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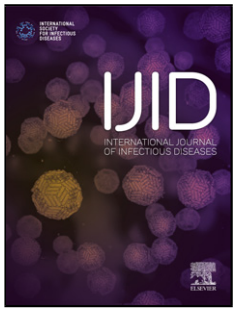

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Derivation and validation of a risk score predicting early-onset risk of peritonitis among patients initialising peritoneal dialysis: a cohort study

Running title: Risk score predicting early-onset peritonitis

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HIGHLIGHTS

- EOP relates to high risk of complications, technique failure and death in PD patients
- Although some risk factors were examined, no risk score was derived to predict EOP
- A well-discriminated and calibrated score for EOP has been derived and validated
- As a tool the score could identify high-risk patients for further intervention

ABSTRACT

Objectives

Early onset peritonitis (EOP) increases risk of clinical complications in patients initialising peritoneal dialysis (PD). This study aimed to develop and validate a risk prediction model for EOP among patients initialising PD.

Methods

3,772 patients registered with the Henan Peritoneal Dialysis Registry (HPDR) between 2007-2015 were included. The main outcome, EOP was defined as the incident peritonitis occurred within 6 months since the initialisation of PD. Multivariable logistic regression modelling was applied to derive the risk score. All accessible clinical measurements were screened as potential predictors. Assessment of the developed model regarding model discrimination and calibration was performed by C statistics and calibration slope, respectively, and validated internally through bootstrapping (1000-fold) method to adjust for over-fitting.

Results

The absolute risk of EOP was 14.5%. Age, cardiac function measurements, serum electrolyte test items, lipid profiles, liver function test items, blood urea nitrogen, and white cell count were significant predictors of EOP in the final risk score. Good model discrimination with C statistics above 0.70 and calibration of agreed observed and predicted risks were identified in the model.

Conclusion

The prediction model that quantify risks of EOP has been developed and validated. It is based on a small number of clinical metabolic measurements that are available for patients initialising PD in many developing countries and could serve as the tools to screen the population at high risk of EOP.

Keywords: Early-onset peritonitis; Peritoneal dialysis; Prognostic model; Cohort

Introduction

Technological advances have allowed peritoneal dialysis (PD) to be increasingly applied to end-stage renal disease (ESRD) patients, especially in developing countries [1]. As a common and serious complication of peritoneal dialysis, peritonitis was estimated to be ranging from 0.06 to 1.66 episodes per patient-year over different countries [2,3]. Severe or

persistent peritonitis can result in peritoneal membrane injury, promoting the progress of encapsulating peritoneal sclerosis [4,5].

Early-onset peritonitis (EOP) is a clinical term that has been recently widely used in emerging studies due to the growing interest as patients with EOP appear to be placed at an increased risk of clinical complications, covering technique failure and all-cause mortality, when compared to those patients who develop to peritonitis later since their initialisation of PD treatment [6,7]. The period to define the EOP ranged from 3 months to 2 years across studies [8,9]. Most commonly, the definition of 'early-onset' has been 6 months [2,3,8].

Although several prognostic factors for EOP have been reported in several studies, including modifiable risk factors and non-modifiable risk factors [10-12], few risk prediction algorithm to predict the individual-level risk of EOP have been derived among patients initialising PD. Risk algorithms based on clinical measurements collected by the initialisation of PD care could help the identification of patients initialising PD with high probability of EOP and provide tailored education program and anti-infection therapies. Furthermore, different from patients registered in PD care settings in developed countries, among many developing countries like China, validated health records are very difficult to be accessible due to restricted primary or secondary care systems which are unable to accurately record pre-existing comorbidities and treatments [13,14]. Relying on patients' self-reported medical history could be misleading in PD care settings, this current study therefore aimed to develop and validate a risk prediction model that can be used to predict individual-level risk of 6-month EOP among patients initialising PD mainly

utilising objective routinely recorded clinical measurements potentially to be accessible in most developing countries.

Methods

Data setting

Registry data the Henan Peritoneal Dialysis Registry (HPDR) were used derive and validate the risk prediction model [1]. HPDR is administrated under the auspices of the Department of Nephrology, the First Affiliated Hospital of Zhengzhou University which is in charge of an independent audit and analysis of medical care for renal disease in the province [1,15].

Over the study period, patients' information was prospectively collected electronically from all renal departments across the province [1]. All data at the HPDR are subjected to an extreme-value detection process which identifies suspicious measurements, which are then further examined and corrected where necessary by contacting the nephrological department [1]. This study was designed as a cohort study, which included all patients aged ≥ 18 years (n=3,772) who commenced PD between 2007-2015 and who had at least 6-month follow-up after baseline measurement [13].

Ethics approval was granted by the Clinical Research Ethics Committee of the First Affiliated Hospital of Zhengzhou University (REF No.: KY-2017-22). Written informed consent was obtained from all participants before inclusion.

Defining outcome, predictors, missing data and power calculation

The outcome was defined as recorded EOP, peritonitis within 6-months since the start of PD care. Potential prognostic factors (predictors) including demographic characteristics,

self-reported comorbidities, and clinical measurements collected by the initialisation of PD care were reviewed and screened by 3 clinicians. Prognostic factors consented to be clinically relevant by ≥2 clinicians were chosen in the analysis for further evaluation as candidate predictors. Logistic regression model with backward elimination, with all candidate predictors, was applied to decide the parameters for the final prediction model. For prognostic factors included in the final model, our cohort had missing information on body mass index (12.36%), phosphate (16.76%), albumin (15.28%), total protein (12.36%), total cholesterol (20.06%), low density lipoprotein (20.17%), fasting glucose (12.37%), sodium (3.26%), systolic blood pressure (3.16%), and diastolic blood pressure (3.36%). We applied multiple imputation to replace missing values by using a chained equation method based on all prognostic factors and outcome to improve the model accuracy [16]. We generated twenty imputed datasets for missing prognostic factors that were then combined across twenty datasets by using Rubin's rule to derive final model estimates [16]. With 546 EOP during the first 6 months since the start of PD and 23 parameters in the final model, a sample size was estimated with 24 final events per predictor, higher than the minimum requirement suggested by Peduzzi et al. [17].

Model development and validation

In our study, having an incident episode of peritonitis within the first 6 months of initialising PD was treated as a binary outcome measure. Candidate prognostic factors that were not statistically significant were excluded from the backward elimination Logistic regression model (P> 0.1 based on change in log likelihood)[13]. Two-degree fractional polynomial terms were used to model non-linear associations between outcomes and continuous predictors [18]. Fractional polynomial parameters were also re-checked at this stage and re-estimated when necessary [18]. The term of continuous predictors (cut-off or

polynomial term) was decided by the model fitness and performance based on joint by parameters[19]. The risk algorithm is estimated as the log odds from the final model with the selected prognostic factors (and polynomials), and the estimated risk (probability) is derived from the log odds [20].

We assessed model calibration by plotting the mean predicted risk (probability) against the mean observed proportion of EOP by tenth of predicted risk [21]. We used the concordance statistic (C-statistic) to evaluate model discrimination [20]. Model discrimination was internally validated by calculating the bootstrap optimism-corrected c-statistic with 1000 bootstrap replications [13].

To facilitate model utilisation in clinical practice, the logistic regression equations were transformed into prognostic score charts [13]. The coefficients in the logistic regression equation were multiplied by 50 and rounded to the nearest integer to obtain the prognostic score per predictor [21]. Multiplication by 50 was chosen to ensure that a majority of the coefficients were close to be an integer, thereby minimizing the effects of rounding. The sum of all prognostic scores reflects patients' probability of EOP [21].

Stata MP V15.1 (StataCorp, College Station, TX, USA) were used for all statistical analyses. Our study was conducted and reported in line with the Transparent Reporting of a multivariate prediction model for Individual Prediction Diagnosis (TRIPOD) guidelines [22].

Results

Study participants

546 newly diagnosed EOP episodes since the start of PD were identified from this current cohort that incorporates 3,772 patients initialising PD. The characteristics and clinical measurements recorded at baseline among patients initialising PD were presented in **Table-1**. 57.8% of patients were male gender.14.8% and 39.9 of patients had existing type 2 diabetes and cardiovascular diseases, respectively. The median (interquartile range) for age, body mass index, estimated glomerular filtration rate, systolic and diastolic blood pressure was 48.0 (37.8 to 59.0) years, 22.6 (20.7 to 24.8) kg/m^2, 4.9 (3.4 to 7.9) $mL/min/1.73m^2$, 145 (136 to 159)mmHg, and 87 (78 to 86)mmHg, respectively.

Model derivation and performance

The association between each predictor and EOP was estimated by univariable model analysis and presented in **Supplemental Table-1**. 20 predictors (23 parameters) were selected from the 38 candidate predictors by backward elimination and kept in the final risk prediction model (**Table-2**). Age, cardiac function measurements (blood pressure, heart rate, ejection fraction), serum electrolyte test items (sodium, potassium, carbon dioxide combining power), lipid profiles (total cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein), liver function test items (total protein, alanine aminotransferase, aspartate transaminase), blood urea nitrogen, and white cell count were predictors remained in the final prediction model.

Our final risk prediction model can discriminate patients initialising PD with and without EOP as the optimism-adjusted C statistics was 0.759 (95% confidence interval 0.756 to 0.762) (Table-3). After the optimism adjustment, the calibration slope was calibration

slope was 0.991 (0.973 to 1.009) (Table-3). The agreement between the predicted and observed proportion of EOP indicated the good calibration (Figure-1). A real clinical example was given in the Table-4 and Supplemental Figure-1 gives interpretation of the application of prognostic score charts with graphical illustrations for the developed prediction model to predict the EOP.

Discussion

The risk algorithm to predict the individual-level risk of future EOP among patients initialising PD has been developed and validated in this present cohort study. Good model calibration and good discrimination with C-statistics of greater than 0.70 for the model was presented in this study. To our knowledge, this is the first prediction tool for predicting EOP among patients initialising PD in prospective cohort data.

The majority of previous studies focused on one or more potential risk (potential causal) factors for peritonitis. Few studies have previously derived and reported a multivariable prediction model for incident risk of EOP based on clinical measurements routinely collected and recorded by the start of PD care. Although the overall performance of the prediction model is of the most importance, the direction and magnitude of associations between some predictors and outcome always deserve some comments. It should be recognised though that those associations are not aimed to be, and cannot be interpreted as, any type of causal effect estimations on EOP: they were selected for their informativeness in predicting EOP [23]. They might or might not be causal or reversible; all

such associations were conditioned on the start of PD care; each model coefficient was adjusted for all other parameters in the prediction model, but the minimally sufficient set of covariables should be adjusted for confounding would likely differ for each [24]. Bearing those concerns in mind, we noted that decreased risk of EOP was found among those with higher level metabolic measurements, like triglyceride, total cholesterol and glucose, which might include a very small direct causal effect but which otherwise we would interpret as reflecting a mixture of a proxy of health status [25], risk of future progression of EOP, as patients at low health status (having high measurement of metabolic measurements) would more like adhere to standard PD techniques comparing those at relatively high health status (having low measurement of metabolic measurements) [26,27].

Instead of investigating the causal association between cut-offs of prognostic factor (predictor) and the outcome in terms of clinical interpretation and application, the aim of this study was to make the accurate individual-level risk prediction based on joint-by cut-offs of predictors in terms of model fitness and performance[19]. The investigation of causal association and further clinical interpretation and utilisation for cut-offs of predictors will be made in further studies.

This newly developed risk algorithm could have potentially important application in clinical practice by helping direct monitoring, intensive care and timely assessment. This algorithm can specifically identify the individual patients who, in terms of current health-insurance policies and resource, are at higher risk of future EOP and therefore can be targeted for tailored care ranging from HR refer to hygiene education program that might alter the potential risky trajectory or postpone the progression to EOP [28].

The hypothetical higher risk individual might, for instance, be targeted for a programme of more intensive monitoring and interventions that might prevent such future progression of EOP, for example, re-training (covering hand-washing, technique recall, protocol adherence, and exit-care) that has been found to significantly delay the onset of EOP as studies have demonstrated that PD techniques progressively deteriorate [26].

In the routine PD care, a precise strategy based on individual-level risk of EOP would be helpful for clinical decision. Surveillance of patient who initialising of PD care for development of EOP is considered as a vital aspect of PD clinical practice quality, however, the current guidance of International Society for Peritoneal Dialysis would result in intensive intervention being provided to the majority of patients initialising PD [29]. Although emerging evidence advocates the clinical effectiveness for intensive therapy among patients initialising PD, the health burden or over-treatment for all patients initialising PD could be another issue that would need aids from individual-level precise prediction tool to recognise the high-risk patients.

Among most patients initialising PD, an earlier identification of individual-level patients' risk of upcoming EOP might be helpful to more timely evaluation and discussion of proper intensive preventive therapy [28,30]. However, it should be cautious against over-dependence on the current risk prediction model, especially for patients initialising PD whose baseline measurements or characteristics indicate they would not be defined as potential high-risk patients to accept further intensive therapy although they were experiencing some progressive peritonitis. Moreover, although the model developed in this study could identify patients at high-risk of incident EOP within 6 months, there

would be a subgroup of these high-risk individuals with potential risk of recurrent EOP even within the 6 months, which suggest further study to develop another new model for prediction of recurrent EOP.

There are some advantages in our newly developed risk prediction algorithm in terms of its utilisation in most developing countries. The risk algorithm is based in individual-level risk developed and validated in a prospective cohort. It is derived from objective validated clinical measurements that are routinely tested and recorded for patients initialising PD, suggesting that this algorithm can be readily utilised in routine clinical practice and is potentially amendable to further validation in many regions and countries that practice routine PD. The derivation and validation methods used in this prediction model are very close to other that wide-applied prediction models, like QRISK models and prediction models developed from CPRD [18,31]. The current registration dataset used in this study was one of the largest data used to predict EOP among patients initialising PD. As the only PD registration dataset in the province, the HPDR incorporated all ESRD patients treated by PD in the province, which suggesting a good representativeness. The lifetime follow-up since the initialisation of PD was processed for each registered PD patient, which suggesting potential low information bias.

This study had several limitations. First, ESRD patients incorporated in this study were different from ESRD patients in European studies in terms of age, BMI, comorbidities (as Chinese ESRD patients having lower onset-age, lower level of BMI, fewer comorbidities and poorer clinical management or treatment). Therefore potential amendments in the algorithm might be needed when applying this model in European ESRD patients who

initialising PD. Second, some traditional risk factors, like smoking and prior health information were not accessible in our study. Third, the volume of missing values in some predictors (for example, phosphorus and albumin) are relatively high in current model. Although the multiple imputation was applied in the model derivation, there still might be some information bias impacting the model external application. Fourth, no individual-level risk threshold to identify 'high-risk' EOP patients was provided in our model, as risks of EOP and patients' benefit would have to be balanced in defining the risk threshold, which was not in the scope of this study. Finally, there might be uncertain in the application in the external population due to the lack of external validation, the need of external validation of our prediction model was highlighted.

Conclusions

This study has developed and validated a new risk prediction equation to quantify the individual-level risk of EOP among patients initialising PD. This risk prediction model has the advantage of being based on health records routinely collected in PD care setting, making this potentially applicable for automatic risk assessment in electronic medical record software. This model can also be used to identify patients at high individual-level risk of EOP for further assessments, monitoring and intensive therapy. This prediction model is also readily modifiable to further external validation in many developing countries that have routinely collected records available for research. Further researches are warranted to external validate the model and assess its cost-effectiveness of using this risk equation in PD care.

Authors' contribution

Conception and design of the study: SM, JX, ZZ, YC and DY. Acquisition of data: SM and ZW. Analysis of data: SM and YC. Interpretation of data: SM, YC, ZW, JX, ZZ and DY. Drafting the article: SM, YC and DY. Revising the article critically for important intellectual content: SM, YC, ZW, JX, ZZ and DY. Final approval of the article: all author

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethics Approval

Ethics approval was granted by the Clinical Research Ethics Committee of the First Affiliated Hospital of Zhengzhou University (REF No.: KY-2017-22).

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References

1. X Zhang, Y Chen, Y Cai, X Tian, J Xiao, Z Zhao, et al. Characteristics of Patients Initializing Peritoneal Dialysis Treatment From 2007 to 2014: Analysis From Henan Peritoneal Dialysis Registry data. Iran J Kidney Dis 2018;12:178-84.

2. HC Gan, EJ Lee, MM Tay, N Yusuf. A study on early onset peritonitis in CAPD patients. Singapore Med J 2003;44:138-40.

3. H Wu, R Huang, C Yi, J Wu, Q Guo, Q Zhou, et al. Risk Factors for Early-Onset Peritonitis in Southern Chinese Peritoneal Dialysis Patients. Perit Dial Int 2016;36:640-6.

4. MC Brown, K Simpson, JJ Kerssens, RA Mactier, Scottish Renal Registry. Encapsulating peritoneal sclerosis in the new millennium: a national cohort study. Clin J Am Soc Nephrol 2009;4:1222-9.

5. Y Cho, DW Johnson. Peritoneal dialysis-related peritonitis: towards improving evidence, practices, and outcomes. Am J Kidney Dis 2014;64:278-89.

6. S Feng, Y Wang, B Qiu, Z Wang, L Jiang, Z Zhan, et al. Impact of early-onset peritonitis on mortality and technique survival in peritoneal dialysis patients. Springerplus 2016;5:1676,016-3369-9. eCollection 2016.

7. E Vargas, PG Blake, M Sanabria, A Bunch, P Lopez, J Vesga, et al. Early Peritonitis in a Large Peritoneal Dialysis Provider System in Colombia. Perit Dial Int 2017;37:30-4.

8. Z Wang, L Jiang, S Feng, L Yang, S Jiang, Z Zhan, et al. Early peritonitis is an independent risk factor for mortality in elderly peritoneal dialysis patients. Kidney Blood Press Res 2015;40:298-305.

9. Z Harel, R Wald, C Bell, JM Bargman. Outcome of patients who develop early-onset peritonitis. Adv Perit Dial 2006;22:46-9.

10. WH Lim, DW Johnson, SP McDonald. Higher rate and earlier peritonitis in Aboriginal patients compared to non-Aboriginal patients with end-stage renal failure maintained on peritoneal dialysis in Australia: analysis of ANZDATA. Nephrology (Carlton) 2005;10:192-7.

11. SP McDonald, JF Collins, M Rumpsfeld, DW Johnson. Obesity is a risk factor for peritonitis in the Australian and New Zealand peritoneal dialysis patient populations. Perit Dial Int 2004;24:340-6.

12. JR Ghali, KM Bannister, FG Brown, JB Rosman, KJ Wiggins, DW Johnson, et al. Microbiology and outcomes of peritonitis in Australian peritoneal dialysis patients. Perit Dial Int 2011;31:651-62.

13. X Zhang, D Yu, Y Cai, J Shang, R Qin, X Tian, et al. Derivation and Validation of Risk Scores to Predict Cerebrovascular Mortality Among Incident Peritoneal Dialysis Patients. Kidney Blood Press Res 2018;43:1141-8.

14. X Zhang, D Yu, Y Cai, J Shang, R Qin, J Xiao, et al. Dose-Response Between Cardiovascular Risk Factors and Cardiovascular Mortality Among Incident Peritoneal Dialysis Patients. Kidney Blood Press Res 2018;43:628-38.

15. D Yu, Y Cai, R Qin, X Tian, J Xiao, Z Zhao. Dialysate Creatinine Response Patterns During Peritoneal Equilibration Test and the Association Between Cardiovascular Mortality: Findings from a Prospective Cohort Study. Kidney Blood Press Res 2018;43:162-9.

16. IR White, P Royston, AM Wood. Multiple imputation using chained equations: Issues and guidance for practice. Stat Med 2011;30:377-99.

17. P Peduzzi, J Concato, E Kemper, TR Holford, AR Feinstein. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol 1996;49:1373-9.

18. D Yu, KP Jordan, KIE Snell, RD Riley, J Bedson, JJ Edwards, et al. Development and validation of prediction models to estimate risk of primary total hip and knee replacements using data from the UK: two prospective open cohorts using the UK Clinical Practice Research Datalink. Ann Rheum Dis 2019;78:91-9.

19. EW Steyerberg, KG Moons, DA van der Windt, JA Hayden, P Perel, S Schroter, et al. Prognosis Research Strategy (PROGRESS) 3: prognostic model research. PLoS Med 2013;10:e1001381.

20. AA Sultan, J West, MJ Grainge, RD Riley, LJ Tata, O Stephansson, et al. Development and validation of risk prediction model for venous thromboembolism in postpartum women: multinational cohort study. BMJ 2016;355:i6253.

21. D Yu, Y Cai, J Graffy, D Holman, Z Zhao, D Simmons. Development and External Validation of Risk Scores for Cardiovascular Hospitalization and Rehospitalization in Patients With Diabetes. J Clin Endocrinol Metab 2018;103:1122-9.

22. KG Moons, DG Altman, JB Reitsma, JP Ioannidis, P Macaskill, EW Steyerberg, et al. Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD): explanation and elaboration. Ann Intern Med 2015;162:W1-73.

23. LC Martin, JC Caramori, N Fernandes, JC Divino-Filho, R Pecoits-Filho, P Barretti, et al. Geographic and educational factors and risk of the first peritonitis episode in Brazilian Peritoneal Dialysis study (BRAZPD) patients. Clin J Am Soc Nephrol 2011;6:1944-51.

24. W Tang, B Grace, SP McDonald, CM Hawley, SV Badve, NC Boudville, et al. Socio-Economic Status and Peritonitis in Australian Non-Indigenous Peritoneal Dialysis Patients. Perit Dial Int 2015;35:450-9.

25. K Hanazaki, H Maeda, T Okabayashi. Relationship between perioperative glycemic control and postoperative infections. World J Gastroenterol 2009;15:4122-5.

26. R Russo, L Manili, G Tiraboschi, K Amar, M De Luca, E Alberghini, et al. Patient re-training in peritoneal dialysis: why and when it is needed. Kidney Int Suppl 2006;(103):S127-32. doi:S127-32.

27. MF Gadallah, G Ramdeen, J Mignone, D Patel, L Mitchell, S Tatro. Role of preoperative antibiotic prophylaxis in preventing postoperative peritonitis in newly placed peritoneal dialysis catheters. Am J Kidney Dis 2000;36:1014-9.

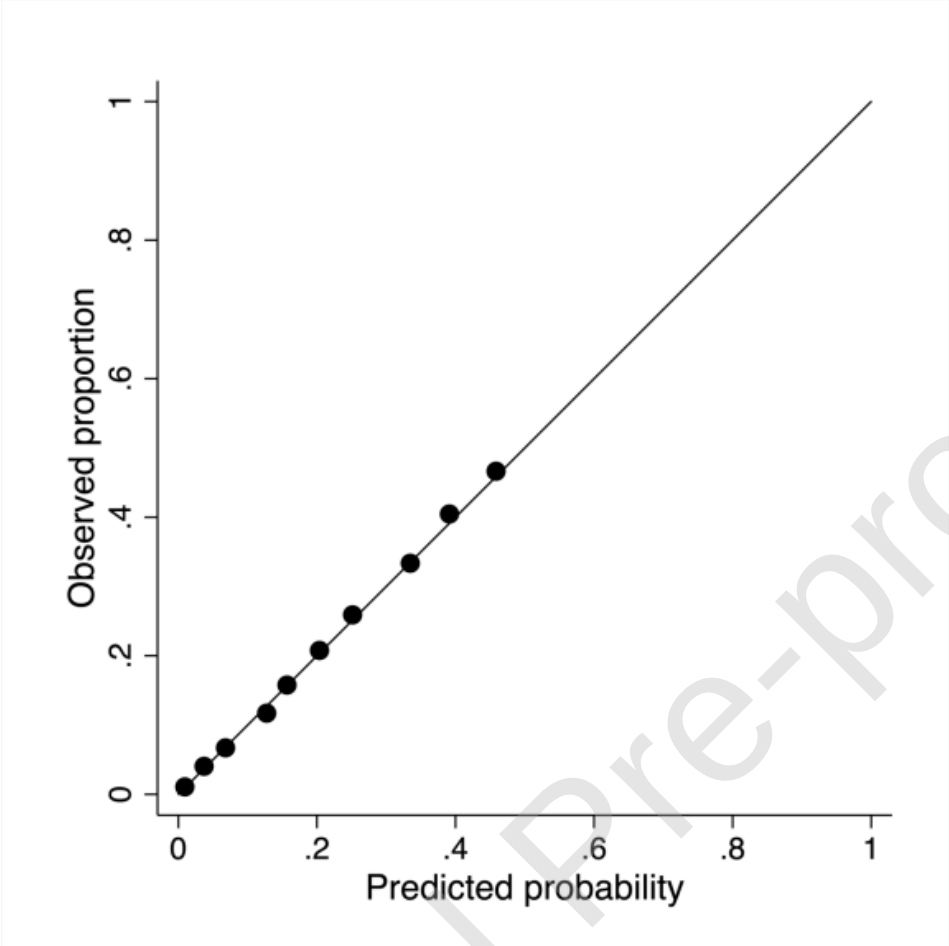
28. JH Crabtree. Selected best demonstrated practices in peritoneal dialysis access. Kidney Int Suppl 2006;(103):S27-37. doi:S27-37.

29. B Piraino, J Bernardini, E Brown, A Figueiredo, DW Johnson, WC Lye, et al. ISPD position statement on reducing the risks of peritoneal dialysis-related infections. Perit Dial Int 2011;31:614-30.

30. A Benabed, C Bechade, M Ficheux, C Verger, T Lobbedez. Effect of assistance on peritonitis risk in diabetic patients treated by peritoneal dialysis: report from the French Language Peritoneal Dialysis Registry. Nephrol Dial Transplant 2016;31:656-62.

31. J Hippisley-Cox, C Coupland, P Brindle. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study. BMJ 2017;357:j2099.

Figure-1. Calibration of the prediction model—the observed 6-month probability of peritonitis by tenths of model-predicted probability



The distributions of actual 0 and 1 values are shown at the bottom and at the top of the graph. The ideal 45° line indicates the observed risk equals the predicted risk. The actual outcomes by deciles of risk are shown by dots.

Table-1. Baseline Characteristics of study cohort.

Candidate Predictors	Derivation Cohort
N	3,772
Early-onset peritonitis, n (%)	546 (14.5)
Male Gender, n (%)	2,180 (57.8)
Primary Glomerular Disease, n (%)	1,833 (48.6)
Age, years	48.0 (37.8 to 59.0)
Haemoglobin, g/L	89.0 (75.0 to 103.0)
Packed cell volume	20.0 (2.8 to 28.0)
Reticulocyte, %	36.0 (13.1 to 62.8)
Phosphate, mg/dl	1.8 (1.4 to 2.1)
Albumin, g/L	33.8 (30.1 to 37.6)
Total iron binding capacity, µmol/L	44.3 (34.4 to 52.0)
FeTIBC, mmol/L	26.0 (21.2 to 41.6)
Creatinine, µmol/L	868.0 (664.0 to 1079.0)
estimated Glomerular Filtration rate, mL/min/1.73 m^2	4.9 (3.4 to 7.9)
Transferrin, mg/dl	188.0 (104.4 to 388.4)
Total protein, g/L	57.6 (52.3 to 62.6)
Prealbumin, mg/L	293.0 (200.0 to 360.0)
Total Cholesterol, mmol/L	4.4 (3.6 to 5.2)
Low density lipoprotein, mmol/L	2.5 (2.0 to 3.2)
High density lipoprotein, mmol/L	1.1 (0.9 to 1.4)
Alanine aminotransferase, U/L	15.0 (10.0 to 22.0)
Aspartate transaminase, U/L	17.0 (12.0 to 23.0)
Fasting glucose, mmol/L	4.8 (4.2 to 5.6)
carbon dioxide combing power, mmol/L	22.2 (19.1 to 25.7)
Sodium, mmol/L	140.0 (137.0 to 142.3)
Potassium, mmol/L	4.3 (3.8 to 4.9)
C-reaction protein, mg/dl	2.4 (1.0 to 5.3)
Body mass index, kg/m2	22.6 (20.7 to 24.8)
Systolic blood pressure, mmHg	145.3 (135.5 to 159.0)
Diastolic blood pressure, mmHg	87.0 (80.0 to 95.0)
Erythrocyte sedimentation rate, mm/hr	22 (12 to 41)
Hear rate, /min	80 (78 to 86)
Ejection Fraction, %	60 (56 to 66)
Blood urea nitrogen ≥ 24mg/dl	23.6 (18.1 to 31.1)
White cell count, 10^9/L	6.0 (4.9 to 7.5)
Triglyceride, mmol/L	1.2 (0.9 to 1.8)
Magnesium, mmol/L	1.0 (0.9 to 1.1)
Cardiovascular diseases, n (%)	1,503 (39.9)
Type 2 Diabetes, n (%)	558 (14.8)
Taking antihypertensive treatment, n (%)	1,595 (42.3)

Table-2. Final multivariate analysis for risk of peritonitis within 6-month of initialisation of peritoneal dialysis

Predictor	Coefficients	95% Confidence interval
(age/10)^2	0.2117308	(0.194291 to 0.229171)
(age/10)^2*ln(age/10)	-0.1141053	(-0.122562 to -0.105649)
(diastolic blood pressure/100)^3	0.3894896	(0.227608 to 0.551372)
(diastolic blood pressure/100)^3*ln(diastolic blood pressure/100)	-1.205053	(-1.673582 to -0.736524)
(Sodium/100)^-2	-1.118932	(-1.645308 to -0.592555)
(Sodium/100)^-2*ln(Sodium/100)	-0.4350019	(-0.637212 to -0.232792)
Alanine aminotransferase ≥ 15 U/L	-0.4272603	(-0.463637 to -0.390883)
Aspartate transaminase ≥ 17 U/L	-0.3352946	(-0.371045 to -0.299544)
Total protein ≥ 58g/L	0.3829204	(0.349473 to 0.416368)
Erythrocyte sedimentation rate ≥ 28mm/hr	0.3119003	(0.279601 to 0.344200)
White cell count ≥ 6×10^9/L	-0.1684228	(-0.201098 to -0.135748)
Triglyceride ≥ 1.26mmol/L	-0.3836425	(-0.418634 to -0.348651)
Magnesium ≥ 0.98mmol/L	0.4827478	(0.449384 to 0.516111)
Total cholesterol ≥ 4.43mmol/L	-0.0654031	(-0.105478 to -0.025328)
Fasting glucose ≥ 5.0mmol/L	-0.9677222	(-1.004691 to -0.930753)
Hear rate ≥ 80/min	-0.3486695	(-0.384037 to -0.313302)
Ejection Fraction ≤ 60%	-0.3853148	(-0.417759 to -0.352871)
Blood urea nitrogen ≥ 24mg/dl	0.6670026	(0.633130 to 0.700875)
Potassium ≥ 4.3mmol/L	0.0730316	(0.039482 to 0.106581)
Low density lipoprotein ≥ 2.6mmol/L	0.1397471	(0.101377 to 0.178117)
Systolic blood pressure ≥ 145mmHg	0.0053947	(-0.031752 to 0.042542)
High density lipoprotein ≤ 1.1mmol/L	0.0336835	(0.000669 to 0.066698)
carbon dioxide combing power ≥ 22.3mmol/L	0.430856	(0.396910 to 0.464802)
Constant	-1.578509	(-1.931018 to -1.226001)

Table-3. Final multivariate analysis for risk of peritonitis within 6-month of initialisation of peritoneal dialysis

Measure	Apparent performance	Optimism corrected performance
C-statistics	0.761 (0.757 to 0.764)	0.759 (0.756 to 0.762)
Calibration slope	1.000 (0.982 to 1.018)	0.991 (0.973 to 1.009)

Table-4. Prognostic score chart for predicting early onset peritonitis among patients initialising peritoneal dialysis. Clinical example: 76 years old, 60mmHg of diastolic blood pressure, 140.34mmol/L of sodium, 8.42 U/L of Alanine aminotransferase, 14.50 U/L of Aspartate transaminase, 51.16g/L of total protein, 8.4*109/L of white cell count, 0.95mmol/L of magnesium, 4.23 mmol/L of total cholesterol, 4.89mmol/L of fasting glucose, 70/minute of heart rate, 71.58% of ejection fraction, 20.60mg/dl of blood urea nitrogen, 5.01 mmol/L of potassium, 1.54 mmol/L of low density lipoprotein, 130 mmHg of systolic blood pressure, 3.24 mmol/L of high density lipoprotein, and 17.28 mmol/L of carbon dioxide combing power.

Predictor	**Value**	**Score**
(age/10)^2	12.229571	611
(age/10)^2*ln(age/10)	-13.366961	-668
(diastolic blood pressure/100)^3	0.08412975	4
(diastolic blood pressure/100)^3*ln(diastolic blood pressure/100)	0.13296354	7
(Sodium/100)^-2	-0.5681263	-28
(Sodium/100)^-2*ln(Sodium/100)	-0.0748506	-4
Alanine aminotransferase ≥ 15 U/L	0	0
Aspartate transaminase ≥ 17 U/L	0	0
Total protein ≥ 58g/L	0.3829204	19
Erythrocyte sedimentation rate ≥ 28mm/hr	0.3119003	16
White cell count ≥ $6*10^9$/L	-0.1684228	-8
Triglyceride ≥ 1.26mmol/L	0	0
Magnesium ≥ 0.98mmol/L	0	0
Total cholesterol ≥ 4.43mmol/L	0	0
Fasting glucose ≥ 5.0mmol/L	0	0
Hear rate ≥ 80/min	0	0
Ejection Fraction ≤ 60%	0	0
Blood urea nitrogen ≥ 24mg/dl	0	0
Potassium ≥ 4.3mmol/L	0.0730316	4
Low density lipoprotein ≥ 2.6mmol/L	0	0
Systolic blood pressure ≥ 145mmHg	0	0
High density lipoprotein ≤ 1.1mmol/L	0	0
carbon dioxide combing power ≥ 22.3mmol/L	0	0
Constant	-1.578509	-79
Sum Score		-127
Predicted probability for peritonitis		7.29