Analysis of Factors Predicting Mortality of New Patients Commencing Dialysis Therapy in a Single Year after 10 Years Follow-Up

Oliver T Browne¹
Prof Sunil Bhandari¹²
Victoria Allgar³

²Department of Renal Medicine
Hull and East Yorkshire Hospitals NHS Trust, Kingston upon Hull, HU32JZ, UK
¹Hull York Medical School, East Yorkshire,
³Department of Statistics, Hull York Medical School and University of Hull
United Kingdom.

Phone: 01482674566
Fax: 01482674998
Email: sunil.bhandari@hey.nhs.uk

Correspondence to Prof Sunil Bhandari
Background
The natural history of patients commencing dialysis in East Yorkshire is not well characterised and there is little convincing evidence studying the impact of potential pre-dialysis factors predicting mortality during dialysis. Aim: To update previously published 5-year data on pre-dialysis and co-morbid risk factors for mortality to 10 years.

Methods
A longitudinal study of subjects commencing dialysis in 2001/02 in East Yorkshire with a mean follow up of 11.8 years. Mortality was evaluated at 126 months. Predictors of mortality were determined by uni-variate, multi-variate analysis and survival via Kaplin-Meier analysis.

Results
Baseline characteristics and the preferred mode of dialysis remained concordant with the original trial. The mortality rate at the end of the study period was 60% (56/94) with 30% (29) of patients having been transplanted. Highlighted in the 5 year data the significant proportion of mortality was made up of vascular disease and sepsis (71%) but this proportion had decreased to (56%) by 10 years. Cardiac disease was the commonest cause of death but notably in 18% of patients death was related to dialysis or withdrawal of treatment. Vascular disease and diabetes remained as independent risk factors and predictive of mortality.

Conclusions
Although diabetes and vascular disease remained predictive of mortality, interestingly calcium-phosphate levels are no longer significant and may be a more specific predictor of early cardiac mortality. Key to the impact of survival in this cohort was aggressive management of cardiac risk factors in addition to early transplantation.

Key Words: diabetes, dialysis, mortality, risk factors, vascular.

Short summary: Vascular and Diabetic risk factors are strongly predictive of mortality in dialysis patients at 10 years, calcium phosphate is no longer so. Treatment withdrawal has become a more salient feature. A patient’s risk profile changes over time, identifying modifiable risk factors at different stages of disease progression will help reduce morbidity and mortality of those on dialysis.
**Introduction**

Chronic kidney disease (CKD) has been increasingly recognized as a risk factor for mortality and cardiovascular disease. In the United Kingdom at least 7% of the adult population have an eGFR of less than 60mls/min and over forty thousand patients are receiving treatment for end stage renal disease (ESRD) [1], with an increasingly aging population suffering from a significant number of co-morbidities these figures continue to increase at 5% per annum [2].

Despite advances in the treatment of chronic renal failure the prognosis remains poor. Identification of risk factors that predispose or exacerbate CKD will help to reduce the morbidity and mortality of those who will need dialysis. In particular, there is strong evidence for cardiovascular disease risk factors being associated with deterioration in patients’ renal function and is predictive of those who will go on to require dialysis [3]. This generates scope for primary preventative interventions, ameliorating not only classical modifiable risk factors such as; smoking, hypertension, diabetes mellitus and hyperlipidaemia but also non-traditional risk factors such as; functional iron deficiency, anaemia, insulin resistance and vitamin D deficiency [4,5,6]. Preventive measures are not only needed to prevent disease states occurring but also are required to modify outcomes once disease has been established. Secondary and tertiary preventative measures show that modifying a patient’s risk factors on dialysis improves survival and quality of life [7,8,9].

Previously we have described the 1 and 5-year results of an analysis of factors and co-morbidities predictive of mortality in a prospective study of a cohort of 94 dialysis patients [10]. Risk factors, which were analysed at 5 years, confirmed that an elevated calcium phosphate product, diabetes mellitus, vascular disease and older age at the start of dialysis were independently predictive of mortality. In addition, the study identified low haemoglobin and lower pre-dialysis GFR as good predictors of early mortality reflecting findings and discussion from other investigators [11,12]. We now present the extended ten-year data to highlight the impact and changes in risk factor profile.

**Subjects and Methods**

The design of the study remained longitudinal, taken from a cohort receiving dialysis from the Hull and East Yorkshire services over a 10-year period. Re-analysis of the data was performed on the same cohort of 94 patients, the database from the 5-year period having been updated to include changes in patient outcome. Previously analysed risk factors were sought for revalidation of predicting mortality.

The trust research and development committee approved the study as part of regional development of its dialysis service. All patients are globally consented for use of patient data prior to initiating dialysis with the service as set out by the trust’s renal handbook policy. Formal written consent was not required as any subsequent interventions made during the longitudinal study were aimed at improving clinical care based on the current guidelines, best evidence and clinical expertise.

The 94 patients had been selected from the East Yorkshire region having commenced renal replacement therapy (RRT) in the form of haemodialysis or peritoneal dialysis in the year 2001/2002. All patients presenting for dialysis therapy were included except patients dialysing for less than 90 days, who were considered to be acute. Patient characteristics are described in the original study [10]. All cause mortality was the primary outcome measure and was used as a comparison to the previous 5-year data.

Pre-dialysis factors analysed included; age at the start of dialysis, gender, smoking status, referral and pre-dialysis eGFR (measured by the four-variable Modification of Diet in Renal Disease equation), duration of renal care, renal disease aetiology, dialysis mode (haemodialysis and peritoneal dialysis), form of access, dialysis planning, diabetes and left ventricular hypertrophy (diagnosed by ECG or trans-thoracic echocardiography).

Presence of significant co-morbidity at the start of RRT including; diabetes, vascular disease, chronic obstructive pulmonary disease, ischaemic heart disease, cerebrovascular disease and visceral
malignancy were studied together to stratify subjects into low-medium and high risk groups on mortality.

Modifiable biochemical markers of haemoglobin, serum albumin, triglycerides, cholesterol, calcium and phosphate at the start of RRT were also included in the analysis. Calcium phosphate product was split into quartiles and the upper quartile was compared to the 3 lower quartiles when comparing effect on mortality.

Statistical analysis

All statistical analyses were completed on SPSS for Windows – version 19. All dependent variables are expressed as means, medians, interquartile ranges and standard deviations. All independent variables are expressed as percentages of total study population. Predictors of mortality were determined by uni-variate, multi-variate analysis by MANOVA and using a Cox-Regression model. For survival over 10 years the Kaplan-Meier method was used, with a negative log rank test (Mantle-Cox) to secure the p-value. A p-value of < 0.05 was considered statistically significant. Data is represented a means +/-SEM or medians with ranges.

Results

The cohort of patients was followed up for a median of 8.7 years [mean of 8.8±0.3 years] from the date each patient commenced dialysis therapy in 2001/2002 and a median of 10.5 years [mean of 11.9±4.2 years] from presentation to a nephrologist.

Baseline characteristics and the preferred mode of dialysis remained concordant with the original trial (10), consisting of a mean age of 63±1 yrs and predominantly Caucasian ethnicity (98.2%). Mortality was evaluated at a median of 126 months (mean of 146±4.2 months) from presentation to the renal service.

30% (29/94) of patients had been transplanted during the follow-up period and were therefore censored in the survival cumulative analysis. At the time of last follow-up 18 of the transplant patients were still alive with a functioning renal allograft (62%); 2 had experienced transplant failure and returned to haemodialysis and 9 of those who received transplants died (31%; 6 cardiac deaths, 1 sepsicaemia, 1 calciphylaxis and 1 related to treatment withdrawal). For transplant patients, the median time from first presentation to death was 8.9 years [mean of 9.8±5.1 years], with an average wait of 1.3±0.4 years between first dialysis and transplant. Survival from transplant using Kaplan-Meier showed a mean of 75 months (95% CI 57-92) and compared with non-transplantation 63 months (95% CI 51-75), however this was not statistically significant (p=0.263). These patients were then censored from the data when examining mortality on further survival analysis.

The mortality rate at the end of the 10-year study period was 60% (56/94). Causes of death are described in Table 1 with cardiac related and infection accounting for the majority (56%). There was an increase in the percentage of deaths from treatment withdrawal (13%) and deaths from other causes (14%). The other categories included malignancy and deaths related to chronic renal failure whilst on dialysis.

Table 2 shows the cross-sectional comparison between survivors and non-survivors at 10 years of dialysis. Survivors have a lower mean age (53 years) compared to non-survivors (69 years). Chi-squared analysis of the ordinate variables compared vascular disease, diabetes, co-morbidity and haemoglobin stratified into categories <11g/dL and >11 g/dL. At 10 years, those with vascular disease, diabetes and >3 co-morbidities were more likely to have a greater percentage of non-survivors. There was no difference in percentage survival between groups based on haemoglobin over 10 years. ANOVA analysis of continuous variables showed a difference between serum creatinine (µmol/L), albumin (g/L) and haemoglobin concentration (g/dL) all at the start of RRT. Non-survivors at 10 years had a lower serum creatinine, lower albumin and haemoglobin at the start or RRT. There was no significant difference between triglycerides, calcium phosphate product, cholesterol, GFR or
creatinine at referral to a nephrologist. Multivariate analysis using MANOVA and a Cox-regression model showed a lack of statistical significance in this cohort (Table 3).

On 10-year analysis, vascular disease and diabetes remained independent risk factors and were predictive of mortality (Table 4). From Kaplan-Meier survival curves, patients with vascular disease had a cumulative survival of 20% compared to 37% of those without vascular disease (Figure 1A; p=0.01). Diabetic patients had a cumulative survival of 22% compared to 31% without diabetes (Figure 1B; p=0.03). Those aged greater than 65 had a mean survival time of 51 months compared to those less than 65 years who had a mean survival of 85 months (p=0.001). No significant difference was seen between those with the upper 3 quartiles of calcium phosphate product and the lowest 3 quartiles (Figure 1C; p=0.7).

Additionally, patients stratified into high (>3) and low (<3) co-morbidities, unplanned or referred presentations and age groups stratified into greater and less than 65 yrs had marked differences in overall survival. From Kaplan-Meier survival curves showed those with high co-morbidities (>3) had a cumulative survival of 46% compared to 9% (p<0.0001). Comparing presentations those with planned presentations had a cumulative survival of 43% compared to 12% of those with unplanned presentations (p=0.004). Finally, those who were older (>65) had worse survival rates after 10 years of 15% compared to those in the younger age group, which showed just over half of these patients were still alive (52%) at 10 years (p=0.001). Notably those who were aged over 65 represented 73% of the high co-morbidity (30/41). Survival analysis of factors including LVH, duration of follow up, smoking status and type of dialysis and individual co-morbidities such as cancer were non-significant at 10 years (data not shown).

Discussion

In this single centre study of a relatively elderly Caucasian population receiving dialysis therapy, we have demonstrated that diabetes and vascular disease remain strong predictors of mortality, however contrary to the 5 year data a high calcium-phosphate product no longer correlates with mortality at 10 years. Vascular disease and sepsis account for the majority of causes of death at all stages of dialysis, accounting for 72% of the mortality seen at 5 years reducing to 56% at 10 years with a quarter of all mortality (14/56) represented by cardiac disease. The data from this does not fully highlight the protection conferred from a renal allograft; indeed the observation that kidney graft is protective may be a result of selection bias.

At 10 years, treatment withdrawal and other causes of death (including respiratory failure, pulmonary oedema and sudden death) collectively have shown the greatest proportional increase over the last 5 years (Table1). Treatment withdrawal has become a more significant feature and is common sequelae for those with end stage renal failure (ESRF) on long-term dialysis. In some cohorts, treatment withdrawal has been described as an increasingly common cause of death and is related to an aging population with increased co-morbidities, such as diabetes, or occurs in young individuals with severe disease [13,14]. Indeed the poor projected survival reduced added benefit of therapy and increased cognitive impairment seen in ESRF coupled with changing views of clinicians has increased dialysis withdrawal rates. Although we have investigated all-cause mortality as our primary outcome, it is important to note that other end-points for palliative care such as quality of life, ability to make advanced directives and symptom management are more clinically relevant.

The 5 year cumulative survival of diabetes and non-diabetics was 47% vs. 67% (p=0.03) and then at 10 years was of 22% vs. 31% respectively (Figure 1B; p=0.03). At 5 years the paths of the two groups were divergent, however the 10 year graph is following a divergent-convergent path showing that therapy may be delaying the natural progression of the underlying disease or that those with diabetes may be experiencing early mortality.

The prevalence of diabetes mellitus in chronic kidney disease (CKD) continues to increase and remains a strong independent cardiovascular risk factor for patients in the general population as well as on dialysis [15]. Hyperglycaemia, in combination to traditional risk factors not only potentates endothelial damage and inflammation but in addition to diabetic mediators such as reactive oxygen
species and cytokines, affects gene structure and function, generating targets for novel epigenetic therapeutics [16]. In addition to the recognised atherosclerotic processes responsible for these cardiac events, a decreased cardiac velocity reserve has also been observed in diabetic patients with CKD [17]. The importance of atherosclerosis in this cohort has been well documented and the presence of microalbuminuria has been recognised as a surrogate marker of endothelial injury and hence vascular damage seen in diabetic patients [18].

Intensive intervention of diabetes within a multidisciplinary team, in comparison to a conventional therapeutic approach, has been shown not only to reduce mortality from cardiovascular disease but also reduce the micro and macro-vascular complications of diabetes such as neuropathy, nephropathy and retinopathy [19, 20].

Debate remains about the optimal level of glycaemic control for diabetics on dialysis [21]. Poor glycaemic control has been associated with increased cardiovascular deaths seen after transplantation [22], in our study 67% of those transplanted suffered cardiac deaths (30% of whom were diabetic). Aggressive glycaemic control has been shown to be detrimental generating a U-Shaped curve for HbA1c. When a patient’s HbA1c is persistently lowered below 6% this is associated with adverse outcomes, demonstrated not only in the general population, but in those receiving dialysis randomised to this group as publicised in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial [23,24]. Although initially aimed at reducing microvascular complications the increasing cardiovascular mortality that was seen meant the ACCORD trial had to be terminated prematurely. Although near-normal glycaemia has not been shown to reduce cardiovascular events in the short-term [25], indeed the majority of our cardiovascular disease mortality was seen within the first 5 years; follow up of long-term randomised control studies is needed to determine optimal glycaemic control.

Our data correlates with previous studies demonstrating that patients on dialysis with atherosclerotic vascular disease have higher mortality rates [26,27]. Also the number of risk factors for cardiovascular disease increases with the stage of CKD [28]. Given that the pre-dialysis diagnosis of cardiovascular disease predicted both early and late mortality, the reemphasis of both prompt recognition and management of cardiovascular risk factors during the early stages of CKD is key to improving survival.

The importance of tight blood pressure regulation has been shown to significantly reduce mortality and morbidity [29]. However studies have raised concerns about over aggressive blood pressure reduction as blood pressure in relation to mortality, in a situation analogous to diabetes, also follows a U-shaped curve [30,31]. Statins have been used successfully in the general population to reduce cardiovascular events by around 34%. In CKD and dialysis patients the data is more complex, initial studies have shown reduced LDL levels in dialysis patients with no cardiovascular benefit [32], while the more recent SHARP study has shown a 17% reduction in cardiovascular events in the overall cohort [33]. Sub-group analysis however suggests once again no benefit in dialysis patients [34].

Traditional risk factors have been the mainstay of cardiovascular disease primary prevention identified in the Framington Heart Study. However there is debate whether the same relative risks apply to a dialysis population in the secondary prevention of cardiovascular disease. The presence of “renal-specific” non-traditional risk factors including endothelial dysfunction, inflammation, oxidative stress, insulin resistance, anaemia and changes in vitamin D metabolism may play an even more important role in cardiovascular disease progression in CKD [35]. Therefore in considering the overall cardiovascular risk factors, a risk score specific to this population whilst incorporating a wide range of factors, including those prior to dialysis (such as renal function at the start of dialysis and microalbuminuria), may aid the stratification of high risk patients [36,37].

Although, in the previous analysis an elevated calcium phosphate product had a significant effect on early mortality and at 5 years, validating previous findings in patients with ESRF [38], this was no longer the case after 10 years follow up (Figure 1C; p= 0.7), reflecting other studies with a similar case mix and follow up [39]. One hypothesis is perhaps that calcium phosphate is an independent risk factor, or proxy, for those already with significant vascular disease. Those with higher proportions of
vascular disease coupled with calcium phosphate’s strong association with cardiac calcification and mortality may have already perished at 1 and 5 years [40]. Indeed more aggressive management of vascular risk factors may account for the reduced mortality seen at 10 years. This is, however, speculation of an independent risk factor recorded on first dialysis and would require serial calcium phosphate measurements within a randomised control trial to validate this hypothesis.

There is emerging interest between vitamin D, FGF-23 and Klotho and their relation to cardiovascular risk in dialysis patients, understanding how these factors modulate signalling pathways of mineral metabolism may be influential in modifying patients’ overall vascular risk [41,42]. A reduction in Klotho and elevation in FGF-23 culminate in reduced vitamin D levels and increased phosphate with subsequent increased risk of vascular calcification [43]. From our study perspective, levels of these signalling messengers may have changed with dialysis therapy or been influenced by the inherent genetic variations seen in different patient sub-groups altering expression of these factors and conferring protection - a concept proposed by those undertaking molecular biological assays with Klotho [44,45].

**Conclusions**

Diabetes and vascular disease remain challenging risk factors in dialysis patients. Vascular calcification in relation to a higher calcium phosphate product is a potential and important modifiable risk factor to prevent early mortality on dialysis for those patients already at significant cardiovascular risk. Early aggressive intervention will be necessary to influence mortality in subsequent cohorts.

The burden of vascular disease remains of key importance for patients, modifying the risk profile and intensive intervention accounts for the reduced numbers of cardiovascular disease seen in the last 5 years of this study. Determining modifiable risk factors and optimal management for those who are more likely to suffer from early demise will be central to changing the overall mortality.

**Limitations to the study**

This study has several limitations. One acknowledges that this was an observational longitudinal study in a relatively elderly Caucasian cohort of patients and that small numbers were used. However it does highlight some interesting findings. Therefore prospective studies are necessary to investigate any potential causal relationships between both traditional and non-traditional risk factors that we have described with cardiovascular end-points. Larger numbers would be necessary to remove possible type 2 errors occurring and to see if interventions to reduce risk factors lead to overt reductions in cardiovascular risk.

*Conflict of interest*: None declared

**References**


41. Mirza MA, Larsson A, Melhus H, Lind L and Larsson TE. Serum intact FGF23 associate with left ventricular mass, hypertrophy and geometry in an elderly population. *Atherosclerosis* 2009; 207: 546-51
Table 1  Mortality of study population over 10 years:

<table>
<thead>
<tr>
<th>Factor</th>
<th>Alive at 10 Years</th>
<th>Dead at 10 years</th>
<th>P-value</th>
<th>Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>53</td>
<td>69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular Disease – no (%)</td>
<td>52</td>
<td>48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular Disease – yes (%)</td>
<td>28</td>
<td>72</td>
<td>0.02</td>
<td>5.5 (X²)</td>
</tr>
<tr>
<td>Diabetes – no (%)</td>
<td>48</td>
<td>52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes – yes (%)</td>
<td>27</td>
<td>73</td>
<td>0.03</td>
<td>4.3 (X²)</td>
</tr>
<tr>
<td>Co-morbidity (&gt;3) – no (%)</td>
<td>60</td>
<td>40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Co-morbidity (&gt;3) – yes (%)</td>
<td>15</td>
<td>85</td>
<td>&lt;0.001</td>
<td>20.1 (X²)</td>
</tr>
<tr>
<td>Haemoglobin &gt;10g/dl (%)</td>
<td>50</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoglobin &lt;10g/dl (%)</td>
<td>40</td>
<td>61</td>
<td>0.5</td>
<td>.426 (X²)</td>
</tr>
</tbody>
</table>

*Deaths have been censored for live and deceased donor renal transplantation.*

Table 2  Univariate comparison of Factors between patients alive and dead at 10 years

<table>
<thead>
<tr>
<th>Factor</th>
<th>Alive at 10 Years</th>
<th>Dead at 10 years</th>
<th>P-value</th>
<th>Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
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<td>69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular Disease – no (%)</td>
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<td>Diabetes – no (%)</td>
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<td>52</td>
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<tr>
<td>Diabetes – yes (%)</td>
<td>27</td>
<td>73</td>
<td>0.03</td>
<td>4.3 (X²)</td>
</tr>
<tr>
<td>Co-morbidity (&gt;3) – no (%)</td>
<td>60</td>
<td>40</td>
<td></td>
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<tr>
<td>Co-morbidity (&gt;3) – yes (%)</td>
<td>15</td>
<td>85</td>
<td>&lt;0.001</td>
<td>20.1 (X²)</td>
</tr>
<tr>
<td>Haemoglobin &gt;10g/dl (%)</td>
<td>50</td>
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<td></td>
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<tr>
<td>Haemoglobin &lt;10g/dl (%)</td>
<td>40</td>
<td>61</td>
<td>0.5</td>
<td>.426 (X²)</td>
</tr>
</tbody>
</table>


Creatinine at referral (µmol/l) \(^c\) 483 (±77) 411 (±28) 0.3
GFR at referral (ml/min/1.732 m\(^2\)) \(^c\) 18.6 (±2.8) 19.3 (±1.8) 0.84
Creatinine at start of RRT (µmol/l) \(^c\) 903 (±60) 757 (±27) 0.02
GFR at start of RRT (ml/min/1.732 m\(^2\)) \(^c\) 6.35 (±0.4) 6.35 (±0.2) 0.99
Albumin at start of RRT (g/L) \(^c\) 32.0 (±4.9) 28.6 (±5.7) 0.004
Haemoglobin at start of RRT (g/dl) \(^c\) 9.56 (±0.28) 8.78 (±0.22) 0.03
Cholesterol at start of RRT (mmol/l) \(^c\) 5.2 (±0.21) 5.0 (±0.2) 0.69
Triglycerides at start of RRT (µmol/l) \(^c\) 2.12 (±0.22) 2.19 (±0.16) 0.82
Calcium Phosphate Product at start of RRT (mmol\(^2\)/l\(^2\)) \(^c\) 4.84 (±0.29) 4.44 (±0.22) 0.26

\(^a\) Age: analysis using T-test  
\(^b\) Ordinate variables Chi-squared test  
\(^c\) Continuous variables compared using ANOVA (SEM)

### Table 3  Multivariate Analysis: Cox-Regression Model

<table>
<thead>
<tr>
<th>Factor</th>
<th>Wald</th>
<th>Sig.</th>
<th>95.0% CI for Exp(B)</th>
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<tr>
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<td>.036</td>
<td>.849</td>
<td>.290</td>
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<tr>
<td>High versus Low Comorbidity</td>
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<td>.493</td>
<td>.344</td>
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<tr>
<td>Diabetes</td>
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<td>.013</td>
<td>.193</td>
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<tr>
<td>Ischaemic Heart Disease</td>
<td>.380</td>
<td>.538</td>
<td>.564</td>
</tr>
<tr>
<td>Cerebrovascular Accident</td>
<td>.666</td>
<td>.414</td>
<td>.304</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>.754</td>
<td>.385</td>
<td>.626</td>
</tr>
<tr>
<td>Vascular Disease</td>
<td>1.158</td>
<td>.282</td>
<td>.215</td>
</tr>
<tr>
<td>Cancer</td>
<td>1.212</td>
<td>.271</td>
<td>.298</td>
</tr>
<tr>
<td>Chronic Obstructive Pulmonary Disease</td>
<td>.621</td>
<td>.431</td>
<td>.167</td>
</tr>
</tbody>
</table>

### Table 4  Kaplan-Meier survival analysis of factors affecting mortality:

<table>
<thead>
<tr>
<th>Factor</th>
<th>Mean survival (Months)</th>
<th>95% CI</th>
<th>P-value (Log rank test –Mantel Cox)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;65 Years</td>
<td>85</td>
<td>(69-101)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age &gt;65 Years</td>
<td>51</td>
<td>(40-63)</td>
<td></td>
</tr>
<tr>
<td>Description</td>
<td>Count</td>
<td>Range</td>
<td>p-value</td>
</tr>
<tr>
<td>--------------------------------------------------</td>
<td>-------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>Vascular Disease</td>
<td>52</td>
<td>(39-66)</td>
<td></td>
</tr>
<tr>
<td>No Vascular Disease</td>
<td>77</td>
<td>(64-91)</td>
<td>0.01</td>
</tr>
<tr>
<td>Highest quartile of the calcium phosphate product</td>
<td>60</td>
<td>(38-82)</td>
<td></td>
</tr>
<tr>
<td>Lowest quartile of the calcium phosphate product</td>
<td>65</td>
<td>(55-77)</td>
<td>0.7</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>50</td>
<td>(34-66)</td>
<td></td>
</tr>
<tr>
<td>No Diabetes Mellitus</td>
<td>74</td>
<td>(62-86)</td>
<td>0.03</td>
</tr>
</tbody>
</table>
Figure 1. Kaplan-Meier Survival curves over 10 Years for (A) Vascular disease versus no vascular disease; (B) Diabetes versus no diabetes; (C) Calcium phosphate product quartiles.