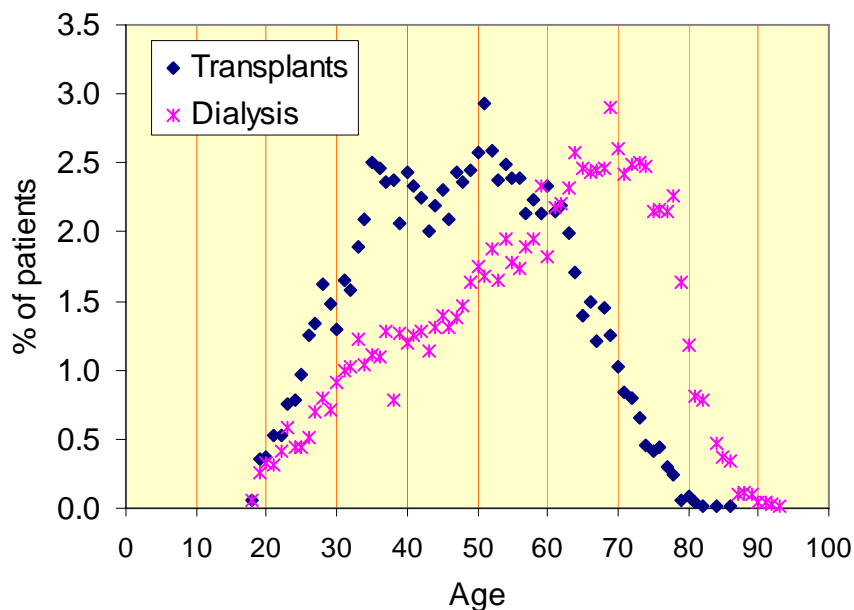
	New transplants in 1998		Established transplants 1/1/98	
	%	No	%	No
Aetiology uncertain/GN not proven	18.6	122	24.0	1508
Glomerulonephritis	23.5	154	18.7	1175
Pyelonephritis	14.5	95	18.6	1171
Diabetes	10.5	69	6.0	380
Renal Vascular disease	1.2	8	1.1	70
Hypertension	3.7	24	5.1	320
Polycystic Kidney	11.3	74	11.4	713
Not sent	4.7	31	1.4	85
Other	12.0	79	13.7	859

**Table 11.2 Primary diagnosis of transplant patients.**

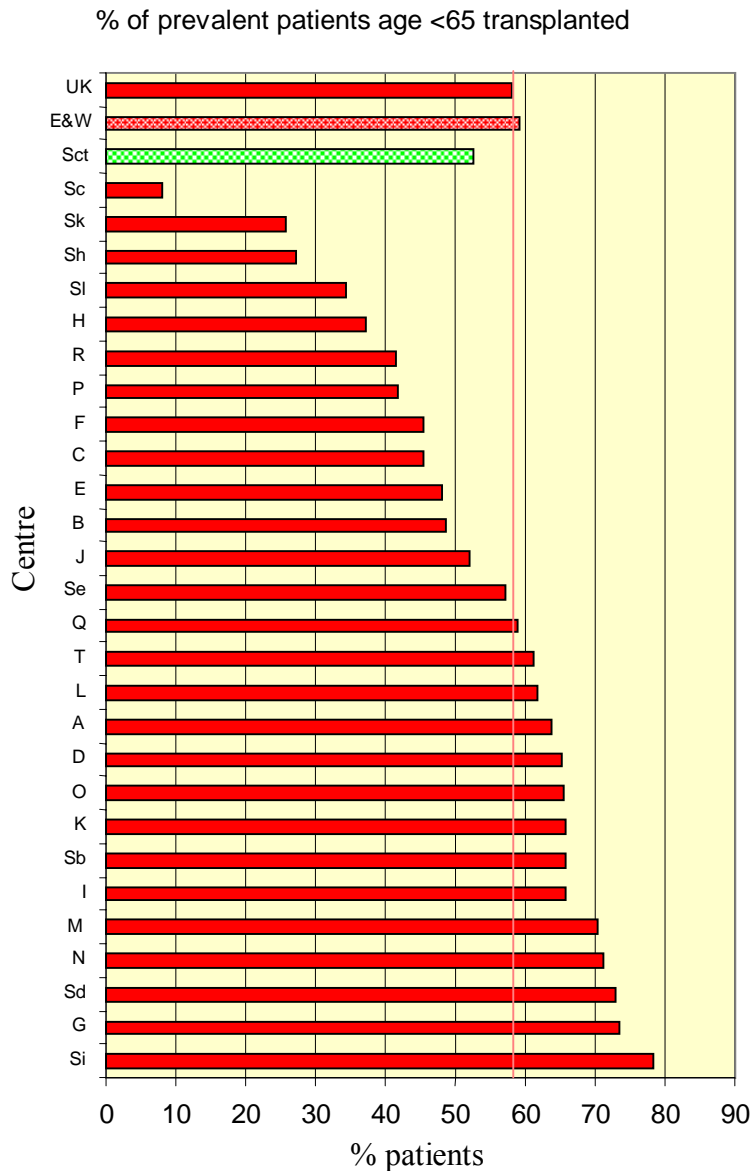
***Patients with established renal transplants***

The age distribution of the prevalent transplanted patients is shown in figure 11.1. The median age was 48 compared with 60 for the dialysis population from which they were drawn.

**Age distributions of adult dialysis and transplant patients**



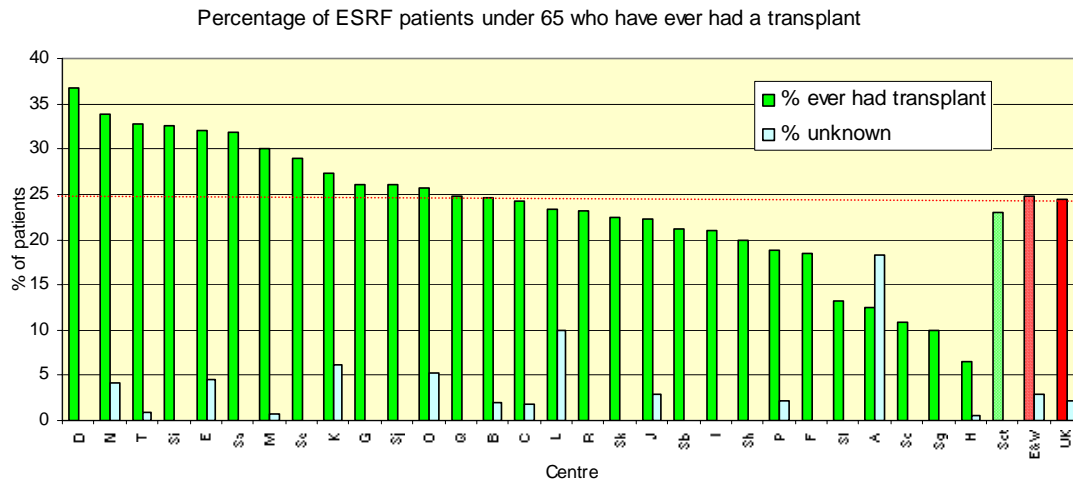
**Figure 11.1 Age histogram of dialysis and transplant patients**



**Figure 11.2 Percentage of prevalent RRT patients age >65 with a functioning transplant on 31/12/98**

The percentage of all renal replacement therapy patients age less than 65 years with a functioning renal transplant at the end of 1998 is shown for each participating centre in figure 11.2.

For individual registry units, the proportion of the prevalent dialysis patients under 65 years old that had ever had a renal transplant is illustrated in figure 11.3. These figures are an underestimate, as some patients had no information regarding previous transplantation when transferring in on dialysis from a non-registry unit and are treated as unknown.



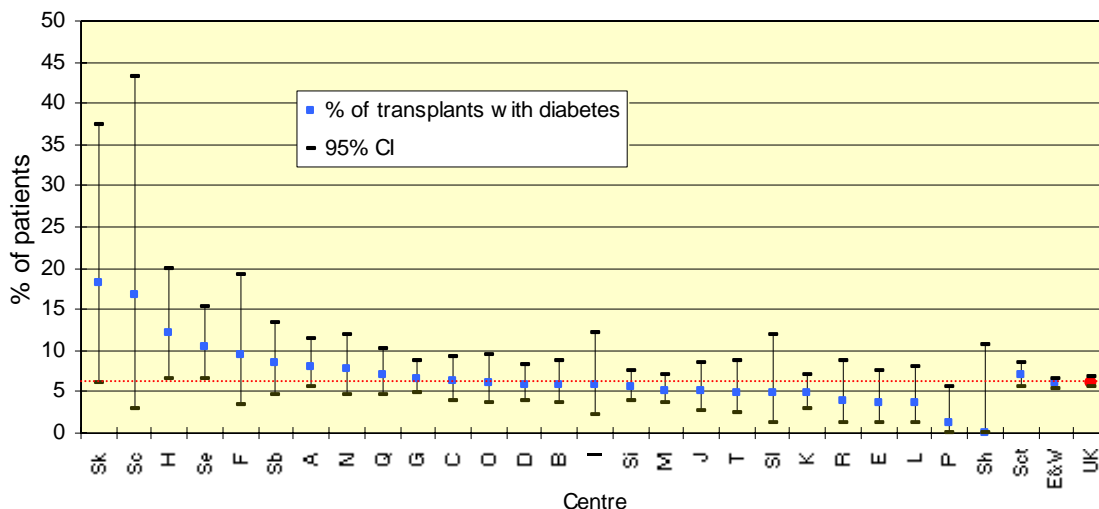
**Figure 11.3 Percentage of current renal replacement therapy patients age < 65 who have ever received a renal transplant – currently functioning or not**

The Registry cannot explain the different proportions observed between units. Plausible explanations include differences in age of units (patients in older units likely to have had a longer exposure to possible transplantation than in newer units) and differences in the proportion of prevalent dialysis patients made up by ethnic minorities which are harder to HLA match and thus transplant. The Registry does not currently have sufficient data to test these hypotheses.

### ***Transplantation in patients with diabetes mellitus***

Diabetics are a group of patients with End Stage Renal Failure whose prognosis has been shown to improve with renal transplantation. Some physicians therefore would give priority to diabetics awaiting transplantation. However the prognosis of diabetics transplanted is less than that of non-diabetics, largely due to death with a functioning graft. As there is shortage of organs some transplant practitioners feel it is more appropriate to give the organs to recipients who will survive longer. Figure 11.4 shows the proportion of patients in each registry centre with a functioning renal transplant on 31/12/98 with a primary diagnosis of diabetes mellitus.

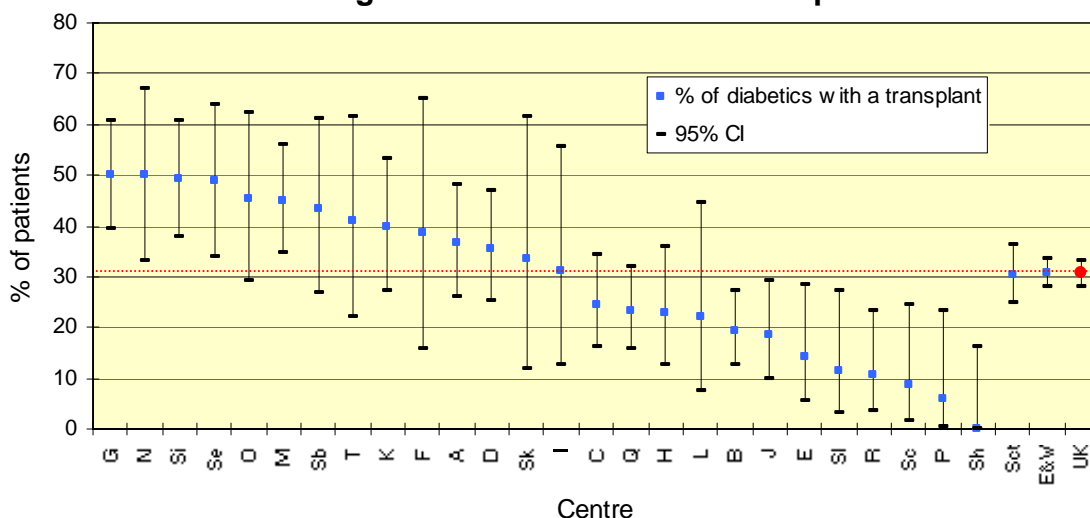
### Percentage of transplant patients with diabetes



**Figure 11.4 Percentage of current transplant patients with diabetes mellitus, by centre**

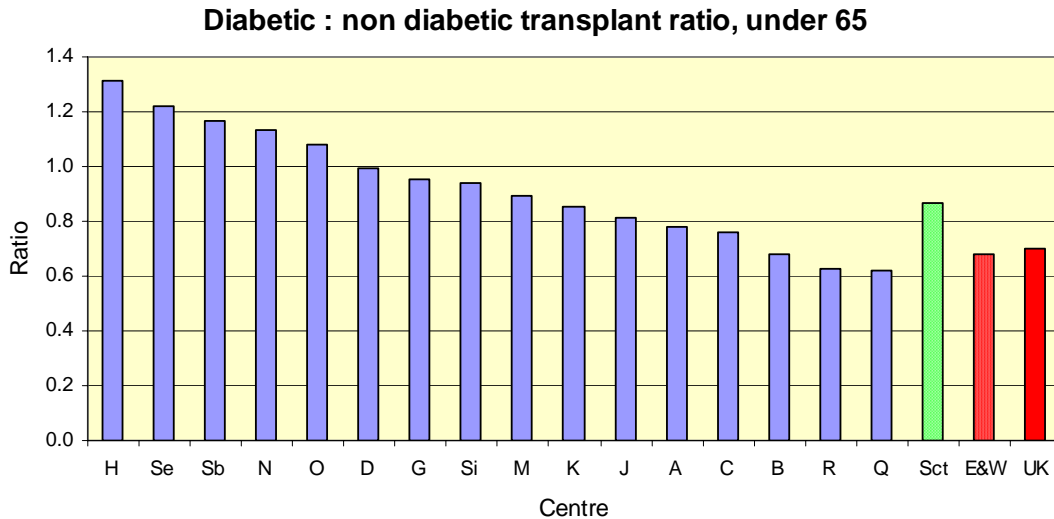
The percentage of prevalent endstage renal failure patients in each centre with a primary diagnosis of diabetes mellitus with a functioning renal transplant on 31/12/98 is illustrated in figure 11.5.

### Percentage of diabetic ESRF with transplant



**Figure 11.5 Percentage of diabetic ESRF patients with a transplant**

To compare the differences within each unit between diabetic and non-diabetic patients, the ratio of % diabetics under 65 with a transplant to non-diabetics under 65 was calculated. The age limit was used in an effort to make the populations comparable, as most patients receiving a transplant are under 65, and diabetics have a lower median age than non-diabetics on RRT. These figures are demonstrated in figure 11.6. Centres with fewer than 20 diabetic patients aged under 65 have been excluded from the graph.



**Figure 11.6 Ratio of % patients with a transplant under 65, diabetics: non-diabetics**

In order to identify reasons for these observed differences between centres, a number of variables need to be examined, including the overall percentage of live ESRF patients with diabetes, the median age of this diabetic cohort, and the percentage of the cohort originating from ethnic minorities (and thus likely to experience difficulty in HLA matching). Some of the difference in the proportion of transplant patients with a primary diagnosis of diabetes mellitus observed between centres could be accounted for by differences in these variables. There will be sufficient patients on the Registry for this analysis to be presented in next year's report.

Overall diabetics seem less likely to receive a transplant than non-diabetics, but there appear to be differences of approach between units with regard to attitudes towards transplantation of diabetics.

### ***Failed transplants***

Within the participating centres, approximately 9% of all patients commencing dialysis in 1998 were patients whose renal transplants had failed during the year as opposed to new patients on Renal Replacement Therapy.

Dialysis modality 90 days after a transplant had failed was related to the dialysis modality before transplantation. Of those restarting dialysis, 77% of patients on haemodialysis before transplantation returned to haemodialysis after transplant failure, while 66% of CAPD patients returned to peritoneal dialysis. This analysis considered patients whose transplants failed between 1/10/1997 and the 30/9/1998, who resumed dialysis at a Renal Registry centre, regardless of where the patient had been transplanted. Patients whose transplant failed on the day of transplant have not been considered.

## ***Survival of patients with established renal transplants***

The UKTSSA annual report provides information on graft survival within the UK although follow-up information is not collected on patients once they return to dialysis.

The one-year survival figures presented are for those patients alive on 1/1/98. Patients who had been transplanted within six months prior to this date were excluded from these figures as they were still considered to be in the post-operative transplant risk group. Survival was calculated both censoring at return to dialysis and with continuing follow-up of patients after return to dialysis (Table 11.3).

	<b>No. of patients</b>	<b>No patients died</b>	<b>Death rate (95% CI)</b>	<b>K-M 1 yr survival (95% CI)</b>
Transplant	4853	121	2.6	97.4%
Censored at dialysis			(2.1- 3.1)	(97.0% - 97.9%)
Transplant	4853	141	3.0	97.1%
Incl dialysis return			(2.5 –3.5)	(96.6% - 97.5%)

**Table 11.3 Survival during 1998 of established transplant patients alive 1.1.98**

## ***Quality of transplant function***

Future reports will compare the quality of graft function between units by prospectively comparing creatinine and calculated creatinine clearance at set time points after transplantation. Correlation of graft function with pre- and post-transplant variables such as blood pressure, CMV status, serum cholesterol etc. will be possible as the Registry accumulates data over a longer time period. At present there are insufficient data to perform such analyses.

This analysis considered transplant patients on the 31/12/1998 who had had their transplant for more than a year. The most recent serum creatinine within 6 months was used in the analysis.

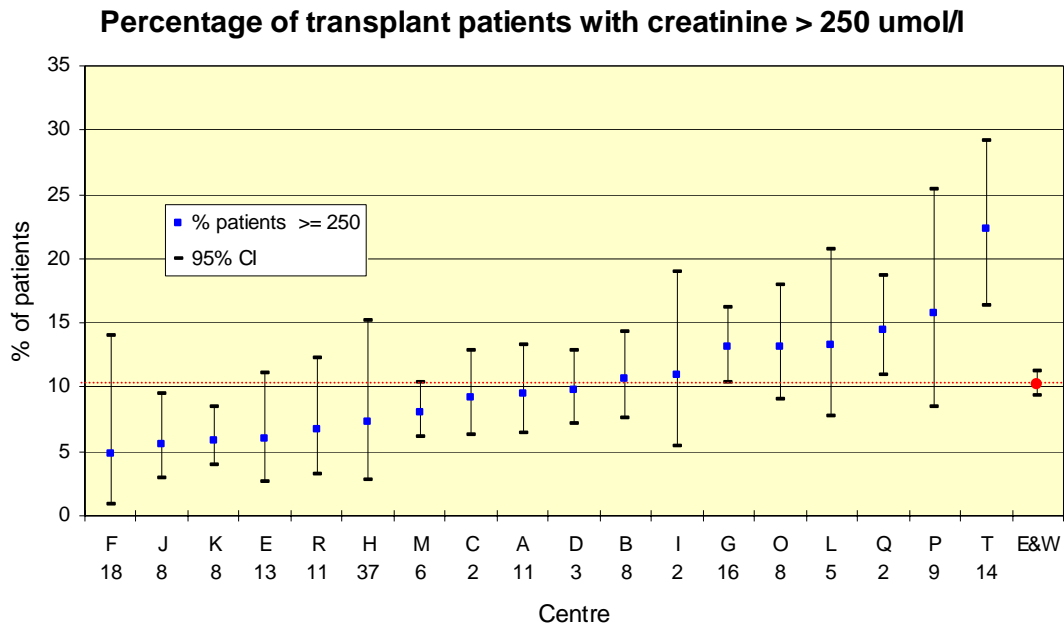
There was no relationship between primary diagnosis and graft function (Table 11.4).

<b>Diagnosis</b>	<b>% with creatinine &lt; 200</b>
Aetiology uncertain*	80.5
Glomerulonephritis	76.6
Pyelonephritis	78.0
Diabetes	72.0
Renal Vascular disease	88.0
Hypertension	77.2
Polycystic Kidney	82.7
Not sent	83.1
Other	78.4

\* Includes “glomerulonephritis– not histologically proven”

**Table 11.4 Relationship between transplant function and primary renal diagnosis**

A crude examination of graft function is demonstrated in figure 11.7 where the percentage of established transplant patients with a serum creatinine greater than 250 micromols/l is shown for each unit. There differences between units are significant but as yet unexplained.

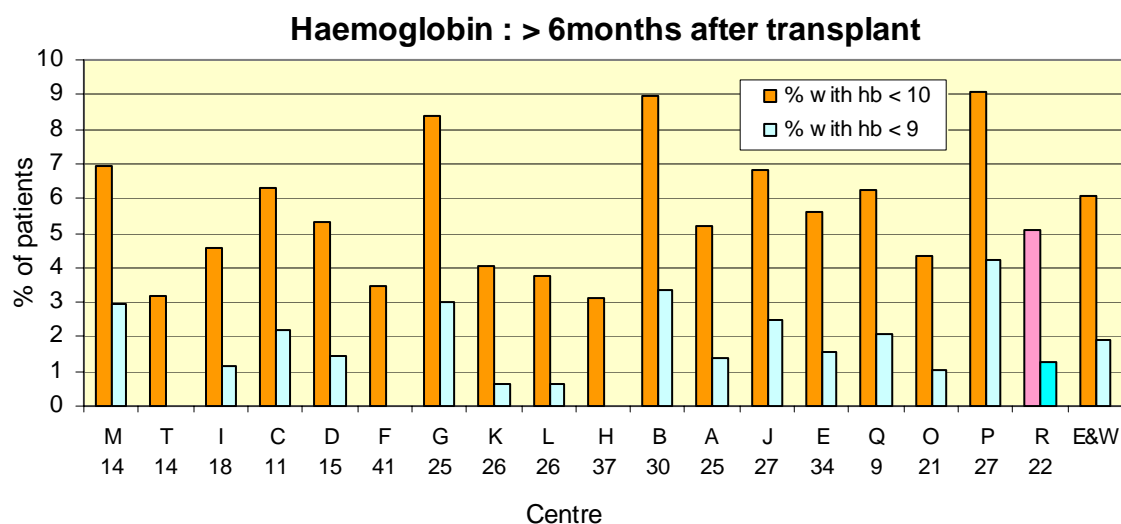


**Figure 11.7 Percentage of established transplant patients with serum creatinine greater than 250 micromols/l**

### ***Haemoglobin in transplanted patients***

There are no recommended haemoglobin standards for renal transplant patients. Figure 11.8 shows the percentage of transplant patients in each participating Registry unit with haemoglobin less than 10g/dL and 9g/dL respectively, at least 6 months after transplantation. The variation is unexplained (1-10% of transplant patients with Hb <10g/dL depending on unit) but possible reasons include quality of graft function, type of immunosuppression (use of azathioprine and mycophenolate mofetil) and use of erythropoietin in where there are failing grafts.





**Figure 11.8 Haemoglobin of established transplant patients – by centre**

As expected haemoglobin is lower in women and those with higher serum creatinine (Table 11.5).

		Haemoglobin							
Gender	Creatinine	Mean Hb	Std dev	5th centile	Lower quartile	Median Hb	Upper quartile	95th centile	No. with data
Male	<250	13.5	1.6	10.8	12.3	13.5	14.6	16.1	1913
Male	250+	11.4	1.9	8.7	10.0	11.2	12.6	14.8	284
Female	<250	12.4	1.6	9.9	11.2	12.4	13.4	15.1	1235
Female	250+	10.6	1.7	7.5	9.4	10.8	11.7	13.3	142

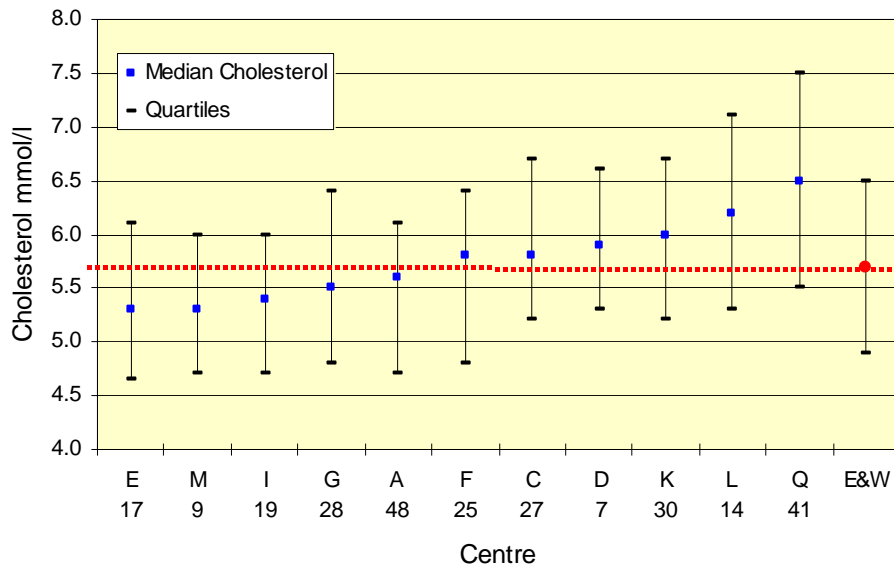
**Table 11.5 Renal transplant patients: relationship of haemoglobin and creatinine**

### ***Serum cholesterol***

The distribution of serum cholesterol in transplantees according to centre is shown in figure 11.9.

This analysis considered transplant patients on the 31/12/1998 who had had their transplant for more than a year. The most recent serum cholesterol over a 12 month period was used and the cholesterol was harmonised for inter-laboratory variation.

### Transplants : Serum Cholesterol mmol/l in 1998



**Figure 11.9 Serum cholesterol levels for transplant patients – by centre**

The total death rate in the population with established renal transplants whilst the graft is functioning is surprisingly low at around 2-3% per annum. The overall death from cardiovascular disease in the UK transplant population is at least 8-10 fold more common than in the gender and aged-matched general population. However the relationship between serum cholesterol and prognosis in transplant patients has not been studied. Nevertheless, in the general population, total cholesterol is an important risk factor for cardiovascular disease. Current recommendations for primary prevention in the *high-risk* general population advise a total cholesterol above 5.5 mmol/l as a trigger for prescribing cholesterol-lowering agents. Transplantees have usually experienced a period of dialysis, frequently with concomitant hypertension, and have a high incidence of hypertension post transplantation. Considering this together with the known high death rate from cardiovascular disease they could be considered high risk and suitable for primary prevention of cardiovascular disease.

In most units the median serum cholesterol of transplantees is above the recommended level for primary prevention in high-risk patients. Serum cholesterol in these patients is not related to serum creatinine (Table 11.6)

Serum Creatinine	Serum cholesterol					No. with data
	5th centile	Lower quartile	Median cholesterol	Upper quartile	95th centile	
<150	4.0	4.9	5.7	6.4	7.8	1388.0
150-250	3.8	4.9	5.7	6.5	8.0	953.0
250+	3.9	5.1	5.8	6.6	8.5	274.0

**Table 11.6 Renal transplant patients: relationship of serum cholesterol and creatinine**

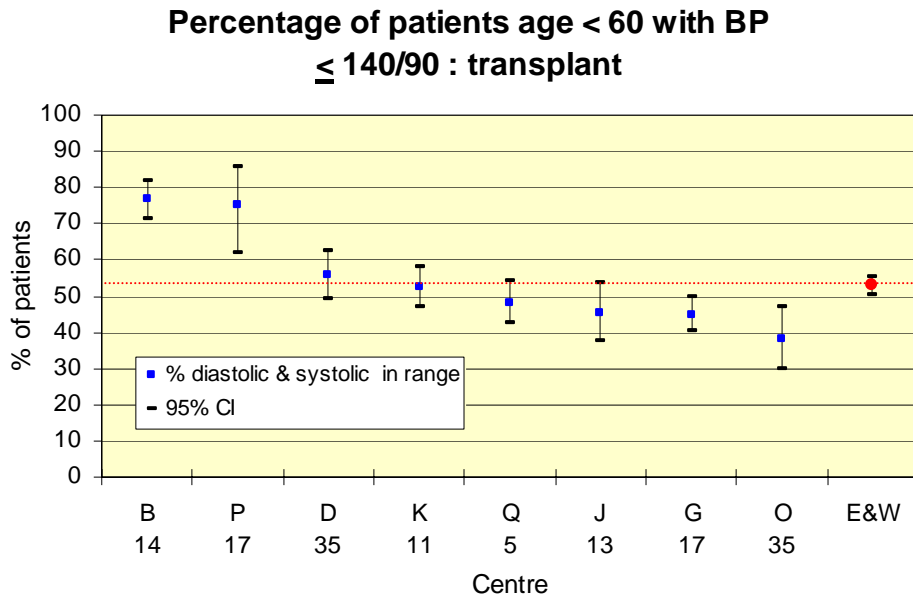
## **Blood pressure**

Neither the Renal Association nor the British Transplantation Society has recommended standards for blood pressure control in transplanted patients. In the following analysis the standards recommended for dialysis patients have been adopted, although many would argue that the acceptance of higher blood pressure in the elderly is not appropriate (British hypertensive society guidelines).

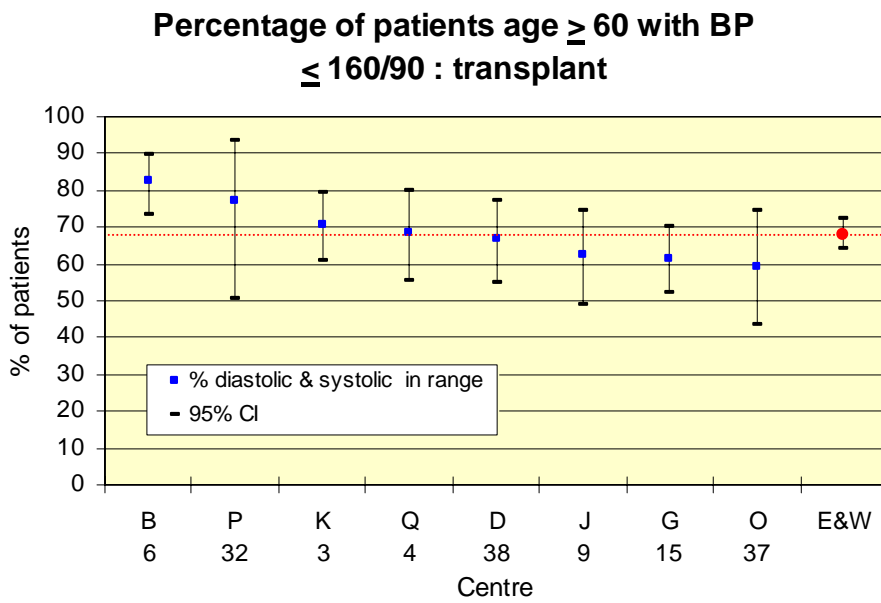
There may be errors due to incomplete data. Table 11.7 shows the percentage of renal transplant recipients with blood pressure data. Blood pressure recordings are also likely to be subject to a variety of biases. Fit patients with infrequent clinic attendance will have infrequent BP assessment. High BP readings may be selectively included or excluded from computer records depending on operator bias. The following data must be interpreted with this in mind.

Centre	% with BP return from last 6 months	
	Age < 60	Age > 60
A	0	0
B	86	94
C	2	1
D	65	57
E	3	0
F	0	0
G	83	83
H	3	0
I	3	0
J	87	91
K	89	95
L	6	0
M	34	27
N	0	0
O	65	60
P	83	68
Q	95	96
R	0	0
T	26	24
E&W	50	47

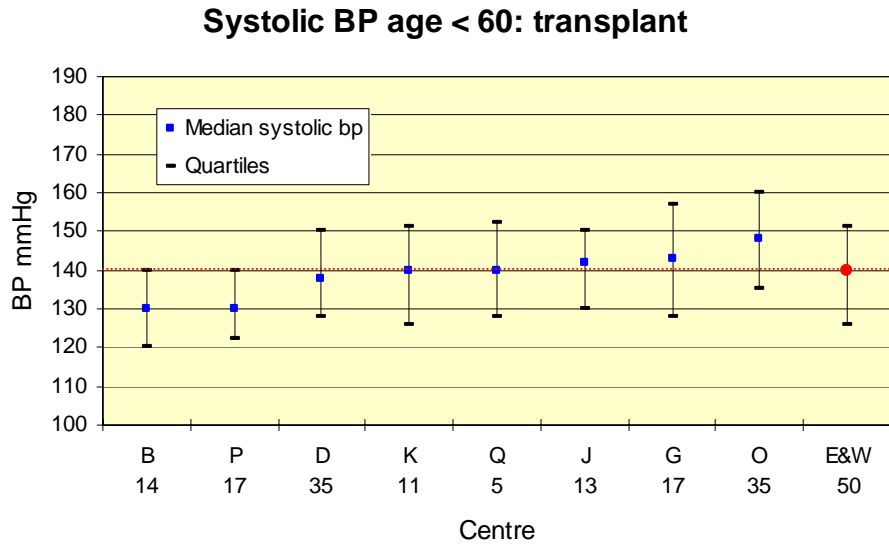
**Table 11.7** Completeness of BP returns for transplant patients



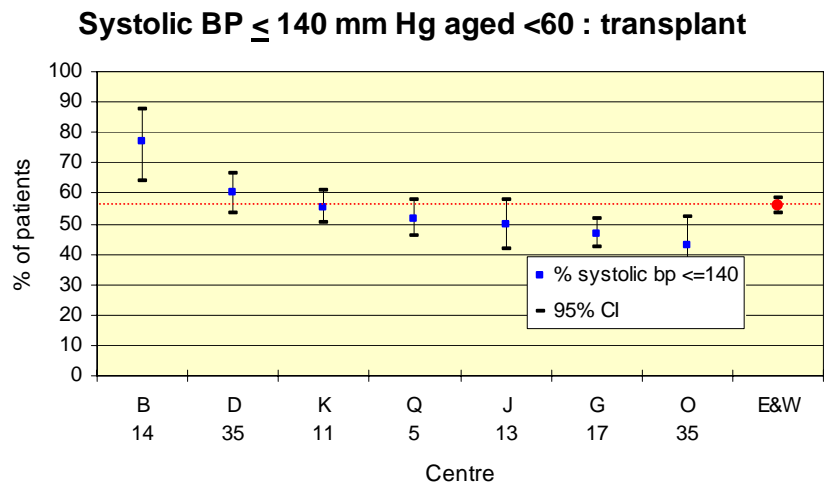
**Figure 11.10** % patients under 60 with systolic and diastolic BP below 140/90 mmHg



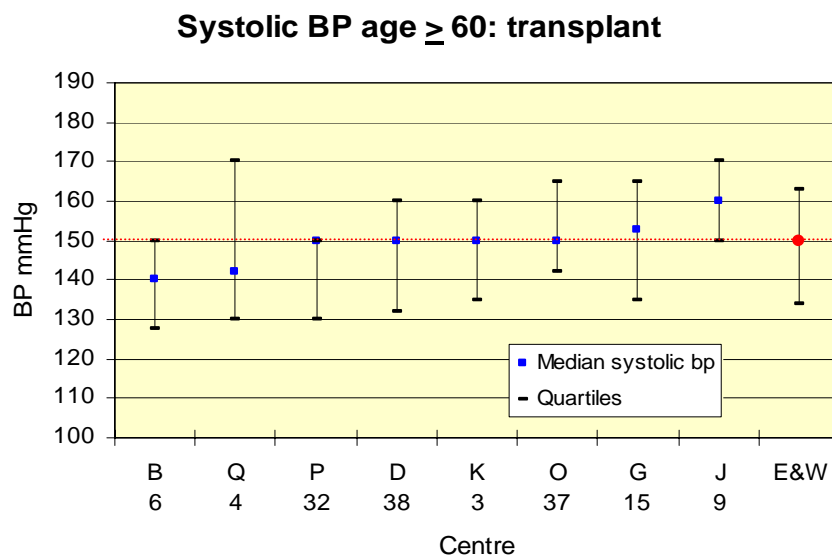
**Figure 11.11** % patients over 60 with systolic and diastolic BP below 160/90 mmHg



**Figure 11.12** Transplant patients under 60: median systolic pressure



**Figure 11.13** Percentage transplant patients under 60 with systolic BP  $\leq$ 140 mmHg



**Figure 11.14** Transplant patients over 60: median systolic pressure

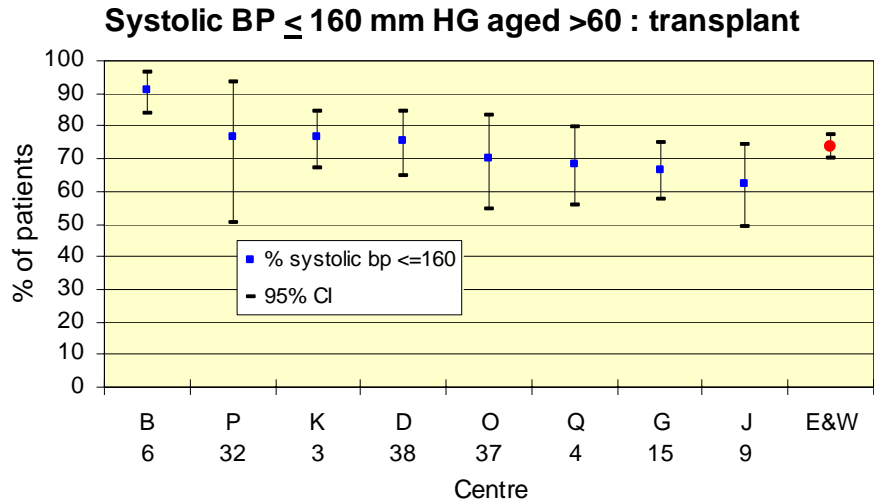


Figure 11.15 % patients over 60 with systolic BP  $\leq$  160 mmHg

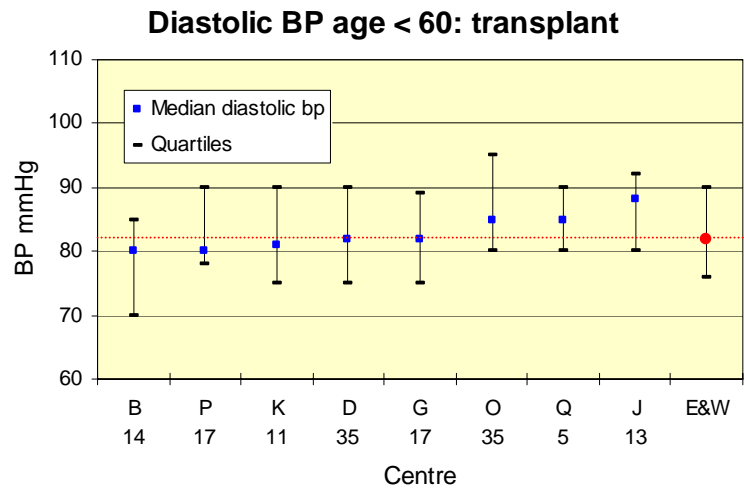


Figure 11.16 Transplant patients under 60; median diastolic pressure

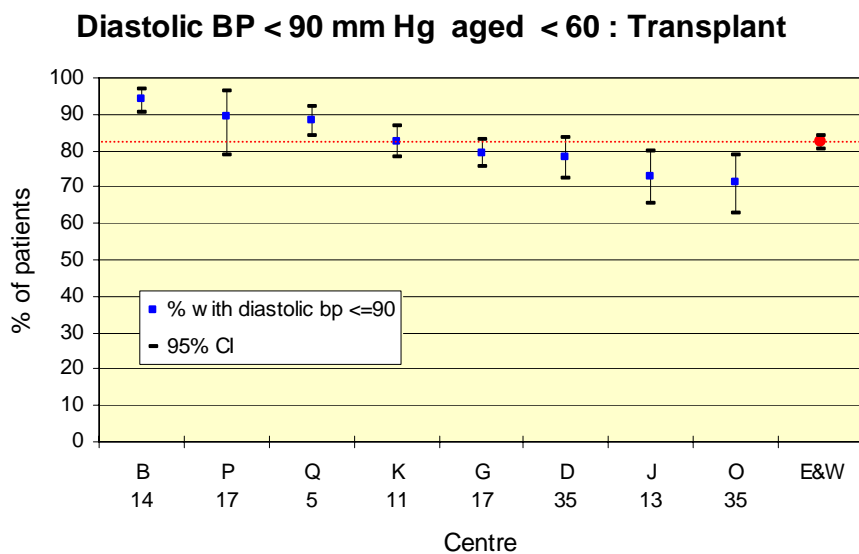


Figure 11.17 % patients under 60 with diastolic pressure  $\leq$  90 mmHg

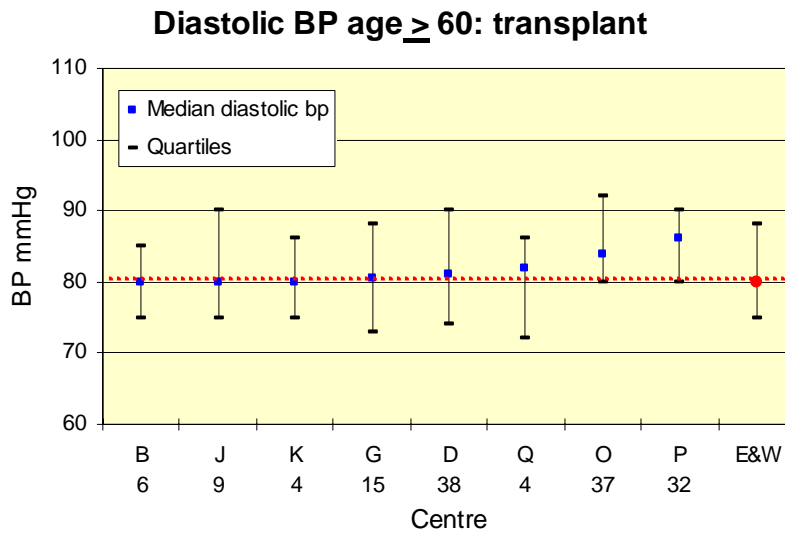


Figure 11.18 Transplant patients over 60: median diastolic pressure

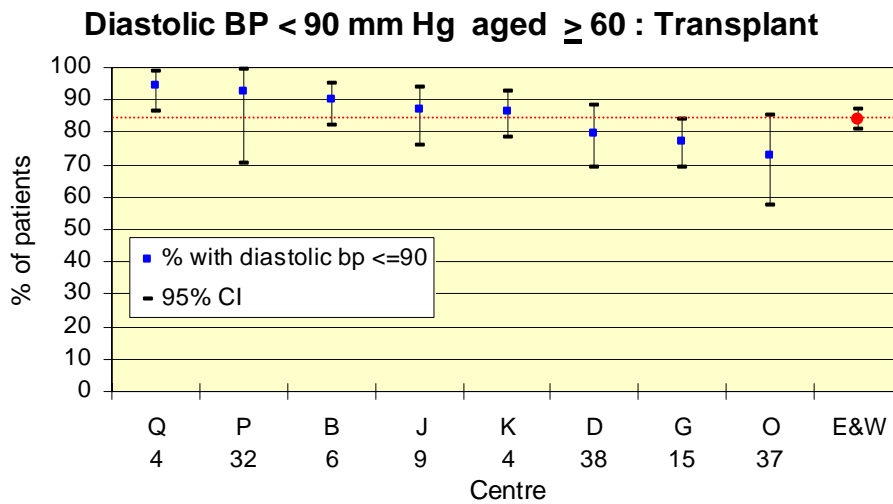


Figure 11.19 % patients over 60 with diastolic pressure  $\leq$  90mmHg

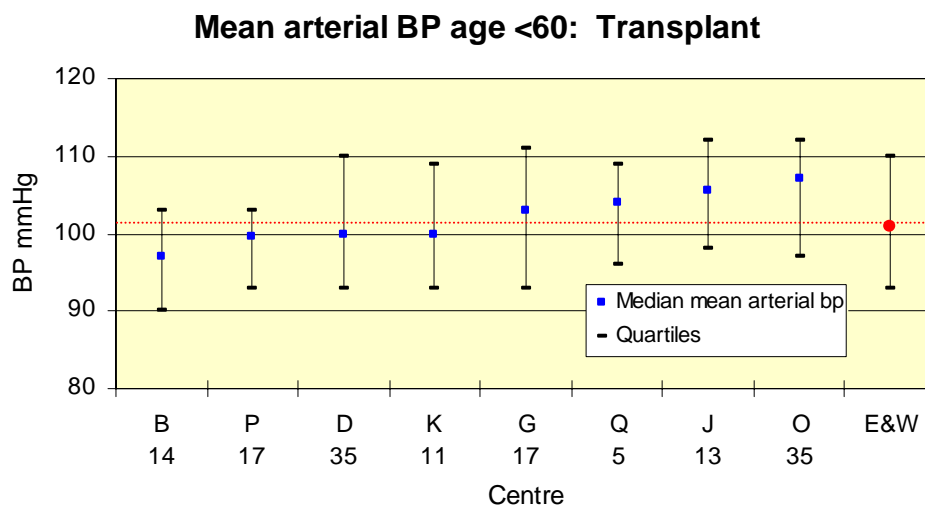


Figure 11.20 Transplant patients under 60: median mean arterial pressure

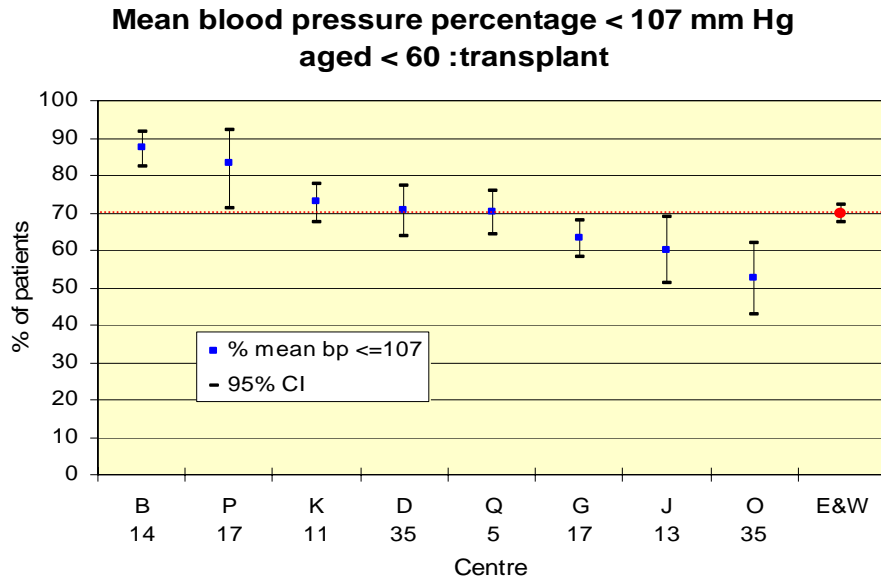


Figure 11.21 % patients under 60 with mean arterial pressure ≤107 mmHg

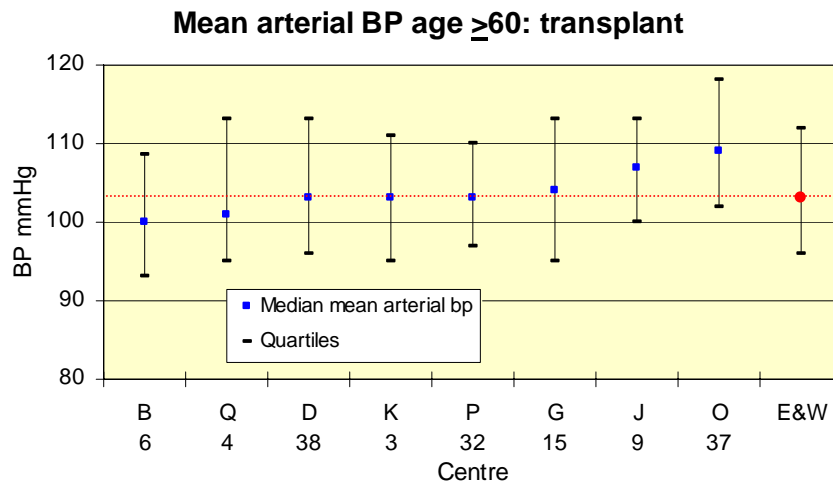


Figure 11.22 Transplant patients over 60: median mean arterial pressure

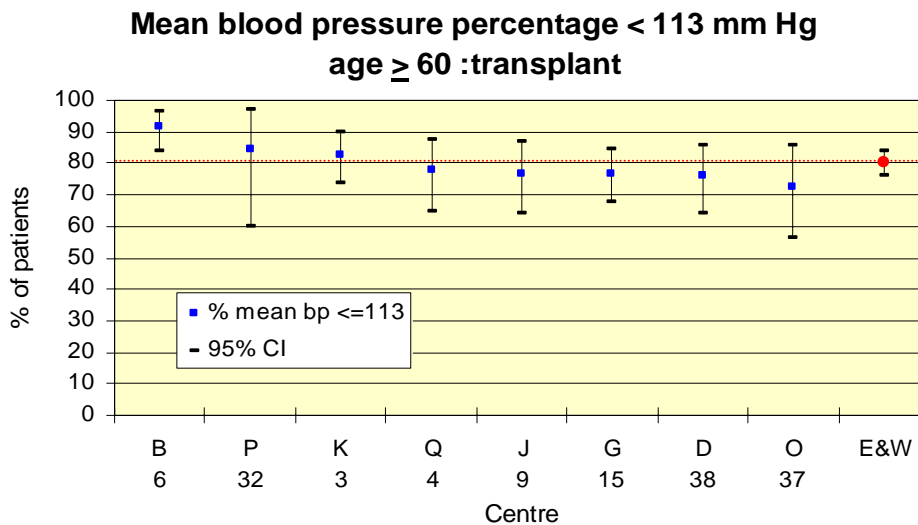


Figure 11.23 % patients over 60 with mean arterial pressure ≤113 mmHg`



There is more variation between centres in blood pressure achieved in the younger patients than the older ones, and more variation in the systolic pressure achieved than diastolic. Control of systolic hypertension seems more difficult to achieve than control of diastolic hypertension.

The overall median diastolic pressure in those above and below age 60 is similar at 83 mmHg. and 84 mmHg. Overall achievement of the standard in younger and older patients is 82.9% and 84% respectively. There is variation between units in the proportion of patients with blood pressure within the desired range which is significant for younger patients.

Considering all the transplant patients in the Registry, systolic pressures achieved are different in the two age ranges. For younger patients the median systolic pressure is 140 mmHg., for older patients 150 mmHg. The percentage achieving the “standard” is 56% for younger patients and 73% for older patients. This reflects the more liberal standard for older patients. If more rigorous criteria were used for older patients, i.e. upper limit 140 mmHg, then the proportion achieving the standard would be less than for younger patients. The variation between units is again significant for younger patients.

The Registry median for mean arterial pressure is 101 mmHg. for younger patients and 103 mmHg. for older patients. 70% of younger patients are within the desired range, with a significant variation between units. 80% of older patients are within the more liberal range for this age group, but the variations between units may not be significant in these older patients.

From these figures some units seem to control both systolic and diastolic pressure to significantly lower levels than others. This may have important implications for subsequent cardiovascular disease and long-term patient survival. As the Registry collects further sequential data on these patients, the relationship of blood pressure to graft and patient survival will be investigated