

Table 1 | Blood pressure and heart rate responses to pressor maneuvers

	Blood pressure ^a (mm Hg)	Heart rate (bpm)
<i>Mental stress^b</i>		
Baseline	152/82	100
End	144/78	100
<i>Handgrip (30 s)</i>		
Baseline	126/62	75
End	158/80	88
<i>Cold pressor (30 s)</i>		
Baseline	132/60	78
End	160/78	88

All tests performed in the supine position. They are reported above in the order they were performed. 5 min of rest separated each maneuver from the next.

^aValues reflect the average of three readings at each point of measurement.

^bMental stress: serial 7s counted down from 300.

different maneuvers are described in Table 1. As he no longer exhibited the previously observed BP fall with pressor stimulation, we did not feel compelled to draw arterial blood gas samples. Of note, his respiratory rate was unchanged, though we did not measure his tidal volume.

1. Raj SR, Luther JM, Sato K *et al.* Response to labile hypertension can be due to autonomic nervous system failure. *Kidney Int* 2009; **75**: 860.
2. Zar T, Peixoto AJ. Paroxysmal hypertension due to baroreflex failure. *Kidney Int* 2008; **74**: 126–131.
3. Imai Y, Abe K, Munakata M *et al.* Does ambulatory blood pressure monitoring improve the diagnosis of secondary hypertension? *J Hypertens* 1990; **8**(suppl. 6): S71–S75.

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Death or hospitalization of patients on chronic hemodialysis is associated with a physician-based diagnosis of depression

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To the Editor: The article by Hedayati *et al.*¹ is relevant in that it addresses the important but underrecognized problem of depression in the dialysis population. The goal of the study was to investigate whether an association exists between physician-diagnosed depression and poor outcomes. The paper underscored the high prevalence of depression in this population and illustrated the significant morbidity and mortality associated with the combined diagnosis of depression and dialysis.

The authors did a good job of addressing most of the clinical characteristics that could affect the outcome of hospitalizations and mortality. However, phosphorus and calcium, two clinical characteristics associated with mortality outcomes in the dialysis population were not addressed.

The inclusion of phosphorus and calcium is highly important in the analysis, as these biochemical markers are associated with the outcome.² Phosphorus in particular should have been evaluated, as it is more difficult for the observer to control relative to parathyroid hormone and calcium and is dependent on the behavior of the subject, in regard to both dietary discretion and adherence to binder therapy. Depression by definition influences behavior; it is essential to know if the difference in mortality between the two patient groups can be attributed to at least in part to a difference in phosphorus and or calcium.

1. Hedayati SS, Bosworth HB, Briley LP. Death or hospitalization of patients on chronic hemodialysis is associated with a physician-based diagnosis of depression. *Kidney Int* 2008; **74**: 930–936.
2. Danese M, Belzeroff V, Smirnakis K *et al.* Consistent control of mineral and bone disorder in incident hemodialysis patients. *Clin J Am Soc Nephrol* 2008; **3**: 1423–1429.

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Response to 'Death or hospitalization of patients on chronic hemodialysis is associated with a physician-based diagnosis of depression'

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The letter by Brown¹ appropriately highlights the significance of calcium and phosphorus as predictors of poor outcomes in end-stage renal disease patients on chronic dialysis, and inquires why these variables were not included in the multivariable model for outcomes in our study. We recognize that previous observational studies have shown a correlation between phosphorus and calcium-phosphorus product and death in this patient population.² Earlier studies have also shown a direct relationship between depressive symptoms and non-adherence to diet and interdialytic weight gain in chronic hemodialysis patients, although to our knowledge, no published data exist to show an association between higher phosphorus, in particular, and presence of depression.^{3,4} It is also known that decreased behavioral adherence is in turn associated with decreased survival.⁴

In our study, mean calcium, phosphorus, and parathyroid hormone levels were not significantly different among depressed vs non-depressed patients. The baseline

characteristics of the cohort based on the presence or absence of depression has been previously published.⁵ Given the lack of correlation between these variables and depression in bivariate models, these variables were not included in the multivariable model. In addition, the number of events (52) limited the inclusion of too many covariates at the risk of over-fitting the model. We agree with Brown that perhaps one mediator between depression and poor outcomes could be that those with depression are more non-adherent to dietary and fluid restrictions, which in turn leads to worse outcomes.⁶ Future larger studies are warranted to address these important questions.

1. Brown CG. Death or hospitalization of patients on chronic hemodialysis is associated with a physician-based diagnosis of depression. *Kidney Int* 2009; **75**: 861.
2. Block GA, Klassen PS, Lazarus JM *et al*. Mineral metabolism, mortality and morbidity in maintenance hemodialysis. *J Am Soc Nephrol* 2004; **15**: 2208–2218.
3. Sensky T, Leger C, Gilmour S. Psychosocial and cognitive factors associated with adherence to dietary and fluid restriction regimens by people on chronic haemodialysis. *Psychother Psychosom* 1996; **65**: 36–42.
4. Kimmel PL, Peterson RA, Weihs KL *et al*. Psychosocial factors, behavioral compliance and survival in urban hemodialysis patients. *Kidney Int* 1998; **54**: 245–254.
5. Hedayati SS, Bosworth HB, Kuchibhatla M *et al*. The predictive value of self-report scales compared with physician diagnosis of depression in hemodialysis patients. *Kidney Int* 2006; **69**: 1662–1668.
6. Cukor D, Peterson RA, Cohen SD *et al*. Depression in end-stage renal disease hemodialysis patients. *Nat Clin Pract Nephrol* 2006; **2**: 678–687.

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⁹Note that this work was completed while L.P. Briley was a nephrology fellow at Duke University Medical Center and before she joined Quintiles.
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Bilirubin as a predictor of albuminuria and atherosclerosis in type 2 diabetic patients: misleading data

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To the Editor: We read with great interest the article by Fukui M and colleagues¹ evaluating the relationship between serum bilirubin and albuminuria in patients with type II

diabetes. In this paper, the authors performed a number of correlations and a multiple regression analysis and concluded that the serum bilirubin level is associated with microalbuminuria and subclinical atherosclerosis in type II diabetic patients.

However, these results should be interpreted with caution, as in most of the correlations, the Pearson's *r* value was below 0.2, implying a very poor correlation.² For example, the coefficient of determination (r^2) for bilirubin pulse wave velocity and bilirubin ankle brachial index, which are early preclinical markers of atherosclerosis, are $0.114^2 = 0.013$ and $0.118^2 = 0.0139$, respectively. That is, the proportion of variance that the variables have in common is 1.3 and 1.39%, respectively; the remaining 98.7 and 98.61% would probably be explained by other factors, perhaps by HbA1c levels or other parameters common and sufficiently proven to be atherogenic in diabetic patients. The fact that these weak correlations were statistically significant can be explained by the large sample size of the study but does not mean that these values are fair enough to imply any important correlation between the examined variables. Similarly, the adjusted R^2 as well as the tolerance values in the multiple regression model should be presented, as there seems to be a degree of co-linearity (between age and duration of diabetes, BMI, or systolic blood pressure) that might destabilize the model and lead to indefinite results (for example, triglycerides but not cholesterol were independent determinants of log (urinary albumin excretion)).

In our opinion, it is quite venturesome and unwarranted to discuss the potential preventive and therapeutic applications of bilirubin or its diagnostic utility as a new risk factor for diabetic nephropathy and atherosclerosis based on the current data.

1. Fukui M, Tanaka M, Shiraishi E *et al*. Relationship between serum bilirubin and albuminuria in patients with type 2 diabetes. *Kidney Int* 2008; **74**: 1197–1201.
2. Wayne DW. *Biostatistics*, 6th edn. John Wiley & Sons: New York, 1995.

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Response to 'Bilirubin as a predictor of albuminuria and atherosclerosis in type 2 diabetic patients: misleading data'

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We would like to thank Drs Kassimatis and Moutzouris¹ for their interest in our article,² and the editor for the opportunity to clarify the several points raised.

Certainly, the Pearson's *r*-value between serum bilirubin concentration and pulse wave velocity and between serum