Survival and Technical Failure in a Large Cohort of Thai CAPD Patients

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Objective: *To evaluate patient and technique survival, and to analyze factors influencing survival in a large Thai CAPD program.*
Material and Method: *A single center, retrospective, observational cohort study was carried out to examine the baseline factors affecting patient and technique survival.*
Results: *From January 1995 to December 2005, 322 incident CAPD patients were recruited for study. One hundred and thirteen patients (35.1%) died during the study period of 7,706 patient-months. Median patient survival time was 46.4 months. The major cause of death was related to infection. In multivariate analysis, only age at enrollment and baseline serum albumin were strong risk factors of death. Median technique survival was 41.2 months. The major cause of technique failure was peritoneal dialysis related infection. History of peritonitis, baseline serum albumin, and dialysis commencement in recent era were technique failure predictors. A neutral effect of self and caregiver performer was observed in the present study.*
Conclusion: *Patient survival in the presented institute is similar to that reported in Western countries. Age and baseline serum albumin were the strongest predictors of death.*

Keywords: *Continuous ambulatory peritoneal dialysis, Patient survival, Technical failure, Risk factors*

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CAPD is a well-established renal replacement therapy for end stage renal disease (ESRD), and has been used for the last 15-20 years in Thailand. This mode of treatment needs less resource compared to hemodialysis[1]. For many rural people with renal failure who have limited access to hemodialysis centers, CAPD may be particularly suitable. However, success of the treatment requires low peritonitis rate, long technique survival, good quality of life (QoL) and low mortality rate. In situations of limited resource, patient evaluation is an important way to improve outcome of treatment.

Several baseline factors appear to be clear predictors of poor outcome, including the presence of diabetes mellitus (DM), old age, and hypoalbuminemia[2]. The need for a partner to perform peritoneal dialysis (PD), and co-morbidities were associated with an increased risk of death[3].

Cueto-Manzano et al analyzed mortality risk factors for patient and technique survival in a cohort study of 627 patients (37% with diabetes) in a large Mexican single-center CAPD program[4]. Univariate analysis showed that DM, old age, hypoalbuminemia, low serum creatinine, low serum phosphate, and lymphopenia were associated with mortality ($p < 0.05$). The only significant mortality risk factors found from multivariate analysis were diabetes, old age, hypoalbuminemia, and lymphopenia. Peritonitis, hypoalbuminemia, lymphopenia, old age, and DM were all significantly associated ($p < 0.05$) with technique failure in the univariate analysis, while in the multivariate analysis, only DM, peritonitis, lymphopenia and hypoalbuminemia were technique failure predictors.

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Srinagarind Hospital is a large 650-bed public tertiary-care referral medical center in the northeast of Thailand. Its CAPD program has been operating for more than ten years. Most of the patients are elderly and many need caregivers to perform CAPD. Thus, the patients' characteristics in the present study may be somewhat different from previous studies.

In Thailand, there has previously been no significant report on long-term CAPD survival. In the present study the authors retrospectively evaluated factors affecting patient survival and technique failure in Thai CAPD patients. Such understanding could yield insights for the improvement of patient care, particularly if the CAPD program is to be expanded as first line renal replacement therapy for the whole country.

Material and Method

Three hundred and twenty two CAPD patients attended Srinagarind Hospital from January 1995 to December 2005 and were included in the present study. A standard Tenckhoff catheter was used in most patients by both peel-away sheath bedside insertion and mini-exploration by the surgeon. Prophylactic antibiotic with cefazolin was administered prior to Tenckhoff catheter placement in almost all cases. CAPD was started in most patients without a break-in period due to uremic condition and scant availability of hemodialysis back up. Most of the connecting system was a single bag (both standard spike and safe lock). Peritoneal dialysis solution used was a standard 1.5% dextrose 1.5-2 liters with lactate buffer at 4 exchanges per day. Patients and at least one caregiver were trained to do CAPD exchange by dialysis nurses. The training program lasted for 3-5 days. The training processes were composed of a video demonstration, simulation with a mannequin, and an evaluation of the trainee's performance.

The data collection consisted of demographic details, primary renal disease, baseline laboratory data within one month prior to CAPD, and the requirement of a helper for dialysis exchange. The latter was defined by the requirement of a helper at least one time per day. Patients with severe co-morbidities such as cerebrovascular disease, malignancy, dementia and severe obstructive airway disease were not eligible for CAPD in the presented center. Therefore, co-morbidities other than DM were not considered in the analysis. Due to incomplete information on dialysis adequacy and peritoneal membrane transport status, these data during follow-up were not included in the present study.

Patients were followed up until death, technique failure, receiving kidney transplantation, or until 31 December 2005. The cause of death of each patient was determined by reviewing the medical record, autopsy report and interviewing the patient's relatives in cases of death outside the hospital. In the analyses, the cause of death was classified into three categories; cardiovascular death, infection including peritoneal dialysis-related infection, and unknown. Technique failure was defined by changing the treatment to hemodialysis for at least one month. Re-entry to the CAPD program after technique failure was not counted as a new incident case. The cause of failure was classified as ultrafiltration/clearance failure, peritonitis related infection, and socioeconomic problem including patient and family burn-out.

The present study was approved by the Ethics Committee of Khon Kaen University.

Statistical analysis

All data were expressed as mean $\pm$ SD for normally distributed data, and median or range for skewed data. Statistical comparison was performed using Student t-test, and comparison of percentage between groups was made with the Chi-square test or Fisher-exact test. Analysis of patient survival was terminated at transplantation, loss to follow up and transfer to hemodialysis. Technique survival was terminated at death or loss to follow up. Actuarial survival curves were made according to the Kaplan-Meier method. Comparison of the survival curves of the different subgroups was made using log rank test. The following indicator variables were tested; gender, age, baseline values of serum albumin and hematocrit, body mass index, underlying disease with diabetes mellitus, type of connection, performer by self or caregiver, and year starting CAPD. Variables that remained significant at a p value less than 0.2 were retained in the final model of Cox regression model for the multivariate analysis. Statistical analysis was performed using STATA software. All probabilities were two-tailed and the level of significance was set at 0.05.

Results

Three hundred and twenty two incident CAPD patients were studied over a total observation period of 7,706 patient-months (mean 23.9 months, median 18.1 months). Mean age at commencement of CAPD was 56.7 $\pm$ 12.5 years (range 14 - 85 years). Etiologies of ESRD were diabetic kidney disease (49.4%), hypertension (14.6%) chronic glomerulonephritis (9.0%), obstructive

uropathy and interstitial nephropathy (9.0%), and unknown primary renal disease (17.7%). At the end of the present study, 209 patients were still alive, 113 patients were dead, 27 patients had been referred to other centers, and 3 patients were lost to follow up. Fifteen patients (32.61%) received kidney transplantation.

Patient survival

Among 322 CAPD patients, 113 patient (35.1%) died during the observation period. Of these deaths, 32 (28.8%) were related to cardiovascular events, 38 (34.2%) were from peritoneal dialysis-related infection, and 41 (36.94%) were unknown cause. This last category occurred outside the hospital and the cause could not be verified. Median survival time was 46.4 months. Patient survival at 1, 3, 5, 7 years was 84.0%, 61.1%, 44.0% and 25.7%, respectively.

By univariate analysis (Table 2), significantly lower survival was found among older age and diabetes patients, those with lower baseline albumin levels, and those starting CAPD during the years 2000-2005. A marginally significant better survival rate was observed in self-performed CAPD. These findings were consistent for year 1 and year 3 follow-up. Type of connection and body mass index were not found to be statistically associated with risk of death. Fig. 1 shows patient survival of the various subgroups.

In the multivariate analysis (Table 3), age and baseline serum albumin were strongly associated with an increased risk of death. When age increased by 1 year, the risk of death among CAPD patients increased by 3% (95%CI 1.012-1.05). If the level of baseline albumin increased by 1 g/dL, the risk of death decreased by 43% (Hazard ratio 0.57, 95%CI 0.42-0.77). In the present study, the status of diabetes mellitus and starting CAPD during the period 2000-2005 were associated with an increased risk of death of about 45%, however, they did not reach statistical significance ($p = 0.087$).

Technique survival

Technique failure was found in 132 patients (41.0%). Causes of technique failure were as follows: peritoneal dialysis related infection (69.5%), ultrafiltration/clearance failure (15.3%), and socioeconomic problems (15.2%). Median technique survival time was 41.2 months. Technique retention at 1,3,5,7 years was 80.1%, 54.4%, 32.6%, and 23.7%, respectively. Unlike patient survival, technique survival was not related to diabetic kidney disease.

The results of the univariate analyses are presented in Table 2 and technique failure free survival of various subgroups are shown in Fig. 2. Baseline albumin at low level, starting CAPD during the years 2000-2005, and patients with normal body mass index were strongly associated with higher risk of technique failure. Differences in technique failure free survivals of the above subgroups were evident at both year 1 and year 3 follow-up. In addition, experience with peri-

Table 1. Baseline clinical characteristics and laboratory data of the cohort

	All patients	Starting CAPD before year 2000	Staring CAPD during year 2000-2005
Patients (N)	322	198	124
Age, mean ± SD (years)	56.7 ± 12.5	58.1 ± 12.5	54.4 ± 12.2
Gender, (%male)	177 (55.0)	106 (53.5)	71(57.26)
Cause of end stage renal disease, N (%)			
Diabetes mellitus	159 (49.4)	111 (56.1)	48 (38.7)
Glomeronephritis	29 (9.0)	8 (4.0)	21 (16.9)
Hypertension	47 (14.6)	31 (15.7)	16 (12.9)
Polycystic kidney disease	1 (0.3)	0 (0)	1 (0.8)
Obstructive uropathy or interstitial nephropathy	29 (9.0)	12 (6.1)	17 (13.7)
Unknown	57 (17.7)	36 (18.2)	21 (16.9)
Weight, mean ± SD (kg)	58.7 ± 10.3	59.0 ± 10.6	58.1 ± 9.7
Body mass index, mean ± SD (kg/m^2)	22.9 ± 3.1	23.0 ± 3.1	22.8 ± 3.1
Serum albumin, mean ± SD (g/dL)	3.1 ± 0.7	3.1 ± 0.6	3.1 ± 0.7
Hematocrit, mean ± SD(vol%)	29.2 ± 4.8	29.6 ± 4.9	28.5 ± 4.5
Blood urea nitrogen, mean ± SD (mg/dL)	77.6 ± 38.2	79.5 ± 36.5	74.4 ± 40.9
Creatinine, mean ± SD (mg/dL)	10.6 ± 5.4	10.6 ± 6.0	10.7 ± 4.0

tonitis increased the risk of technical failure. At year 1 and year 3, the percentage of patients with peritonitis who had technique failure was 22% and 50.5%, whereas only 14.6% and 31.1% of patients who did not experience peritonitis and had technique failure (p = 0.0018). Type of connection, and performed by self or caregiver were not found statistically associated with risk of technique failure.

In the multivariate analysis (Table 4), baseline albumin, year of starting CAPD, and history of peritonitis were strongly associated with an increased risk of technique failure. Peritonitis was found to be a strong predictor of technique failure with a hazard ratio of 2.34 (95%CI 1.44-3.80). If the level of baseline albumin increased by 1 g/dl, the risk of having technique failure decreased by 27% (Hazard ratio 0.73, 95%CI 0.56-0.95). Patients who started CAPD during the period of year 2000-2005 had a 68% higher risk of technique failure when compared to those who did so before the year 2000. Age and body mass index were associated with an increased risk of technique failure, despite not reaching statistical significance. In the present study, the status of DM was not associated with an increase in risk of technique failure.

Table 2. Subgroup analyses of time to events

Variable	Survival			Technical failure free survival		
	1 year	3 year	p-value	1 year	3 year	p-value
Age ≤ 55 year	90.76	68.77	0.0042	84.72	57.36	0.0614
Age > 55 year	78.69	54.62		76.40	51.39	
Patient with diabetes mellitus	79.50	49.25	0.0008	81.17	50.66	0.3960
Patient without diabetes mellitus	88.79	71.60		78.49	56.60	
Albumin < 3 g/dL	77.57	50.07	0.0011	72.64	46.21	0.0455
Albumin ≥ 3 g/dL	89.63	69.71		85.12	59.81	
Starting CAPD before 2000	91.50	67.89	0.0361	83.20	62.60	0.0319
Starting CAPD year 2000-2005	78.73	55.47		77.48	46.64	
Single bag connection	84.55	59.63	0.4026	80.43	53.43	0.5781
Double bag connection	80.42	71.89		75.59	59.95	
CAPD performer by self	90.94	65.31	0.0813	86.60	55.28	0.4910
CAPD performer by care giver	81.96	59.71		77.80	53.94	
BMI < 25 kg/m^2	84.08	58.39	0.1537	78.41	50.57	0.0331
BMI ≥ 25 kg/m^2	84.15	74.78		85.53	72.20	

Table 3. Multivariate analyses for time to death

Predictors	Hazard ratio	95%CI	p-value
Age	1.032	1.012-1.052	0.001
Baseline albumin	0.568	0.420-0.769	<0.001
Diabetes mellitus	1.443	0.960-2.170	0.078
Starting CAPD during 2000-2005 vs. before year 2000	1.458	0.947-2.246	0.087

Table 4. Multivariate analyses for time to technique failure

Predictors	Hazard ratio	95% CI	p-value
Age	1.013	0.997-1.029	0.102
Baseline albumin	0.728	0.557-0.957	0.020
BMI	1.631	0.965-2.758	0.068
Starting CAPD during 2000-2005 vs. before year 2000	1.682	1.154-2.453	0.007
Experience with peritonitis	2.336	1.436-3.799	0.001

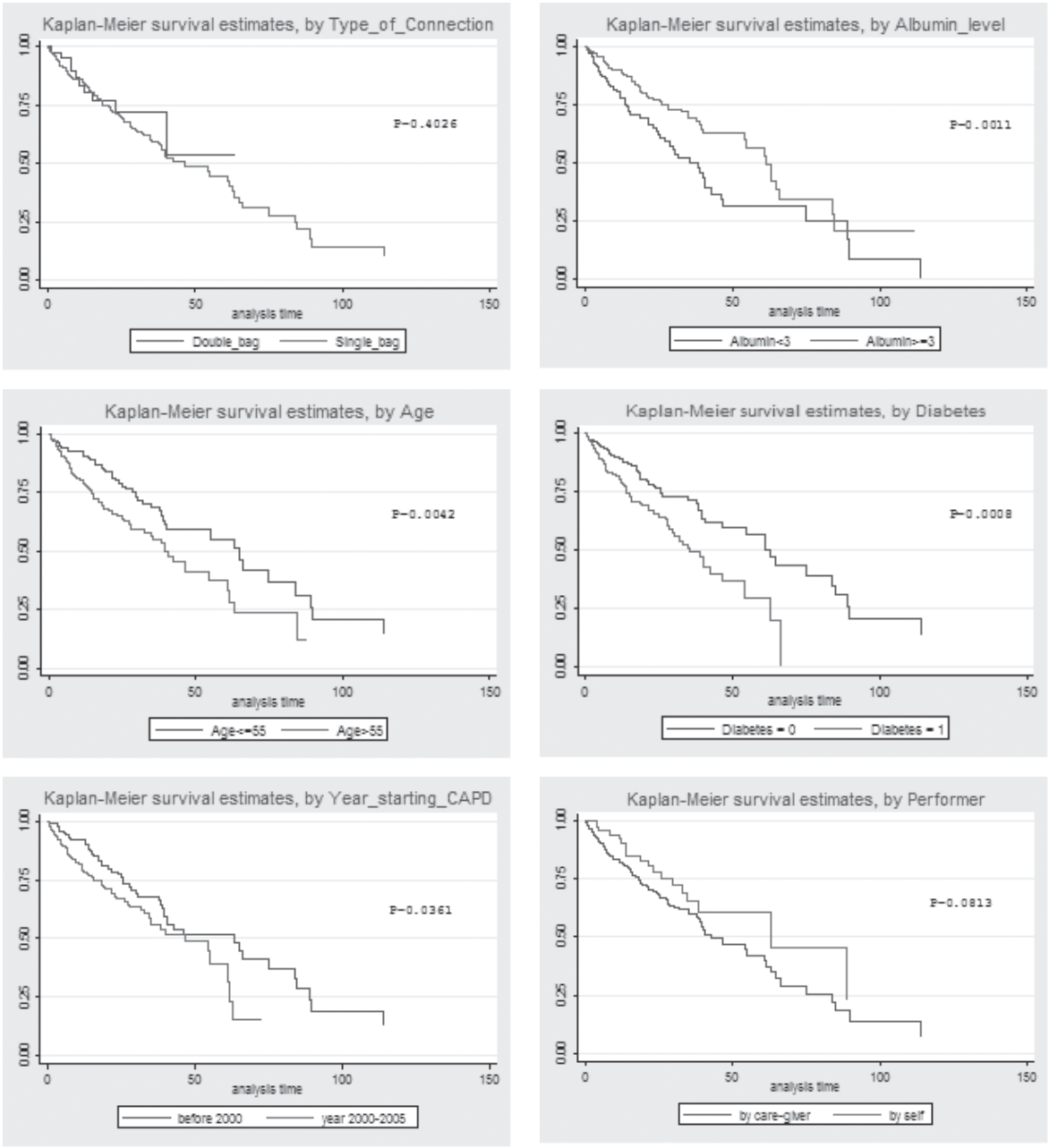

Fig. 1 Time to death analyses

Discussion

This is the first report on the long term experience of a Thai CAPD center. Survival of the patients was similar to previous reports. Reports from large incident cohorts of CAPD patients in the United State[5] and Mexico[4] showed that patient survival at 1 and 3 year of 82.5 and 57.9% and 85 and 68%, respectively, compared favorably to the present study (84.0 and 61.1%). Diabetes, older age, and hypoalbuminemia were the most significant predictors of patient survival in all three large cohort studies. The importance of these three factors was already known from previous studies. In addition to baseline characteristics, treatment effect had an important role on outcome of chronic disease. Adequacy of dialysis and peritoneal transport status has been shown to have a significant effect on

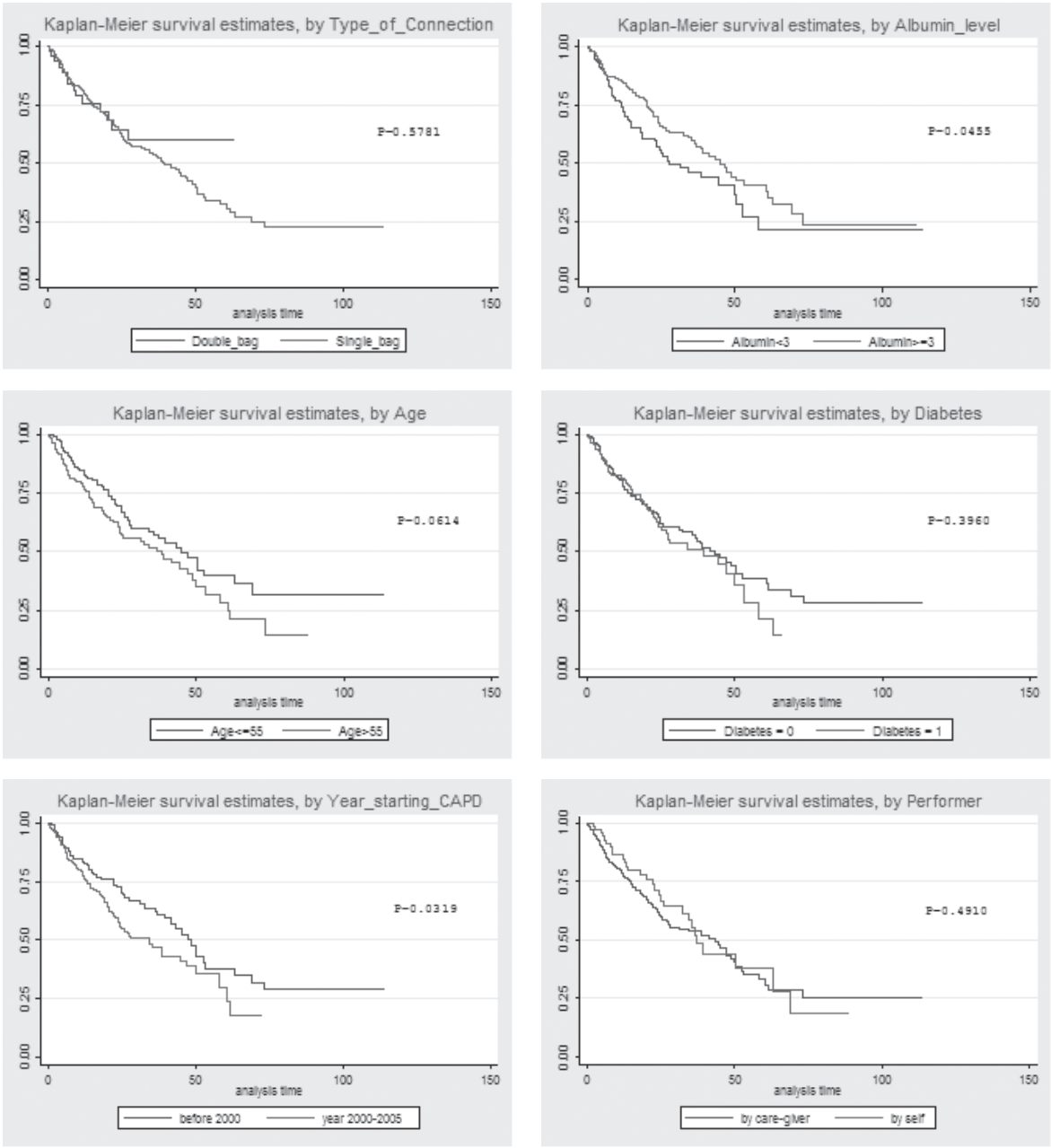

Fig. 2 Time to technique failure analyses

mortality in previous large prospective cohort studies[6,7]. A limitation of the present study is that the authors could not incorporate the data on adequacy and transport status in the analyses. However, the direction of risk factors on mortality were the same, but different in magnitude.

Diabetes affects patient survival by several mechanisms. Glycated product enhances atherosclerosis and leads to cardiovascular disease[8]. At least one-fourth of the deaths in the present cohort were caused by cardiovascular events. This data confirmed the importance of the relationship between diabetes and cardiovascular disease in dialysis patients. Since diabetes is a non-modifiable risk factor, surveillance and prevention of cardiovascular disease in this group of patients is the best way to reduce mortality.

The authors have reaffirmed the independent predictive value of low baseline serum albumin on subsequent risk of mortality in CAPD patients. A difference of 1 g/dL was associated with a 43% change in relative risk of death. The magnitude was less than in the CANUSA study[7] but more than in the study from Mexico[4]. Hypoalbuminemia could be a result of malnutrition and inflammation. Awareness of those two conditions in CAPD patients should be emphasized.

The neutral effect of performer on patient and technique survival led to the break-through for the CAPD program in Thai patients. Most of the performers were younger family members such as patients' offspring and their siblings' children. This result may be explained by the meticulous care given to elderly family members in the Thai culture. It was formerly believed that CAPD may not be appropriate in high dependency patient[3]. Generally, this group of patients can be treated by hemodialysis with minimal effort from a caregiver. In Thailand, especially in rural areas where hemodialysis centers are barely accessible, CAPD could be the most appropriate mode for renal replacement even in high dependency patients.

An unexpected finding is more technique failure in the recent era. Technology advancements and the knowledge of the patient care team should have increased over time and resulted in improvement of outcomes. Migration of skillful nurses and more workload after the introduction of universal coverage policies could be the cause of this paradoxical finding. This could be an opportunity to reassess the presented work and explore the cause of this finding.

Conclusion

Patient survival in the presented institute is similar to that reported in Western countries. Age and baseline serum albumin were the strongest predictors of death. Risk factor of technique failure was infection, low baseline serum albumin, and dialysis commencement in the recent era. A neutral effect of self and caregiver performer on survival was observed in the present study.

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อัตราการรอดชีพและการคงอยู่กับวิธีการรักษาด้วยการล้างไตทางช่องท้องในผู้ป่วยไทย

ชลธิป พงศ์สกุล, ทวี ศิริวงศ์, ทัดสะลัง แก้วบุนมา, ดรุณี จันทร์เลิศฤทธิ์, ปัญจักษร พรมจักร์, จุฬาภรณ์ ลิมวัฒนานนท์

วัตถุประสงค์: *เพื่อหาอัตราการรอดชีพและการคงอยู่กับวิธีการรักษาในผู้ป่วยไตวายเรื้อรังที่ได้รับการรักษาด้วยการล้างไตทางช่องท้องและปัจจัยเสี่ยงต่อเหตุการณ์*

วัสดุและวิธีการ: *ติดตามผู้ป่วยที่เข้ารับการรักษาด้วยการล้างไตทางช่องท้องที่โรงพยาบาลศรีนครินทร์ ตั้งแต่เดือนมกราคม พ.ศ. 2538 - เดือนธันวาคม พ.ศ. 2548 โดยหาอัตราการรอดชีพและการคงอยู่กับวิธีการรักษาของผู้ป่วย*

ผลการศึกษา: *ผู้ป่วยจำนวนทั้งสิ้น 322 ราย เวลามัธยฐานของการรอดชีพคือ 46.4 เดือน สาเหตุของการตายส่วนใหญ่สัมพันธ์กับการติดเชื้อ ปัจจัยเสี่ยงของการเสียชีวิตคือ อายุและระดับอัลบูมินที่ต่ำเมื่อแรกเข้ารับการรักษา เวลามัธยฐานในการคงอยู่กับการรักษาคือ 41.2 เดือน สาเหตุของการหยุดการรักษาด้วยการล้างไตทางช่องท้องคือการติด เชื้อ ปัจจัยเสี่ยงของการล้างไตทางช่องท้องคือ ประวัติของการติดเชื้อในช่องท้อง, ระดับอัลบูมินที่ต่ำเมื่อแรกรักษาและการเริ่มรักษาในช่วง 5 ปีหลัง ไม่พบความแตกต่างระหว่างกลุ่มที่ทำการเปลี่ยนน้ำยาเองกับกลุ่มที่ต้องพึ่งพาญาติ*

สรุป: *อัตราการรอดชีพของผู้ป่วยที่ล้างไตทางช่องท้องในโรงพยาบาลศรีนครินทร์ใกล้เคียงกับรายงานของผู้ป่วยทางตะวันตก อายุที่มากและระดับอัลบูมินต่ำเมื่อเข้ารับการรักษาเป็นปัจจัยเสี่ยงที่สำคัญของการเสียชีวิต ปัจจัยเสี่ยงของการล้มเหลวในการรักษาคือการติดเชื้อและระดับอัลบูมินที่ต่ำ*