CHAPTER 3: DIALYSIS SURVIVAL

Summary

- The survival of all dialysis patients starting dialysis in 1993 to 2002 was 90%, 73%, 60% and 39% at one year, 3 years, 5 years and 10 years respectively.
- CAPD patients had a 74% higher risk of death compared to haemodialysis patients
- Survival of dialysis patients in recent vintage was lower than in earlier vintage. Compared to the 1997-1998 cohort the mortality risk of 1999-2000 and 2001-2002 cohorts were increased by 21% and 27% respectively.
- Diabetics on dialysis had 2.1 times higher risk of death compared to non-diabetics.
- Low serum albumin concentration, low body mass index and low serum cholesterol level were independent risk factors for mortality.
- There was a U-shaped relationship between diastolic blood pressure and risk of mortality.
- The haemoglobin level associated with the lowest risk of mortality was 11-12 g/dl.
- Hyperphosphataemia, hypercalcaemia and low calcium phosphate product were associated with increased risk of death.
- Hepatitis B or Hepatitis C status did not affect patient survival.

Introduction

Despite recent advances, patients on dialysis have higher mortality compared to the normal population. The survival trend and factors affecting the survival of dialysis patients need to be evaluated to assess the effectiveness of this expensive therapy and to allow us to formulate and implement measures to improve the outcome.

3.1 Overall Dialysis Patient Survival

All patients starting dialysis in 1993 to 2002 were included in the analysis for probability of survival. The overall survival of dialysis patients was 90% at one year, 73% at 3-years, 60% at 5-years and 39% at 10-years. (Table 3.2) The 5-year patient survival is similar to those reported from Japan and the UK but higher than those reported by the USRDS and the Netherlands. [1][2] (Table 3.1)

3.2 Patient Survival by Dialysis Modality

Patient survival on haemodialysis (HD) was better compared to CAPD. Haemodialysis patients had a survival probability of 90% at one-year, 63% at 5-years and 41% at 10-years while that for CAPD patients were 88%, 43% and 20% respectively. (Table 3.2 & Figure 3.2) The survival difference between the two modalities was seen after one year on dialysis.

Table 3.1 Unadjusted survival of dialysis patients by country

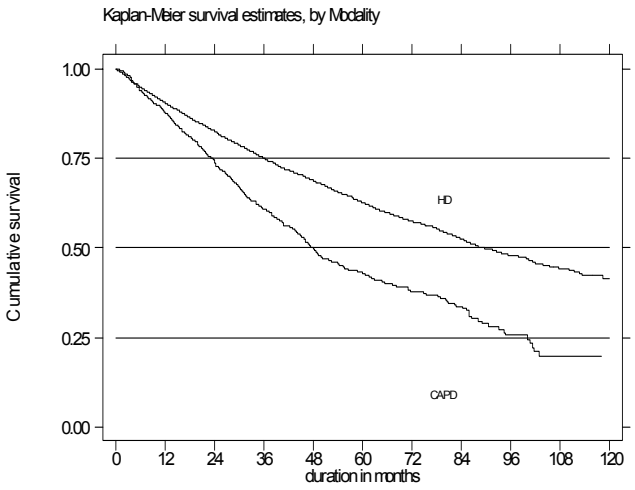
Interval (years)	Malaysia (1993 cohort) (%)	US (1991 cohort) (%)	Japan (%)	UK (%)	Netherlands (%)
1	92	78			
2	85	61			67
5	68	29	61	59	35
10	47	9			11

Table 3.2 Unadjusted ten-year patient survival by Dialysis modality (1993-2002 cohort)

Dialysis modality	CAPD		HD		ALL DIALYSIS	
Interval (months)	% Survival	SE*	% Survival	SE*	% Survival	SE*
6	94	1	95	0	95	0
12	88	1	90	0	90	0
24	74	1	82	0	81	0
36	61	1	75	0	73	0
48	50	2	69	1	66	0
60	43	2	63	1	60	1
72	38	2	57	1	55	1
84	34	2	53	1	50	1
96	26	3	48	1	45	1
108	20	3	44	1	41	1
120	20	3	41	1	39	1

* SE=standard error

Figure 3.2 Unadjusted ten-year patient survival by Dialysis Modality (1993-2002)



3.3 Patient Survival by Year Commencing Dialysis

The survival of haemodialysis and CAPD patients by year of entry into the dialysis programme is shown in Table 3.3. There was no apparent trend in the crude survival of HD patients over the last 10 years despite the increasing intake of older and diabetic patients. In CAPD, long-term survival has gradually improved, perhaps reflecting the improvement in connectology in CAPD treatment resulting in reduced peritonitis rate – the Achilles heel of the peritoneal dialysis programme. The survival at 5 years was 37% and 49% in 1993 and 1997 respectively. (Table 3.3).

3.4 Patient Survival by Age

Not surprisingly, younger patients on dialysis had better survival compared to older patients. The one-year, 5-year and 10-year survival for patients less than 15 years old was 97%, 85% and 56% respectively compared to 84%, 34% and 14% for patients 65 years or older. (Table 3.4 & Figure 3.4)

Table 3.3 Unadjusted ten -year survival of haemodialysis and CAPD patients by year of entry (1993-2002 cohort)

Year	1993		1994		1995		1996	
Interval (months)	HD % (SE)	CAPD % (SE)	HD % (SE)	CAPD % (SE)	HD % (SE)	CAPD % (SE)	HD % (SE)	CAPD % (SE)
6	96 (1)	94 (3)	94 (1)	91 (3)	95 (1)	93 (2)	95 (1)	94 (1)
12	93 (1)	85 (5)	89 (2)	82 (4)	92 (1)	87(3)	92 (1)	88 (2)
24	87 (2)	74 (6)	84 (2)	65 (5)	86 (2)	71 (4)	86 (1)	77 (3)
36	81 (2)	58 (7)	77 (2)	50 (5)	79 (2)	59 (4)	76 (2)	66 (4)
48	77 (2)	44 (7)	72 (2)	43 (6)	75 (2)	46 (4)	70 (2)	52 (4)
60	73 (3)	37 (7)	64 (2)	37 (6)	69 (2)	37 (4)	63 (2)	48 (4)
72	68 (3)	37 (7)	60 (2)	33 (6)	64 (2)	33 (4)	57 (2)	39 (4)
84	63 (3)	37 (7)	53 (3)	31 (6)	60 (2)	29 (4)	52 (2)	35 (4)
96	58 (3)	24 (7)	47 (3)	28 (6)	54 (2)	23 (4)		
108	54 (3)	19 (7)	42 (2)	17 (7)				
120	51 (3)	19 (7)						

Year	1997		1998		1999		2000	
Interval (months)	HD % (SE)	CAPD %(SE)	HD % (SE)	CAPD % (SE)	HD % (SE)	CAPD % (SE)	HD % (SE)	CAPD % (SE)
6	94 (1)	96 (1)	95 (1)	94 (2)	95 (1)	94 (2)	95 (1)	94 (2)
12	90 (1)	92 (2)	92(1)	86 (3)	90 (1)	90 (2)	90 (1)	88 (2)
24	83 (1)	79 (3)	84(1)	73 (4)	83 (1)	73 (3)	81 (1)	77 (3)
36	76 (1)	65 (4)	77(1)	62 (4)	75 (1)	55 (4)	74 (1)	64 (4)
48	70 (1)	56 (4)	70(1)	54 (4)	67 (1)	46 (4)		
60	63 (2)	49 (4)	63(1)	44 (5)				
72	57 (2)	42 (4)						

Year	2001		2002	
Interval (months)	HD % (SE)	CAPD % (SE)	HD % (SE)	CAPD % (SE)
6	94 (1)	93 (1)	96 (1)	94 (1)
12	89 (1)	88 (2)	91 (2)	87 (2)
24	79 (1)	74 (3)		

* SE=standard error

Figure 3.4 Unadjusted ten-year survival of dialysis patients by age (1993-2002 cohort)

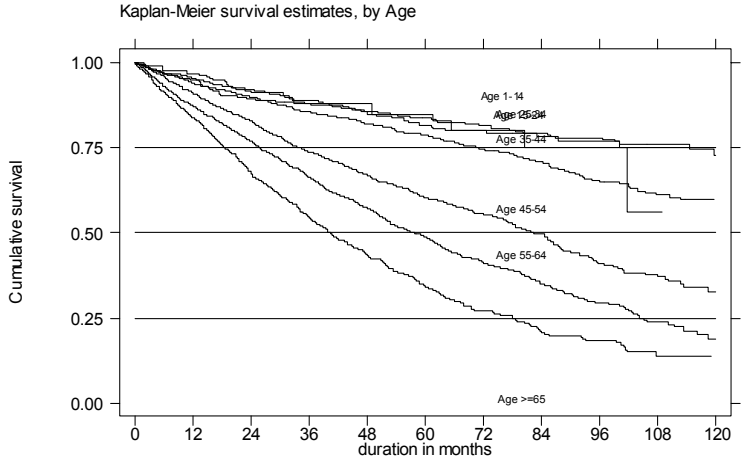


Table 3.4 Unadjusted ten-year survival of dialysis patients by age (1993-2002 cohort)

Age group	≤14		15 - ≤24		25 - ≤ 34		35—≤ 44	
Interval (months)	% Survival	SE*	% Survival	SE*	% Survival	SE*	% Survival	SE*
6	98	1	97	1	97	1	97	0
12	97	1	95	1	95	1	94	1
24	92	2	89	1	92	1	90	1
36	88	3	88	1	89	1	85	1
48	88	3	85	2	86	1	82	1
60	85	3	82	2	84	1	78	1
72	80	4	80	2	81	1	74	1
84	75	6	78	3	79	2	71	1
96	75	6	77	3	78	2	65	2
108	56	17	75	3	76	2	61	2
120	56	17	75	3	73	3	60	2

Age group	45 - ≤ 54		55—≤ 64		≥ 65	
Interval (months)	% Survival	SE*	% Survival	SE*	% Survival	SE*
6	96	0	93	0	91	1
12	91	1	87	1	84	1
24	83	1	78	1	68	1
36	74	1	66	1	54	1
48	67	1	57	1	44	1
60	60	1	49	1	34	1
72	55	1	41	1	27	2
84	49	1	35	1	21	2
96	41	2	29	2	18	2
108	37	2	24	2	14	2
120	33	3	19	3	14	2

* SE=standard error

3.5 Patient Survival by Diabetic Status

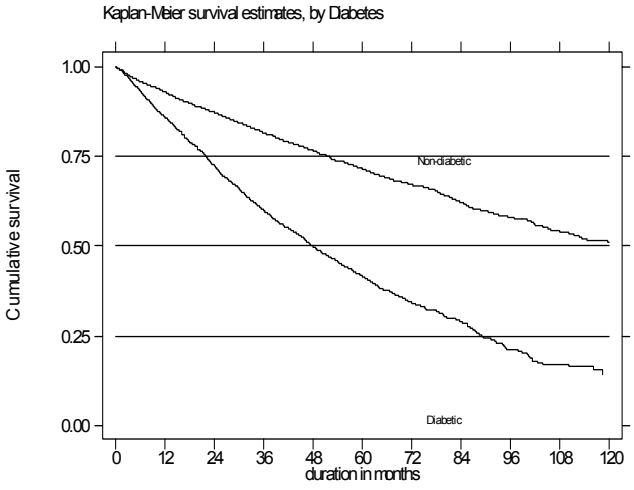
The presence of diabetes mellitus has a major impact on survival. The one-year, 5-year and 10-year survival for non-diabetics were 93%, 71% and 51%, while that for diabetics were 86%, 41% and 14% respectively. The divergence in survival was noted 6 months after commencement of dialysis. The median time of survival for diabetics was 48 months compared to at least 120 months for non-diabetics. (Table 3.5. & Figure 3.5)

Table 3.5 Unadjusted ten-year survival of dialysis patients by diabetic status (1993-2002)

Diabetes status	Non-Diabetic		Diabetic	
Interval (months)	% Survival	SE*	% Survival	SE*
6	96	0	93	0
12	93	0	86	0
24	87	0	73	1
36	82	0	60	1
48	77	1	50	1
60	71	1	41	1
72	67	1	34	1
84	62	1	29	1
96	58	1	21	1
108	54	1	17	2
120	51	1	14	2

* SE=standard error

Figure 3.5 Unadjusted ten-year survival of dialysis patients by diabetic status (1993-2002 cohort)



3.6 Adjusted Mortality of Dialysis Patients

The 1997-2002 dialysis cohort was examined for independent risk factors for death by Cox proportional hazard regression model. The clinical and biochemical data for patients commencing dialysis before 1997 were incomplete and unsuitable for analysis and hence were not included in the analysis. Furthermore the earlier data was only available for patients on dialysis in the Ministry of Health facilities and therefore not representative of the whole dialysis population where about 60% of patients received dialysis therapy in non-Ministry of Health facilities.. The risk of death was adjusted for age, gender, primary diagnosis, time on renal replacement therapy (RRT), modality of dialysis, presence of cardiovascular disease, diabetic status, body mass index (BMI), serum concentrations of albumin, cholesterol, calcium, phosphate, calcium-phosphate product and haemoglobin; blood pressure, and hepatitis status. Time averaged values of biochemical data were used.

Patient characteristics that had significant impact on the hazard of death were age, gender, body mass index, year commencing dialysis, dialysis modality, diastolic blood pressure and presence of diabetes or cardiovascular disease. The significant biochemical risk factors for death were serum albumin, haemoglobin, cholesterol, calcium and calcium-phosphate product. (Table 3.6)

As expected age was an independent risk factor for death. The risk rose progressively with each decade of life. The hazard of death for an elderly patient (more than 65 years of age) was 5.8 times higher compared to a patient less than 15 years of age. This is consistent with the ERA- EDTA registry data. In their report the relative risk of death increased by 5% for each one year increment in age.[3] Female patients had a 14% lower risk of death compared to their male counterparts. This is consistent with the USRDS data.[1] However, the ERA-EDTA registry reported that females had a 5% higher risk of death compared to males.[3]

Diabetic patients on dialysis had about 2 times higher risk of death compared to the non-diabetics. This is comparable with the ERA-EDTA Registry report where the risk of death in diabetics was 2.46 times higher the than non-diabetics.[3] As reported by other authors, dialysis patients with underlying cardiovascular disease had a higher risk of mortality (49%) when compared to patients with no reported history of cardiovascular disease.[4]

CAPD patients had a 74% higher risk of death compared to haemodialysis patients. The ERA-EDTA showed a 25% higher risk of death for those who started renal replacement therapy with peritoneal dialysis.[3] In contrast two other studies did not find any difference in survival between CAPD and haemodialysis patients.[5][6]. The reasons for the lower survival in our CAPD patients are unclear and needs further studies.

The US and European registries have reported improved survival of patients starting dialysis in later vintage. ERA-EDTA data showed that after adjustment for age, gender and diabetes, patient survival for the 1990-1994 (relative risk (RR) 0.94) and the 1995-1999 cohorts (RR 0.88) were better compared to the 1980-1984 cohort.[2] Their improved survival on RRT was attributed to the improved efficiency and safety of dialysis. However our study indicates the reverse - a higher risk of death in patients commencing dialysis from 1999-2002 compared to patients starting dialysis before 1999. Compared to the 1997-1998 cohort the mortality risks of the 1999-2000 and the 2001-2002 cohorts were increased by 21% and 27% respectively. The higher mortality may be due to increased intake of high risk patients into dialysis centres with limited medical care. However, this trend is worrying and more analysis is urgently needed to examine for possible centre-treatment interaction and other as yet unidentified reasons for this trend.

Three nutritional markers (serum albumin concentration, body mass index and serum cholesterol concentration) were identified as independent risk factors for death. Serum albumin concentration was inversely related to the risk of death. Compared to a serum albumin of 40g/l or more, the risk of death was 4.37, 2.24 and 1.38 times higher in patients with serum albumin less than 30g/l, 30-34g/l and 35-39g/l respectively. This relationship has been well described in the literature.[7]

Low body mass index (BMI) and low serum cholesterol concentration were also associated with increased risk of death. Compared to a BMI of 25 kg/m^2 or higher, a BMI of less than 18.5 kg/m^2 was associated with a 41% increased risk of death. The USRDS data also showed higher death rate in haemodialysis patients with lower body mass index. [8][9] Similarly, a serum cholesterol of less than 3.2 mmol/l was associated with a 47% increased risk of death compared to patients with serum cholesterol of more than 5.2 mmol/l. The USRDS data showed similar findings.[1] This inverse relationship in dialysis patients is at variance with the evidence from the normal population. This discrepancy is probably due to the association of low cholesterol with malnutrition and inflammation.[10] Further studies are needed to establish the relationship between higher serum cholesterol and the risk of death from cardiovascular disease.

A prescribed Kt/V_{urea} of less than 1.0 was associated with a 73% higher risk of death compared to a Kt/V_{urea} of 1.2 to 1.4. There was a trend of better survival in patients with $Kt/V_{urea} > 1.4$, but this was not statistically significant.

In the general population high blood pressure is associated with increased mortality. Even borderline high blood pressure has been associated with increased cardiovascular events.[11] Evidence now shows that there is no J-curve relationship between blood pressure and mortality in the general population. In the dialysis population however, several studies have shown a higher risk of death in patients with low blood pressure.[12][13] In our cohort, there is a U-shaped or J-shaped relationship between blood pressure and risk of death. (Figure 3.6a) Compared to the reference range of 80-

90 mmHg, a diastolic blood pressure of less than 70 mmHg was associated with a 28% higher risk of death while a diastolic blood pressure of 90-99 mmHg and 100 mmHg or more was associated with a 1.3 and 2.2 times higher mortality risk respectively. The U-shaped relationship has also been reported in other series. [14][15] After adjustment for diastolic blood pressure and other risk factors, systolic blood pressure and pulse pressure did not independently affect mortality.

Anaemia was associated with increased mortality and poorer quality of life.[16] A haemoglobin level of less than 8g/dl was associated with a 2.2 times higher risk of death compared to a haemoglobin level of 10-12g/dl; while a haemoglobin level of 8-10g/dl was associated with a 31% increase in mortality. The lowest risk of death was recorded in patients with haemoglobin of 11-12g/dl but this was not statistically significant compared to the reference group (haemoglobin 10-11g/dl). There was no significant improvement in survival with haemoglobin level of more than 11g/dl.

The USRDS data showed that serum phosphate of more than 2.08 mmol/l was associated with a 27% increase risk of death.[17] Using a timed average phosphate concentration over 2 years in more than 12,000 patients, Ganesh et al showed that hyperphosphataemia (serum phosphate > 2.08 mmol/l) was associated with a 41% risk of death from cardiovascular disease and a 20% risk of sudden death.[18] Our data showed that hyperphosphataemia had a significant impact on death only when serum phosphate was 2.4 mmol/l or higher - a serum phosphate level of 2.4 to 2.6 mol/l resulted in a 71% increase risk of mortality compared to the reference range of 1.6 to <2.0 mmol/l. Hypercalcaemia (serum calcium 2.6 mmol/l or more) was associated with a 24% increased risk of death compared to the reference range of 2.2 to <2.6 mmol/l in our dialysis population . Foley et al reported that chronic hypocalcaemia was associated with more than two times increased risk of mortality in contrast to our results which did not show any significant increased risk of mortality.[19] The reasons for the discrepancy are unclear.

Patients with a low calcium phosphate product (less than 3.5 $mmol^2/l^2$) was associated with a 31% higher risk of mortality when compared to those with normal calcium phosphate product (3.5-4.5 $mmol^2/l^2$). High calcium phosphate product did not adversely affect survival. This differs from other series where high calcium phosphate product was also associated with increased mortality.[20]

Hepatitis B antigenaemia had no effect on patient survival and this is consistent with other reports.[21] [22] A positive hepatitis C virus (HCV) antibody also did not confer an increase in risk of mortality. However this differs from experience from other centres where a positive HCV antibody was associated with a higher relative risk of death compared to patients negative for HCV antibody. [23-26]

Conclusion

In conclusion survival of our dialysis patients over the last 10 years is comparable to those reported from other centres/registries. The reasons for poorer survival in recent years need to be identified and corrective measures implemented.

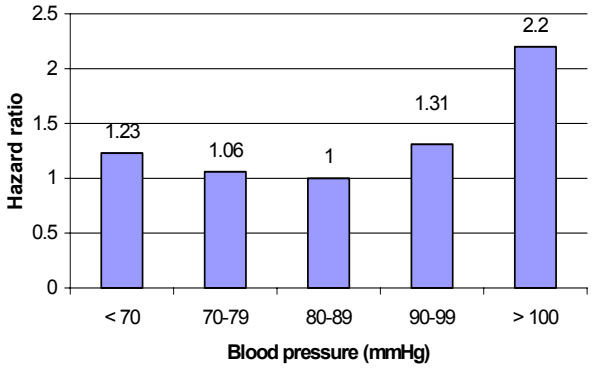
Table 3.6 Adjusted hazard ratio for mortality of dialysis patients (1997-2002 cohort)

Factors	N	Hazard ratio	95% CI	P value
Age (years):				
0-≤14(ref.*)	157	1.00		
15-≤24	417	1.82	(0.89,3.71)	0.100
25-≤34	727	1.58	(0.79,3.16)	0.198
35-≤44	1223	1.97	(1.00,3.89)	0.049
45-≤54	1885	3.12	(1.60,6.09)	0.001
55-≤64	1907	4.03	(2.06,7.89)	0.000
≥65	1094	5.76	(2.92,11.33)	0.000
Gender:				
Male (ref.*)	4113	1.00		
Female	3297	0.86	(0.75, 0.97)	0.015
Primary diagnosis:				
Unknown/Uncertain (ref.*)	2168	1.00		
Diabetes mellitus	2915	2.14	(1.81,2.52)	0.000
GN/ SLE	908	1.04	(0.79,1.35)	0.777
Polycystic kidney	119	1.61	(0.99,2.63)	0.057
Obstructive Nephropathy	361	1.39	(1.05,1.85)	0.023
Others	939	1.23	(0.98,1.53)	0.073
Year start dialysis				
1997-8 (ref.*)	1915	1.00		
1999-2000	2652	1.21	(1.05,1.39)	0.009
2001-2002	2843	1.27	(1.06,1.53)	0.010
Modality:				
CAPD (ref.*)	1243	1.74	(1.51,2.00)	0.000
HD	6167	1.00		
BMI:				
<18.5	1080	1.41	(1.15,1.74)	0.001
18.5-<25	3635	1.27	(1.10,1.46)	0.001
≥25(ref.*)	1444	1.00		

Table 3.6 Adjusted hazard ratio for mortality of dialysis patients (1997-2002 cohort)

Factors	N	Hazard ratio	95% CI	P value
Serum albumin (g/L)				
<30	558	4.36	(3.41,5.56)	0.000
30-<35	1255	2.31	(1.91,2.81)	0.000
35-<40	2861	1.39	(1.17,1.64)	0.000
≥ 40(ref.*)	2170	1.00		
Serum cholesterol (mmol/l):				
<3.2	197	1.45	(1.10,1.92)	0.010
3.2-<5.2	2987	1.00	(0.88,1.13)	0.996
≥5.2(ref.*)	2537	1.00		
KT/V				
<1	274	1.73	(1.23,2.43)	0.002
1.0-1.2	898	1.21	(0.96,1.51)	0.106
1.2-1.4(ref.*)	1439	1.00		
1.4-1.6	1422	0.97	(0.80,1.18)	0.763
≥ 1.6	1823	0.84	(0.67,1.05)	0.126
Diastolic BP:				
<70	824	1.23	(1.01,1.49)	0.036
70-<80	2193	1.06	(0.92,1.22)	0.450
80-<90(ref.*)	2800	1.00		
90-<100	1186	1.31	(1.09,1.58)	0.004
≥100	270	2.20	(1.63,2.98)	0.000
Haemoglobin (g/dl):				
<8	1610	2.17	(1.78,2.64)	0.000
8-<9	1783	1.31	(1.09,1.60)	0.005
9-<10	1803	1.26	(1.04,1.51)	0.016
10-<11(ref.*)	1112	1.00		
11-<12	504	0.89	(0.68,1.20)	0.453
≥ 12	234	1.14	(0.79,1.63)	0.487
Serum Calcium (mmol/l):				
<2.2	1683	1.04	(0.88,1.24)	0.636
2.2-<2.6(ref.*)	4423	1.00		
≥ 2.6	673	1.24	(1.03,1.50)	0.022
Calcium Phosphate product				
<3.5	2130	1.31	(1.08,1.59)	0.006
3.5-<4.5(ref.*)	2335	1.00		
4.5-<5.5	1460	0.84	(0.67,1.05)	0.128
≥ 5.5	813	0.96	(0.64,1.43)	0.824
Serum Phosphate (mmol/l)				
<1.6	2645	1.01	(0.82,1.25)	0.923
1.6-<2.0(ref.*)	2218	1.00		
2.0-<2.2	788	1.17	(0.91,1.50)	0.213
2.2-<2.4	577	1.07	(0.77,1.49)	0.670
2.4-<2.6	329	1.71	(1.11,2.61)	0.014
≥ 2.6	414	1.55	(0.98,2.45)	0.061
HbAsg:				
Negative(ref)	6943	1.00		
Positive	467	1.11	(0.87,1.40)	0.407
Anti-HCV:				
Negative(ref)	6276	1.00		
Positive	1134	0.89	(0.76,1.05)	0.163
Cardiovascular disease (CVD)				
No CVD(ref)	5938	1.00		
CVD	1472	1.49	(1.30,1.70)	0.000

Figure 3.6(a) Adjusted hazard ratio for mortality of dialysis patients by diastolic blood pressure (1997-2002 cohort)



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