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Do differences in clinical conditions affect the nursing care time of dialysis patients?

■ dialysis ■ nursing care time ■ chronic kidney disease

The number of patients in western societies with chronic kidney disease has slowly increased in recent years (Divo et al, 2014). However, the number of in-centre haemodialysis patients in the Netherlands has stabilised (Hoekstra et al, 2017; 2020), partly due to a higher number of renal transplants in the Netherlands. As a result of increased renal transplants, the dialysis population has changed in recent years to an older population with multimorbidity, which means that nurses who work in dialysis centres are working with older patients who need more nursing care time (Kleijn et al, 2020). Furthermore, older patients (over 75 years) with end-stage renal disease are at increased risk for cognitive decline (Berkhout-Byrne et al, 2017) and, additionally, there is an increasing shortage of (renal) nurses.

These challenges mean that generally applicable planning tools for nursing resources are needed.

Several studies have shown that there is a link between staffing, workload and the occurrence of medical errors (Kane et al, 2007; Thomas-Hawkins et al, 2008). Appropriate staffing of nurses is important to improve the quality and safety of care (Cho et al, 2018).

In the Netherlands, there are eight university medical centres that combine a medical faculty with tertiary hospital care and dialysis for patients. Furthermore, general hospitals and independent specialty clinics also offer dialysis for patients. Post-transplant patients, acutely ill patients, complex patients and patients who have many comorbidities, that make them less suitable for treatment in the other hospitals or independent clinics, are treated in the dialysis units of the university medical centres. A classification model has been developed (Kleijn et al, 2015) that focuses on the dialysis routine: vascular access, connecting and closing the fistula and/or the catheter, the independence of the patient, the complexity of the dialysis and whether patients need extra psychological attention. Additionally, the time needed for weekly/monthly activities, such as doctor visits, blood sampling and fistula flow management that nurses work on during a dialysis session, is included. The model has adequately predicted the required care time of a patient for three categories of dialysis centres: general hospitals, satellites of the general hospitals and independent specialty clinics. The classification model is already being used in a number of dialysis centres. Other dialysis centres have indicated that they will start using this model in 2021.

However, nurses in dialysis centres of university hospitals need not only more care time compared to other dialysis centres (Kleijn et al, 2017), but also more time than predicted by the model. A possible explanation for this is that university hospitals treat highly complex dialysis patients and/or more patients who are starting dialysis treatment for the first time. The turnover of

Ria de Kleijn

Postgraduate student, Department of Nephrology, Universitair Medisch Centrum Groningen, University of Groningen, the Netherlands

Email: riadekleijn@home.nl

Carin Uyl-de Groot

Professor, Erasmus School of Health Policy & Management, Erasmus University, Rotterdam, the Netherlands

Chris Hagen

Doctor, Dialysecentrum Midden Nederland, Meander Medisch Centrum, Amersfoort, Harderwijk, the Netherlands

Lianne Messchendorp

Doctor, Department of Nephrology, Universitair Medisch Centrum Groningen, University of Groningen, the Netherlands

Pieterneel Pasker-de Jong

Doctor, Meander Academie, Meander Medisch Centrum, Amersfoort, the Netherlands

Piet ter Wee

Professor, Amsterdam UMC, Vrije Universiteit Amsterdam, Medical Affairs and Nephrology, Amsterdam, the Netherlands

Table 1: Indication for hospital admission

Indication, n (%)	Academic (n=44)	Non-university dialysis centres (n=45)	P-value
Renal	8 (17.8)	2 (4.4)	0.04
Cardiovascular	8 (17.8)	7 (15.6)	0.78
Respiratory	4 (8.9)	6 (13.3)	0.50
Oncological	4 (8.9)	1 (2.2)	0.17
Surgical/vascular access	10 (22.2)	13 (28.9)	0.47
Infectious diseases	8 (17.8)	4 (8.9)	0.22
Other	11 (24.4)	15 (33.3)	0.35

Variables are presented as number (%). P-values were calculated with Chi-square test.
Abbreviations: number (n)

patients in university hospitals was also higher than in other centres. Another observation for this assumption was the fact that 10% of patients admitted to a university hospital died within 3 weeks of the study (Kleijn et al, 2017), while none of the patients admitted to other centres died during the same period (Kleijn et al, 2017).

Malnutrition and inflammation are frequently present in haemodialysis patients worldwide (Rezeq et al, 2018; Zaki et al, 2019). Zaki et al (2019) investigated the nutritional status of haemodialysis patients using Subjective Global Assessment (SGA)—a tool to measure malnutrition. It was found that a decrease in SGA, increase in age, the number of years of dialysis, C-reactive protein (CRP) and a lower level of albumin were associated with a higher prevalence of malnutrition (Gamma-Alexon et al, 2012). Rezeq et al (2018) suggested that dietitians should assess the nutritional status of haemodialysis patients through SGA to monitor the quality of life for these patients. It was also concluded that having diabetes and cardiovascular disorders, as well as the level of education and the profession of the patient, have a significant effect on the nutritional status of the patient undergoing dialysis. Grip strength also appears to be a useful nutritional parameter for evaluating the nutritional status of these patients (Ferreira Garcia et al, 2013). Stenvinkel et al (2007) researched nutritional factors other than albumin, because albumin is also lowered by inflammation. They found that SGA measurement in itself is a good predictor of malnutrition. Grip strength is another useful marker of malnutrition (Normen et al,

2011). The malnutrition inflammation complex syndrome (MICS) (Kalantar-Zadeh et al, 2004) is another predictor of poor outcome and increased number of hospital admissions for a patient. In haemodialysis patients, exposure to dialysis tubing and dialysis membranes, poor water quality, inefficient dialysis and foreign bodies in dialysis access can contribute to inflammatory symptoms. Patients with inflammatory symptoms are more likely to suffer from a loss of appetite, and dietary supplements result in beneficial outcomes of patients undergoing haemodialysis (Kalantar-Zadeh et al, 2011; Ikizler et al, 2013).

The primary aim of this research was to investigate whether the clinical conditions of the dialysis patients affected nursing care time, beyond the dialysis-related activities included in the model. The secondary aim was to confirm the appropriateness of the nursing care time prediction model (Kleijn et al, 2015), given the recent change to the patient population receiving dialysis, and to evaluate whether the discrepancy of measured and predicted time in university dialysis centres versus other dialysis centres can be explained by the difference in clinical characteristics of the patients.

Methods

Classification model development

In 2014, 242 chronic dialysis patients were included in a study in which dialysis characteristics (independence of patients, vascular access, psycho-social aspects, complexity of the dialysis, communication and nursing care) were scored, and time spent on each step of the dialysis procedure was measured with a stopwatch by independent observers, who each followed one nurse during a shift. This resulted in a classification model that adequately predicted the average nursing care time, both in general (Kleijn et al, 2015) and independent dialysis centres (Kleijn et al, 2017).

Study design

For the current study, data were collected in the same way as the previous study (Kleijn et al, 2015) Nurses filled out the classification model. Again, independent observers used a stopwatch and scored in seconds how much time the nurses needed to treat the dialysis patient.

In total, 90 chronic haemodialysis patients were included. A total of 45 patients were included in two university dialysis centres. The other 45 patients were selected from a general hospital (n=15 patients), an independent centre with a nephrologist present (n=15 patients) and an

Table 2: Patient and dialysis characteristics and difference between actual and predicted time

Variable	University dialysis centres (n=242)	Non-university dialysis centres (n=89)	P-value
	Current study	Current study	
Patient characteristics			
Gender (male)	131 (54.1%)	46 (51.7)	0.69
Age (years) (standard deviation)	66 (14.4)	67 (16.4)	0.83
Age ≥75 years	87 (36.0)	31 (35.2)	0.83
Body mass index (kg/m ²)	25.4	25.6	0.67
Number of years on haemodialysis	3.5 (1–24)	3.1 (1–16)	0.27
Previous kidney transplantation	21 (8.7%)	11 (12.6%)	0.29
Previous peritoneal dialysis	31 (12.9%)	6 (7.0%)	0.13
Number of comorbidities	1.8 (1–6)	2.2 (1–6)	0.41
Dialysis characteristics			
Independence			
Mobility—able to walk	166 (68.6%)	45 (50.6%)	0.002
Patient participation	64 (26.4%)	48 (53.9%)	0.000
Vascular access			
Connecting			
Fistula	192 (79.3%)	70 (78.7%)	0.69
Catheter	50 (20.7%)	19 (21.3%)	0.93
Closing by pressure			
Pressure by patient	122 (50.4%)	41 (46.1%)	0.000
Pressure by nurse	70 (28.9%)	29 (32.6%)	0.000
Need for psychosocial attention	193 (79.8%)	39 (43.8%)	0.29
Symptomatic blood pressure drop	101 (41.7%)	43 (48.3%)	0.25
Difference between actual and predicted time			
Actual time mean (sd)	59.06 (23.45)	62.08 (25.26)	0.791
Predicted time mean (sd)	59.92 (9.97)	59.58 (11.92)	0.312
Actual—predicted time mean (sd)	-0.90 (18.77)	2.50 (21.20)	0.159

P-values were calculated with an independent t-test.

independent centre where a nephrologist was only present once a week or on call (n=15 patients).

In the morning or evening dialysis sessions, the observers were matched with a different nurse. Patients were randomly assigned to nurses. This meant that patients had an equal chance of being included. All patients signed a consent form. Not all of the patients and nurses were observed. Patients who underwent dialysis for the first time

and patients in an intensive care setting or in strict isolation were excluded from the research.

Patients were divided into two groups for the analysis: patients from university dialysis centres and patients from other dialysis centres.

Measurements

Observers were instructed to measure the time that the nurses spent on various tasks during dialysis

Table 3: Comparison university dialysis centres versus non-university dialysis centres

	University dialysis centres		non-university dialysis centres		P-value
	First study (n=45)	Current study (n=44)	First study (n=197)	Current study (45)	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Current study
Actual time	75.8 (22.0)	70.3 (28.8)	52.3 (19.9)	54.0 (19.0)	0.003
Predicted time	62.5 (9.31)	63.5 (10.6)	56.6 (9.18)	55.7 (12.0)	0.002
Actual—predicted time	13.3 (18.2)	6.89 (26.6)	-4.3 (16.3)	-1.7 (13.1)	0.06

Variables are presented as mean \pm SD. P-values were calculated with an independent t-test. Abbreviations: Standard deviation (SD)

procedures using a stopwatch. Nurses filled out the form with patient characteristics, such as gender, age, body mass index (BMI), previous transplantation, previous peritoneal dialysis and comorbidities.

A number of other patient characteristics were recorded: laboratory data, SGA measurement, grip strength, current prescriptions and the number of hospital admissions in the past year, including the duration of and reason for admission. The reasons for admission to a hospital were categorised (Table 1).

Finally, the nephrologists were asked to complete the Charlson Comorbidity Index (CCI) for each patient (Charlson et al, 1987). The Charlson Index is used as a measure of comorbidity for a patient population. The index is developed based on the predictive value for mortality after 1 year for various conditions. The Charlson Index is based on ICD-09 codes, and defines 17 comorbidities. Each comorbidity is assigned a weighted score based on the relative risk of mortality after 1 year.

Statistical analyses

Analyses were performed using the statistical package IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, NY US). First, the authors tested whether the current cohort was comparable to the cohort in which the nursing care prediction model was developed. Therefore, differences in patient characteristics, measured care time and predicted care time were tested using an independent t-test in case of normal distribution, a Mann-Whitney U test in case of non-normal distribution and a Chi-square test for categorical variables.

The average difference between measured and predicted time was calculated to evaluate discrepancies between university dialysis centres and other dialysis centres in the current cohort.

Second, the possible differences in characteristics between patients from university dialysis centres versus other dialysis centres were tested. The analyses included age as a continuous variable. Patients over 75 years of age are not a specific item in the analysis (Kleijn et al, 2017; Kleijn et al, 2020).

Subsequently, the authors tested if there were patient characteristics that could possibly explain the differences in measured care time between university dialysis centres and other dialysis centres. Therefore, the authors first tested whether variables were univariably associated with measured care time using linear regression analysis. Thereafter, multivariable linear regression analyses were performed, including variables that had a univariate α of 0.25. Subsequently, a stepwise backward analysis was performed with the variables from the multivariable regression analysis until only variables remained that were statistically significant. A two-sided $p < 0.05$ was considered statistically significant.

Ethical approval

Ethical approval was obtained from the Medical Ethics Committee of University of Groningen (Number METc 2017/234). Patients were informed of the purpose of the study and gave their consent. All data obtained were anonymised.

Results

Of the 45 patients included in the university dialysis centres, one patient was excluded, as this patient had acute kidney injury and had been dialysed only once.

Patient and dialysis characteristics: comparison between the first study and the current study
Table 2 shows characteristics of patients and dialysis procedures, as well as the number of patients for both the former (Kleijn et al, 2017) and the

Table 4: Patient- and dialysis characteristics.

	University dialysis centres (n=44)	Non-university dialysis centres (n=45)	P-value
Variable	Current study	Current study	
Patient characteristics			
Gender (male)	21 (47.7%)	25 (55.6%)	0.46
Age (year) (SD)	65 (16.2)	69 (16.5)	0.24
Age \geq 75 years	10 (22.7%)	21 (46.7%)	0.01
Body mass index (kg/m ²)	24.9 (4.71)	26.4 (5.55)	0.18
Number years haemodialysis	1 (1–4)	3 (1.5–5.0)	0.13
Previous kidney transplantation	6 (13.6%)	5 (11.1%)	0.66
Previous peritoneal dialysis	1 (2.3%)	5 (11.1%)	0.12
Number of comorbidities	2.5 (1–4)	2 (1–3)	0.16
Dialysis characteristics			
Independence			
Mobility—walking	166 (68.6%)	45 (50.6%)	0.002
Patient participation	64 (26.4%)	48 (53.9%)	0.000
Vascular access			
Connecting			
Fistula	31 (70.5%)	39 (86.7%)	0.59
Catheter	13 (29.5%)	6 (13.3%)	0.06
Closing by pressure			
Pressure by patient	10 (22.7%)	31 (68.9%)	0.000
Pressure by nurse	21 (47.7%)	8 (17.8%)	0.000
Need for psychosocial attention	25 (56.8%)	14 (31.1%)	0.02
Symptomatic blood pressure drop	24 (54.5%)	19 (42.20%)	0.25

Categorical variables are presented as number (%). P-values were calculated with an independent t-test in case of normal distribution, Mann-Whitney U test in case of non-normal distribution and Chi-square for categorical variables. Abbreviations: standard deviation (SD).

current study. There were no differences in gender, age, BMI and the average number of years on haemodialysis (HD) treatment between the two study groups. Likewise, the percentage of patients with previous kidney transplantation (NTX) and the percentage of patients with previous peritoneal dialysis (PD) was not significantly different between the two groups.

Compared to the first study (Kleijn et al, 2015; 2017), a significantly higher percentage of patients needed help with their mobility in the current study (31.4% and 49.4%, $p=0.002$). Furthermore, a significantly higher percentage of patients actively participated in their treatment (26.4% and 53.9%,

$p=0.000$). Significantly fewer patients needed psychosocial attention in the present study (79.8% and 43.8%, $p=0.000$). Overall, the predicted care time was similar in both studies, and the actual care time was properly predicted in other dialysis centres, but not in university dialysis centres (Table 3).

Comparison of classification aspects between university dialysis centres and other dialysis centres

In both studies, the average difference between actual and predicted care time was significantly higher in university dialysis centres than in other

dialysis centres (Table 3). The variation in actual time was also larger in university dialysis centres than in other dialysis centres.

The average age of patients was similar, but more patients were older than 75 in the other dialysis group compared to the university dialysis group (Table 4). Analysis of dialysis characteristics showed statistically significant differences for the type of vascular access, closing of vascular access and need for psychosocial attention between university dialysis centres and other dialysis centres. In the other dialysis centres, significantly more patients participated in their treatment (Table 4). All of these differences resulted in a higher predicted care time in the university dialysis centres, but this did not fully explain the longer average actual time needed per patient in the university dialysis centres (Table 3).

Analysis of clinical conditions and their effect on nursing care time

The laboratory results show a lower mean albumin level for patients in university dialysis centres compared to other dialysis centres patients (34.3 versus 36.7 g/L, $p=0.06$). Significantly more patients receive antibiotics (38.6% and 13.3%, $p=0.06$) (Table

5). There were no differences in number of hospital admissions (median 1 (0–3) versus median 1 (0–2) $p=0.46$), or duration of hospital stay (median 11.0 (0.0–19.5 versus 6.0 (median 0.0–12.5) $p=0.26$) between the groups. However, in university dialysis centres, a greater number of patients were admitted to the hospital for renal indications (18.2% versus 4.4%, $p=0.04$). Other indications for hospital admission, for example, cardiovascular, respiratory, surgical/vascular access or oncological, did not differ significantly. Infectious diseases admissions tended to be higher in university dialysis centres, but this was not statistically significant.

In the university dialysis patients, the subjective global assessment was significantly lower compared to other dialysis centres patients (5.3 versus 6.3, $p=0.001$) (Table 5). The number of patients with SGA nutritional status measurement was low, because not every dialysis centre routinely performs this measurement. No difference was seen in grip strength of the dominant hand of patients.

Association between patient characteristics and actual care time

Univariate analysis showed that an increased number of comorbidities means that more time

Table 5: Patient and dialysis characteristics

	University dialysis centres (n=44)	Non-university dialysis centres (n=45)	P-value
Lab value			
Albumin (g/L)	34.3 (6.80)	36.7 (4.83)	0.06
Creatinine (µmol/L)	652 ± 283	724 ± 269	0.23
C-reactive protein (mg/L)	11.0 (4.5–26.0)	7.0 (3–28)	0.44
Haemoglobin (mmol/L)	6.6 ± 0.86	6.7 ± 0.62	0.30
Leucocytes (*10 ⁹ /L)	8.0 (5.5–9.8)	7.8 (5.8–9.0)	0.91
Subjective Global Assessment			
Number	27	25	
Subjective Global Assessment	5.3 ± 1.3	6.3 ± 0.85	0.001
Antibiotics	17 (38.6%)	6 (13.3%)	0.006
Beta blockers	31 (77.3%)	24 (53.3%)	0.09
Angiotensin receptor blocker	2 (4.5%)	2 (4.4%)	0.98
Calcium channel blockers	12 (27.2%)	7 (15.6%)	0.18
Diuretics	18 (40.9%)	13 (28.9%)	0.23
Angiotensin converting enzyme inhibitors	10 (22.7%)	3 (6.7%)	0.03

Variables are presented as mean ± standard deviation (SD) in case of normal distribution, or as median interquartile range in case of non-normal distribution. P-values were calculated with an independent t-test in case of normal distribution, Mann-Whitney U test in case of non-normal distribution.

Variables are presented as mean ± SD.

Table 6: Association between patient characteristics and clinical conditions and actual care time

Variable	Univariate			Multivariate			Stepwise backward		
	B	St β	p-val	B	St. β	p-val	B	St β	p-val
Dialysis centre (non-academic versus academic)									
Gender (male)	-0.88	-0.02	0.87	—	—	—	—	—	—
Age	-0.01	-0.01	0.96	—	—	—	—	—	—
Body mass index	0.17	0.03	0.76	—	—	—	—	—	—
Number years haemodialysis	0.67	0.09	0.39	—	—	—	—	—	—
Previous kidney transplantation	-2.52	-0.03	0.76	—	—	—	—	—	—
Previous peritoneal dialysis	2.32	0.02	0.83	—	—	—	—	—	—
Number of comorbidities	4.20	0.27	0.01	0.73	0.05	0.81	—	—	—
Albumin	-1.27	-0.30	0.005	-0.78	-0.18	0.27	-1.27	-0.30	0.005
Creatinine	-0.01	-0.06	0.61	—	—	—	—	—	—
Leucocytes	0.78	0.15	0.18	0.53	0.10	0.52	—	—	—
CRP	0.07	0.12	0.35	—	—	—	—	—	—
Cholesterol	0.34	0.06	0.63	—	—	—	—	—	—
Haemoglobin	-0.22	-0.06	0.57	—	—	—	—	—	—
Hospital admissions									
Number last year	0.98	0.12	0.26	—	—	—	—	—	—
Days last year	0.09	0.08	0.48	—	—	—	—	—	—
Indication hospital admission									
Renal	-7.61	-0.10	0.38	—	—	—	—	—	—
Cardiovascular	2.03	0.03	0.78	—	—	—	—	—	—
Respiratory	8.28	0.10	0.34	—	—	—	—	—	—
Metabolic/endocrine	—	—	—	—	—	—	—	—	—
Oncological	4.37	0.04	0.71	—	—	—	—	—	—
Surgical/vascular access	-6.44	-0.11	0.30	—	—	—	—	—	—
Infectious diseases	-0.25	-0.003	0.98	—	—	—	—	—	—
Other	3.41	0.06	0.58	—	—	—	—	—	—
Subjective Global Assessment	-5.47	-0.27	0.06	-3.07	-0.15	0.38	—	—	—
Grip strength	-0.51	-0.25	0.03	-0.34	-0.17	0.33	—	—	—

Abbreviations: Betas (β), standardised betas (St β) and p-values were calculated using univariate linear regression. Dependant variable is measured care time. Variables that had a univariate β of 0.25 were included in the multivariable analysis.

is needed per patient (standardised beta 0.27 $p < 0.01$). Furthermore, a low albumin level correlated with an increase in care time (St. β -0.30, $p=0.005$). Another factor that increased measured

care time was a decrease in grip strength (St. β -0.25 $p < 0.03$).

When the authors carried out multivariable analysis, none of these factors remained

CPD reflective questions

- Do you think that better patient nutrition would decrease the nursing care time needed during dialysis?
- What would improve the condition of a patient, especially with regard to hand grip strength?
- Why are patients in university dialysis centres more severely ill than those in non-university dialysis centres?

Key points

- The nursing care time needed for treatment of dialysis patients is higher in university dialysis centres than in non-university dialysis centres in the Netherlands (Kleijn et al, 2017)
- The need for more extensive nursing care in university dialysis centres is not due to differences in the dialysis characteristics or personal characteristics of patients. Rather, the patients at university dialysis centres are more malnourished and have a reduced grip strength, alongside a higher rate of (micro)inflammation, which indicates that they are more severely ill
- Using a model to estimate the nursing time that each patient requires during dialysis can improve the efficiency of dialysis centres

statistically significant. However, in the stepwise backward analysis, only albumin remained significant, indicating that this is the strongest predictor of measured care time during dialysis (Table 6).

Association between patient characteristics and clinical conditions and difference in care time

Univariate analysis showed that there was an association between albumin and the difference between predicted versus measured care time, although this difference did not reach statistical significance (St. β -19 $p=0.07$).

Discussion

This research re-evaluated the appropriateness of the 2015 classification model for estimating the nursing care time needed per dialysis session by recording the nursing time spent per session. In non-university dialysis centres, the predicted care time still equalled the actual measured care time, and was similar to Kleijn et al (2017). Although patients had become older, less mobile and asked for more psychosocial attention (time-consuming characteristics), which lead to more of nurses' time being spent with each patient, this was counterbalanced with time-saving characteristics, because most patients participated actively in their treatment and required less time from the nurses (Kleijn et al, 2020). As a result, both the actual and predicted time were similar to the first study (Kleijn et al, 2017). This confirmed that the most care time for patients was needed

in the university dialysis centres. Similar to the results in the first study (Kleijn et al, 2017), the predicted time underestimated the actual measured time in university dialysis centres, although somewhat less than in the first study.

The decrease in the time spent was mainly due to increased participation of patients in their own treatment (Kleijn et al, 2020). However, the difference had not fully disappeared. Therefore, the authors investigated whether medical indicators of disease severity were able to explain the remaining difference.

Analysis of the clinical data of patients undergoing dialysis showed that patients in university dialysis centres had lower SGA measurements and hand grip strength than patients in other dialysis centres. Additionally, the level of serum albumin was lower compared to patients receiving dialysis in other dialysis centres. In the linear regression analysis, grip strength and albumin were shown to be univariately associated with measured care time. Albumin was associated with the difference in actual and predicted care time, although this did not reach formal statistical significance. This suggests that, compared to patients in other dialysis centres, patients treated in university dialysis centres were more severely ill, and had greater signs of protein energy wasting and muscle loss, which could be a possible underlying explanation for the higher than predicted care time.

It is possible that improvement of dietary intake will reduce the time that nurses are required to spend caring for each individual patient. This could be investigated in future studies. This might lead to an adaptation of the classification model. In the meantime, a standard amount of time of 10 minutes could be added to the care of each patient for the model to be adequate for use in centres with more complex patients.

The classification model can be of value by matching the nursing time needed with the patients presenting for treatment, thus contributing to the efficacy of dialysis centres, especially where there is a shortage of nursing staff.

Strengths

There has been limited research into the required care time for patients undergoing HD based on clinical conditions. Revalidation of the classification model in the changing dialysis population has shown that it is still useful to estimate the nursing capacity needed for patients.

Limitations

The size of the population was relatively small, therefore, associations between detailed comorbidity and nutritional characteristics and the time needed for dialysis were difficult to identify. The authors did not investigate how being observed may have affected the behaviour of the nurses.

Conclusion

The classification tool to predict dialysis care time adequately estimates the nursing care time needed, even in a changing population of patients. It is especially suitable for patients receiving dialysis in non-university dialysis centres. It underestimates care time for patients at university dialysis centres. This may be explained by the fact that patients treated in university dialysis centres have a higher burden of disease, represented in part by a higher prevalence of protein energy wasting, as indicated by lower SGA measurements, a reduced grip strength and lower serum albumin levels. **JKC**

Conflict of interest: None.

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