Factors which may influence cardiovascular disease in dialysis and transplant patients—blood pressure (Chapter 10)

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Abstract

Many renal units still fail to return blood pressure data to the Renal Registry. In England, Northern Ireland and Wales, the percentage of HD patients achieving the combined blood pressure standard (\(<140/90\) predialysis) averages 43\% (inter unit range 16–60\%) and post-dialysis (\(<130/80\)) average 48\% (range 22–66\%). On average 27\% (range 12–48\%) of PD patients achieve the standard of \(<130/80\) and 26\% of renal transplant patients (range 16–40\%).

Over the last 8 years there has been no significant change in systolic or diastolic blood pressure achievement. Better comorbidity data returns are required by the Registry to perform blood pressure survival analyses.

Keywords: blood pressure; chronic kidney disease; dialysis; end stage renal disease; epidemiology; haemodialysis; peritoneal dialysis; registry; transplant

Introduction

International and UK blood pressure guidelines [1,2,3,4] recommend a target blood pressure below 130/80 mmHg for patients with chronic kidney disease (CKD), diabetes and established atherosclerosis. The intention is to reduce cardiovascular complications and progression to renal failure. So far, clinical trials involving CKD patients have all been designed to assess low blood pressure on renal progression as the primary endpoint. Cardiovascular data from these trials are inconclusive and were reviewed in some detail in last year’s report. Blood pressure guidelines take no account of epidemiological data that describe a U-shaped relationship between baseline systolic blood pressure (SBP) and 1 year mortality. Several reports show higher cardiovascular mortality for haemodialysis patients with baseline pre- and post-SBP \(<110\) mmHg [5,6]. The UK Renal Registry has also shown increased all-cause mortality at 1 year for incident haemodialysis patients with baseline pre- and post-SBP \(<120\) mmHg [7]. This raises concern that achieving lower blood pressure targets may be detrimental for some dialysis patients. In 2006, two studies of USA haemodialysis patients analysed the changing relationship of blood pressure with mortality over several years. In the first, hazard ratios for 3-year all-cause mortality for 56,338 incident patients were 2.5 for a baseline SBP \(<120\) mmHg and 1.4 for baseline SBP 120–139 mmHg [8]. Hazard ratios were 5.5 and 1.9, respectively when blood pressure variability was included in the analysis. In the second study \cite{9} the hazard ratio for 2 year all-cause mortality for 16,959 incident patients was 1.7 for baseline SBP 110–119 mmHg. Interestingly, the hazard ratio fell to 0.8 and 0.7 for the third and fourth year, respectively. This is the first data to suggest that achieving low blood pressure guidelines may be beneficial for dialysis patients. In the same study a baseline SBP \(>170\) mmHg was only associated with increased all-cause mortality after 3 years. Intuitively one would expect early deaths to affect patients with established heart failure as hypertension precedes cardiac failure by many years but neither study included comorbidity data to delineate causal associations. Finally, data from the Irbesartan Diabetic Nephropathy Trial [10] showed improved renal function and patient survival down to a SBP of 120 mmHg. Below this, all-cause mortality increased (relative risk 1.25) for both patients with and without pre-existing cardiovascular disease. It will be difficult to prove whether low blood pressure may be beneficial as poor health is a common confounding factor in renal patients.

Last year less than one-third of patients on RRT in England and Wales achieved the blood pressure standard. However, the renal unit at York consistently achieves the best blood pressure results across all treatment modalities suggesting a rational approach to monitoring and therapy. Their patients are sent to a dietician for salt restriction initially. Then patients achieve dry weight by ultrafiltration or diuretics.
Finally, antihypertensive medication is increased. Several publications in the last year support this strategy. An audit of 469 prevalent haemodialysis patients dialysing in seven different centres in the UK compared blood pressure control with varying dialysate sodium concentration [11]. All patients were advised to restrict salt intake to 5 g/day. Patients dialysing with sodium concentration 137–139 mmol/l had significantly lower pre- and post-SBP compared to those dialysed against 140 mmol/l. They also had lower interdialytic weight gains and were prescribed fewer antihypertensive drugs. Intradialytic hypotension correlated with age rather than dialysate sodium concentration. Similarly, a prospective study of 46 prevalent peritoneal dialysis patients in Turkey showed reduced salt intake and use of hypertonic solutions could maintain blood pressure below 130/85 mmHg over a 2-year period without antihypertensive medication [12]. Left ventricular hypertrophy was detected in only 8% of patients after 2 years. No patient lost residual renal function, ultrafiltration rate or dialysis adequacy during the study. The published evidence suggests salt and water balance is important to achieve blood pressure standards in dialysis patients.

**Blood pressure control**

The RA standards for control of hypertension were established in August 2002:

- Pre-haemodialysis blood pressure <140/90 mmHg.
- Post-haemodialysis, peritoneal dialysis and renal transplant blood pressure <130/80 mmHg.

**Methods**

The Registry extracts quarterly blood pressure data electronically from UK renal units. Data from Northern Ireland is included for the first time this year. A single blood pressure reading is extracted for each patient, the last BP recorded in quarter four. If this is not available, the last BP from quarter three is taken. Patients with no blood pressure data for the last two quarters of 2005 are excluded. All patients with data are included in the statistical analysis. Renal units with sparse data for a given treatment modality (data for <50% of patients or less than 20 patients) are omitted from renal unit level results/figures. This approach is taken because small numbers do not skew the data but do give unreliable estimates at the renal unit level.

Each year a number of analyses are performed for the prevalent cohort on RRT (see Appendix at the end of the chapter for definition of prevalent cohort). This report presents data for 2005.

- Completeness of data is analysed at renal unit and national level for patients on haemodialysis, peritoneal dialysis and renal transplant recipients.
- Distributions of SBP, diastolic blood pressure (DBP), mean arterial pressure (MAP) and pulse pressure (PP) are defined for different treatment modalities. Maximum and minimum values are recorded and average values (mean and median), standard deviations and quartiles calculated. The data are presented as caterpillar plots showing median values and quartile ranges for renal units and nations. Data were also analysed by primary diagnosis. The number preceding each centre name indicates the percentage of patients with missing data at that centre.
  - Where applicable, the percentage achieving Renal Association or other surrogate standard is also calculated and represented as caterpillar plots with 95% confidence intervals. For the percentage achieving standards, \( \chi^2 \) testing is used to identify significant variability between centres and countries. Data are also analysed by primary diagnosis.

**Results**

**Data returns**

Poor returns (<50%) were obtained from 20 centres for HD data, 31 centres for PD data and 35 centres for Tx data (Table 10.1). For most renal units, the problem is in transferring the clinical data to their renal IT systems. For a few units, the data may not be extracted from the correct database table within their renal IT system, in which case they should contact the Registry directly.

Overall the completeness of returns is improving but still remains poor for transplant patients. Northern Ireland is omitted from the figures for PD as data is available for only 12 patients.

**Distribution of blood pressure by modality**

Figures 10.1 and 10.2 show histograms of systolic and diastolic blood pressure, for pre-HD data. Blood pressure distributions for post-HD, PD and Tx are also approximately normal. Peaks above the curve indicate digit bias. Figure 10.3 shows systolic, diastolic and PP distributions for each modality (post-HD data is shown).

The median blood pressure pre-HD, post-HD, PD and Tx is 143/75, 128/69, 136/80 and 136/79 mmHg. Median PP for each group is 66, 59, 57 and 57 mmHg, respectively. The HD population has the widest spread for blood pressure. Standard deviations (SBP/DBP) pre-HD, post-HD, PD and Tx are 26/15, 25/14, 23/13 and 19/11, respectively. This compares to 18/10 for a hypertensive population. Last year in a single centre study of 317 prevalent HD patients, the Registry showed blood pressure was significantly higher at the start of the dialysis week. The wider blood pressure distribution for HD may partially therefore reflect the random timing of readings and influence of fluid overload.

**Achievement of combined systolic and diastolic standard**

Figures 10.4–10.7 show a wide variation between renal units achieving the combined blood pressure standard for each modality. In England, Northern Ireland and Wales, the percentage of HD patients achieving...
the standard pre-dialysis averages 43% (range over renal units 16–60%) and post-dialysis averages 48% (range 22–66%). Only 27% of PD patients (range 12–48%) and 26% of Tx patients (range 16–40%) achieve the standard. Chi squared testing indicates the variation between centres for HD and Tx is significant \( (P < 0.001) \) but not for PD. The variation between nations is also significant for HD and Tx \( (P \leq 0.008) \) but not for PD. The results are similar to last year and show control of hypertension remains inadequate across all treatment modalities but is significantly better in the HD population.

**Table 10.1.** Percentage of patients with complete returns of blood pressure values by modality

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National results have been highlighted in boldface.

**Fig. 10.1.** Systolic BP distribution pre-HD.

**Fig. 10.2.** Diastolic BP distribution pre-HD.

**Fig. 10.3.** Summary of BP achievements.

Systolic pressure alone

Figures 10.8–10.15 show wide variation between renal units achieving the SBP standard. In England, Northern Ireland and Wales, the percentage of HD
Fig. 10.5. Percentage of patients with BP < 130/80 mmHg: post-HD.

Fig. 10.6. Percentage of patients with BP < 130/80 mmHg: PD.

Fig. 10.4. Percentage of patients with BP < 140/90 mmHg: pre-HD.

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Fig. 10.13. Percentage of patients with systolic BP < 130 mmHg: PD.

Fig. 10.14. Median systolic BP: Transplant.

Fig. 10.15. Percentage of patients with systolic BP < 130 mmHg: Transplant.
patients achieving the standard pre-dialysis averages
45% (range 19–62%) and post-dialysis averages
51% (range 30–69%). On average 37% of PD
patients (range 12–59%) and 35% of Tx patients
(range 24–55%) achieve the standard. Chi squared
testing indicates that the variation between centres is
significant for each treatment modality (\( P < 0.003 \)).
The variation between nations is significant for HD
(\( P = 0.005 \)) and Tx (\( P = 0.029 \)) but not for PD.
Median SBP for pre-HD, post-HD, PD and Tx is 143,
128, 136 and 136 mmHg, respectively.

Diastolic pressure alone

Figures 10.16–10.23 show wide variation between renal
units achieving the DBP standard. In England,
Northern Ireland and Wales, the percentage of HD
patients achieving the standard pre-dialysis averages
84% (range 69–96%) and post-dialysis averages
77% (range 59–90%). On average 47% of PD
patients (range 27–61%) and 52% of Tx patients
(range 30–74%) achieve the standard. Chi squared
testing indicates the variation between centres for HD
and Tx is significant (\( P < 0.001 \)) but not for PD.
The variation between nations is significant for pre-
HD and Tx (\( P < 0.001 \)) but not for post-HD or PD.
The median DBP for pre-HD, post-HD, PD and
Tx is 75, 69, 80 and 79 mmHg, respectively. The median
data shows...
Fig. 10.19. Percentage of patients with diastolic BP <80 mmHg: post-HD.

Fig. 10.20. Median diastolic BP: post-HD.

Factors influencing cardiovascular disease

N = 7378

Upper 95% CI

Lower 95% CI

N = 1489

Upper quartile

Median diastolic BP

Lower quartile

N = 7378

Upper quartile

Median diastolic BP

Lower quartile

N = 1489

Upper quartile

Median diastolic BP

Lower quartile
approximately half (50.6%) of the observations recorded as exactly 70 mmHg. It is not clear whether DBP is lowest post-HD because HD patients are older (DBP falls after 60 years of age in the general population due to increasing arterial stiffness) or because of the synergistic effect between ultrafiltration and antihypertensive medication.

**Mean arterial pressure**

Figures 10.24–10.31 show wide variation between renal units achieving the desired MAP. MAP is calculated as DBP plus one-third of the PP.

In England, Northern Ireland and Wales, the percentage of HD patients achieving the standard pre-dialysis averages 72% (range 43–89%) and post-dialysis averages 69% (range 43–80%). On average 48% of PD patients (range 32–68%) and 48% of Tx patients (range 34–74%) achieve the standard. Chi squared testing indicates that there is significant variation between centres for HD and Tx ($P < 0.001$). The variation is less marked for PD and is only of borderline significance ($P = 0.052$). The variation between nations is significant for pre-HD ($P = 0.001$) and Tx ($P < 0.001$) but not for post-HD or PD. The median MAP for pre-HD, post-HD, PD and Tx is 98, 89, 98 and 97 mmHg, respectively.
Fig. 10.26. Median MAP: PD.

Fig. 10.27. Percentage of patients with MAP < 97 mmHg: post-HD.

Fig. 10.28. Median MAP: post-HD.
Fig. 10.29. Percentage of patients with MAP < 97 mmHg: PD.

Fig. 10.30. Median MAP: Transplant.

Fig. 10.31. Percentage of patients with MAP < 97 mmHg: Transplant.

Factors influencing cardiovascular disease
**Pulse pressure**

Figures 10.32–10.35 show the variation between renal units for PP. PP is calculated as SBP minus DBP. The median PP for pre-HD, post-HD, PD and Tx is 66, 59, 57 and 57 mmHg, respectively. A high SBP accounts for the wider PP in HD patients pre-dialysis.

**Blood pressure by primary diagnosis**

Figures 10.36–10.43 show the variation in blood pressure control by primary diagnosis for each treatment modality (post-HD data is shown). Each year in the Registry Report, the data have shown a similar pattern. SBP is highest in patients with macrovascular disease (diabetes and renovascular disease), lower in patients with glomerulonephritis and still lower in patients with tubular disorders (PCKD and pyelonephritis).

Diabetics have the poorest blood pressure control of all the diagnostic groups. While salt intake correlates with water intake in non-diabetics, hyperglycaemia accounts for 50% of water intake by diabetics on HD [13] so may exacerbate hypertension. Blood pressure control is significantly better on HD for all diagnostic groups (\(P < 0.0001\) for all groups). Combining groups, the percentage of patients achieving the BP standard on HD compared to PD or Tx are 42% vs 24% for macrovascular disease, 49% vs 26% for glomerulonephritis and 53% vs 26% for tubular disorders (\(P < 0.0001\) for each comparison). This may be due to more frequent monitoring and intervention in the HD population. If so, nephrologists will need to devise more effective strategies for monitoring blood pressure control in out-patient populations.

**Future direction**

The UK Renal Registry needs improved returns of comorbidity data for each patient to perform adjusted survival analyses. The question of whether achieving blood pressure standards is beneficial for all patients receiving RRT can then be addressed. The Registry requests that blood pressure data is logged every
Fig. 10.34. Median PP: PD.

Fig. 10.35. Median PP: Transplant.

Fig. 10.36. Percentage of patients with BP in standards by primary diagnosis.
Fig. 10.37. Median SBP by primary diagnosis.

Fig. 10.38. Percentage of patients with SBP in standards by primary diagnosis.

Fig. 10.39. Median DBP by primary diagnosis.
Fig. 10.40. Percentage of patients with DBP in standards by primary diagnosis.

Fig. 10.41. Median MAP by primary diagnosis.

Fig. 10.42. Percentage of patients with MAP in standards by primary diagnosis.
session for HD patients so it can assess blood pressure variability during the dialysis week.

Conflict of interest statement. None declared.

References


Appendix

Definition of the cohort for blood pressure analyses

Defining the cohort.

- Analysis of prevalent patients.
- Prevalent patients are defined as all patients (including the incident cohort for that year) alive on 31st December for that year.
- Data set called Qtemp.

Qtreat

- Usual UKRR checking programs run on data set.
- Exclusion criteria applied to create data set Qtemp.

Exclusion criteria are:

- Patients who had died before the first day of the quarter.
- Patients on dialysis with a treatment centre of elsewhere (not identified).
- Patients receiving treatment at a non-Registry site.
- Patients with no date of starting ERF treatment.
- Patients who had been receiving treatment for a negative number of days i.e. incorrect starting dates or incorrect patient number on data sent in.
- Patients who had recovered before the start of the quarter.
Where data on a patient are submitted from more than one centre, only data from the primary centre are used.

**Qtemp**

- Further exclusion criteria applied to Qtemp to create data set called **Quarter**.

Exclusion criteria are:
- Patients who have transferred out of the centre (qhcent) by the end of the quarter.
- Patients who had not yet transferred in to the centre (qhcent) by the end of the quarter.
- Patients who had recovered by the end of the quarter.
- Patients who had stopped treatment by the end of the quarter.
- Patients who had died by the end of the quarter.
- Patients who were lost to follow up by the end of the quarter.

**Quarter**

- Further exclusion criteria applied to quarter to create data set called **Bichem**.

Exclusion criteria are:
- Patients who had been on ERF treatment for ≤ 90 days at the end of the quarter.
- Patients who changed treatment modality in the quarter.
- Patients who transferred into the centre (qhcent) at some time in the quarter.