





ORIGINAL ARTICLE

Impact of obesity on the evolution of outcomes in peritoneal dialysis patients

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ABSTRACT

Background. Some studies reveal that obesity is associated with a decrease in mortality in haemodialysis (HD) patients. However, few studies have addressed the association between body mass index (BMI) and peritoneal dialysis (PD) patients.

Methods. We performed this longitudinal, retrospective study to evaluate the impact of obesity on PD patients, using data from the Catalan Registry of Renal Patients from 2002 to 2015 ($n = 1573$). Obesity was defined as $BMI \geq 30$; low weight: $BMI < 18.5$; normal range: $BMI = 18.5-24.99$; and pre-obesity: $BMI = 25-29.99 \text{ kg/m}^2$. Variations in BMI were calculated during follow-up. The main outcomes evaluated were the technique and patient survival.

Results. Obesity was observed in 20% of patients starting PD. We did not find differences in sex or PD modality, with the obesity group being older (65.9% are ≥ 55 years versus 59% non-obese, $P = 0.003$) and presenting more diabetes mellitus and cardiovascular disease (CVD) (47.9% obese versus 25.1% non-obese and 41.7% versus 31.5%, respectively). We did not observe differences in haemoglobin, albumin and Kt/V in obese patients. Regarding peritonitis rate, we did not find any difference between groups, presenting more peritonitis patients on continuous ambulatory peritoneal dialysis and aged ≥ 65 years [sub-hazard ratio (SHR) = 1.75, $P = 0.000$ and SHR = 1.56, $P = 0.009$]. In relation to technique survival, we found higher transfer to HD in the obese group of patients in the univariate analysis, which was not confirmed in the multivariate analysis (SHR = 1.12, $P = 0.4$), and we did not find differences in mortality rate. In relation to being transplanted, the underweight group, elderly and patients with CVD or diabetic nephropathy presented less probability to undergo kidney transplantation (SHR = 0.65, 0.24, 0.5 and 0.54, $P < 0.05$). Obese patients did not present differences in survival with weight changes but in normal-weight patients, a gain of 7% of the basal weight during the first year had a protective effect on death risk (hazard ratio 0.6, $P = 0.034$).

Conclusions. Obese and non-obese patients starting on PD had similar outcomes.

Keywords: epidemiology, obesity, peritoneal dialysis

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INTRODUCTION

The prevalence of obesity [defined as body mass index (BMI) $\geq 30 \text{ kg/m}^2$] has increased in the last decades. In fact, the members of the Global Burden of Disease Obesity Collaborators reported that in 2015, 5% of children and 12% of adult population were obese [1]. In 2015, elevated BMI was related to 7.5% of deaths, with cardiovascular disease (CVD) being reported as the main cause of mortality in this population, followed by diabetes mellitus (DM), chronic kidney disease (CKD) and cancer [1]. Obesity is one of the principal modifiable cardiovascular risk factors (CVRF), at the same time being a risk factor for some chronic diseases such as DM, hypertension and CVD in the general population [2, 3]. However, obesity has been described as a protective factor for death in some groups of patients like elderly individuals in nursing homes, patients with some malignancies and hospitalized patients [4].

In the last decades, in the general population, there has been an increase of obesity in CKD patients and also in those who require renal replacement therapy (RRT), rising from 14.9% to 19.0% in haemodialysis (HD) patients, from 17.4% to 24.6% in peritoneal dialysis (PD) patients and from 11.2% to 16.1% in kidney transplantation (KT) patients from 2005 to 2016 in Catalonia [5]. Multiple epidemiological studies have demonstrated an inverse association between classic CVRF for CVD and mortality in HD patients [4, 6]. In addition, paradox obesity in HD patients has been described as a universal phenomenon that does not differ by sex, age, smoking, diabetic status, race/ethnicity, geographic regions or dialysis dose [7–10].

On the other hand, results among patients undergoing PD have been inconsistent. For a long period of time, obesity has been considered as a relative contraindication for the initiation of PD due to greater possibility of mechanical complications such as abdominal hernia [11], rapid decline in residual kidney function [12] and peritonitis [13]. In terms of technique and patient survival, Ahmadi et al. [14] performed a systematic review and meta-analysis because of the discrepancies observed between different groups and concluded that obese patients present a major risk to transfer to HD and lower mortality during the first year, but these differences in relation to mortality are not maintained over time.

In the present study, we have analysed the influence of obesity and the effect of variation of BMI on PD patients, in terms of technique and patient survival, with data obtained from the Catalan Renal Registry.

MATERIALS AND METHODS

After gaining the approval of the Institutional Review Board, we used data from the Registry of Renal Patients of Catalonia (RMRC). This is a mandatory population-based registry covering 7.5 million people that collects information on all patients with end-stage renal disease (ESRD) requiring RRT in Catalonia. At the time of starting RRT and at every change of treatment throughout RRT, a registration form is filled in. Every year an update has to be carried out and sent to the RMRC up to the finalization of RRT, death of patient or loss of follow-up.

A retrospective observational study has been carried out with the collection of data from patients starting PD in Catalonia from 2002 to 2015. Because the follow-up period is long, we have differentiated the data into two periods, from 2002 to 2006 and from 2007 to 2015. Patients who started PD

during the first 90 days after beginning RRT who were resident in Catalonia, and aged >18 years and <85 years were included and followed-up from the start of RRT until December 2016.

Patients were classified in the following four groups depending on BMI at the moment of initiation of RRT: underweight (BMI <18.5); normal weight (BMI ≥ 18.5 and <25); pre-obesity (BMI ≥ 25 and <30) and obesity (BMI $\geq 30 \text{ kg/m}^2$). A sub-analysis of obese patients in obesity Type I (30–34.9) and obesity Type II (≥ 35) was also carried out. To evaluate the change in weight, we calculated the percentage of change between basal weight and weight during the follow-up for each year and then the mean for the different periods was obtained: $[(\text{Weight at follow-up} - \text{Basal weight})/(\text{Basal weight})] \times 100$.

The collected variables were PD adequacy (Kt/V), nutrition status, which was assessed by serum albumin at the beginning of PD, accumulated probability of developing the first peritonitis based on the technique and initial weight, and also technique and patient survival. Related to technique survival, we considered the following events: death, transfer to HD or end of study period [31 December 2016 (censorship)]. Time for technique survival was evaluated from the start of the RRT to the end of the technique and with competitive risks (the different events compete with each other). To analyse patient survival for intention-to-treat, the time was evaluated from the beginning of the RRT until the death of the patient or time until the end of observation period (censorship). If a patient died within the first 90 days after transfer to HD, then the death was attributed to PD because we considered that this reflected the health status of patients during PD therapy. Transfer to HD was considered when patients were in HD for >90 days.

For the multivariate analysis, the following explanatory variables were taken into account: cause of ESRD, gender, CVRF (DM, age, hypertension and hypercholesterolaemia) and any cardiovascular event (ischaemic heart disease, heart failure, peripheral vascular disease and cerebrovascular disease).

Comparisons between groups by BMI at the time of initiation PD were performed by Chi-square test for categorical data and analysis of variance for continuous data ($P < 0.05$ was considered significant). Baseline characteristics of the study cohort were expressed as a number and a proportion or mean \pm standard deviation (SD). The statistical approach to calculating the adjusted model was done using a generalized estimating equation, which is used to estimate the parameters of a generalized linear model with a possible unknown correlation between outcomes.

Cumulative incidence competing risk functions and competing risk regression were used to calculate the incidence of technique and patient mortality during PD. We also performed a survival analysis for intention-to-treat to evaluate the survival of all patients included in the study from the beginning of RRT, using the Kaplan–Meier in the univariate and the Cox regression in the multivariate analysis. All statistical tests were considered significant if $P < 0.05$ for two-tailed tests. Analyses were performed using STATA software version 13.

RESULTS

Baseline demographic and clinical characteristics

Among the 1573 patients included, weight and/or height information were not reported in 41 patients (2.6%); hence, the study population was 1532 incident patients on PD.

Baseline characteristics are reported in Table 1. Patients were divided in four groups depending on their BMI at the start of PD. There were 307 (20%) obese patients [232 patients (15.1%) obese Type I (BMI 30–34.9) and 75 (4.9%) obese Type II (BMI ≥ 35 kg/m²)]. The profile of an incident obese patient on PD is a man with diabetic nephropathy, aged >55 years with some cardiovascular morbidity who initiated PD in the recent period.

Regarding weight variation from baseline (Table 1), 49.8 and 41.4% of obese patients had some weight loss and gain, respectively. Similar findings were observed in patients who were overweight, whereas weight gain was more frequent in patients who were underweight and normal weight at baseline (75 and 64.5%, respectively). In relation to laboratory data, all groups presented correct control of anaemia (>11 g/dL) and albumin according to the recommendations of clinical guidelines.

Table 1. Baseline demographic and clinical characteristics

Variable	Basal BMI					P-value
	Underweight (n = 35)	Normal (n = 631)	Overweight (n = 559)	Obesity (n = 307)	Total (n = 1532)	
Period						
2002–06	11 (31.4)	195 (30.9)	132 (23.6)	53 (17.3)	391 (25.5)	0.000 ^a
2007–15	24 (68.6)	436 (69.1)	427 (76.4)	254 (82.7)	1141 (74.5)	
PD treatment						
DPCC	19 (54.3)	354 (56.1)	294 (52.6)	163 (53.1)	830 (54.2)	0.648 ^a
DPAC	16 (45.7)	277 (43.9)	265 (47.4)	144 (46.9)	702 (45.8)	
Age, years ^b						
<45	15 (44.1)	170 (28.1)	71 (13.3)	37 (12.8)	293 (20.0)	0.000 ^a
45–54	5 (14.7)	111 (18.3)	100 (18.8)	62 (21.4)	278 (19.0)	
55–64	4 (11.8)	114 (18.8)	115 (21.6)	73 (25.2)	306 (20.9)	
≥ 65	10 (29.4)	211 (34.8)	246 (46.2)	118 (40.7)	585 (40.0)	
Sex						
Men	13 (37.1)	418 (66.2)	406 (72.6)	200 (65.1)	1037 (67.7)	0.000 ^a
Women	22 (62.9)	213 (33.8)	153 (27.4)	107 (34.9)	495 (32.3)	
Cause of CKD						
Standard	14 (40.0)	284 (45.0)	194 (34.7)	89 (29.0)	581 (37.9)	0.000 ^a
DM	3 (8.6)	92 (14.6)	130 (23.3)	107 (34.9)	332 (21.7)	
Others	18 (51.4)	255 (40.4)	235 (42.0)	111 (36.2)	619 (40.4)	
Malignancies ^c						
No	30 (85.7)	575 (93.6)	502 (91.8)	284 (92.5)	1391 (92.5)	0.270 ^a
Yes	5 (14.3)	39 (6.4)	45 (8.2)	23 (7.5)	112 (7.5)	
Cirrhosis and liver disease ^d						
No	29 (82.9)	602 (96.0)	534 (95.7)	297 (96.7)	1462 (95.7)	0.002 ^a
Yes	6 (17.1)	25 (4.0)	24 (4.3)	10 (3.3)	65 (4.3)	
CVD ^e						
No	21 (60.0)	465 (74.0)	350 (62.7)	179 (58.3)	1015 (66.4)	0.000 ^a
Yes	14 (40.0)	163 (26.0)	208 (37.3)	128 (41.7)	513 (33.6)	
DM						
No	31 (88.6)	472 (74.8)	327 (58.5)	133 (43.3)	963 (62.9)	0.000 ^a
Yes	4 (11.4)	159 (25.2)	232 (41.5)	174 (56.7)	569 (37.1)	
BMI variation						
Loss >4	3 (10.7)	94 (16.8)	149 (29.7)	82 (30.0)	328 (24.1)	0.000 ^a
Loss 1–4	2 (7.1)	63 (11.3)	82 (16.3)	54 (19.8)	201 (14.8)	
Remain	2 (7.1)	41 (7.3)	33 (6.6)	24 (8.8)	100 (7.3)	
Gain 1–7	8 (28.6)	169 (30.2)	137 (27.3)	79 (28.9)	393 (28.9)	
Gain >7	13 (46.4)	192 (34.3)	101 (20.1)	34 (12.5)	340 (25.0)	
Dyslipidaemia ^f						
No	21 (63.6)	411 (70.7)	380 (74.2)	213 (76.9)	1025 (73.1)	0.139 ^a
Yes	12 (36.4)	170 (29.3)	132 (25.8)	64 (23.1)	378 (26.9)	
Laboratory data	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Haemoglobin	11.54 (1.88)	12.01 (1.72)	11.87 (1.46)	11.7 (1.35)	11.88 (1.57)	0.039 ^a
Albumin	3.61 (0.72)	3.67 (0.51)	3.73 (0.47)	3.7 (0.44)	3.7 (0.48)	0.469
RCP	13.54 (29.21)	6.63 (18.01)	7.6 (15.5)	8.98 (17.01)	7.63 (17.31)	0.141

^aChi-squared test.

^bTotal = 1462.

^cTotal = 1503.

^dTotal = 1527.

^eTotal = 1528.

^fTotal = 1403.

DPAC, continuous ambulatory PD; DPCC, continuous cycling PD. Asterisks denote statistical significance.

Table 2. Total Kt/V and evolution during 4 years of follow-up

	Basal BMI					P-value
	Underweight n = 29	Normal n = 475	Overweight n = 437	Obesity n = 225	Total n = 1166	
1-year follow-up						
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
ktv_dp_total	2.59 (0.74)	2.59 (0.78)	2.58 (0.90)	2.60 (0.73)	2.59 (0.82)	0.9851
ktv_dp_renal	0.84 (0.57)	0.85 (0.48)	0.86 (0.44)	0.89 (0.40)	0.86 (0.45)	0.6781
ktv_dp_peritoneal	1.75 (0.34)	1.74 (0.59)	1.72 (0.73)	1.71 (0.61)	1.73 (0.64)	0.9161
Second year follow-up	n = 21	n = 264	n = 267	n = 122	n = 674	
ktv_dp_total	2.98 (0.68)	2.42 (0.78)	2.45 (0.74)	2.54 (0.80)	2.47 (0.77)	0.0091
ktv_dp_renal	0.94 (0.56)	0.69 (0.47)	0.79 (0.42)	0.84 (0.40)	0.77 (0.44)	0.0011
ktv_dp_peritoneal	2.03 (0.55)	1.73 (0.60)	1.66 (0.60)	1.70 (0.71)	1.70 (0.63)	0.0471
Third year follow-up	n = 14	n = 153	n = 151	n = 58	n = 376	
ktv_dp_total	4.10 (6.10)	2.30 (0.69)	2.40 (0.88)	2.35 (0.63)	2.41 (1.35)	0.0001
ktv_dp_renal	0.65 (0.52)	0.64 (0.48)	0.74 (0.50)	0.77 (0.38)	0.70 (0.48)	0.1211
ktv_dp_peritoneal	3.45 (5.87)	1.66 (0.50)	1.65 (0.63)	1.58 (0.50)	1.70 (1.21)	0.0001
Fourth year follow-up	n = 6	n = 81	n = 74	n = 34	n = 195	
ktv_dp_total	2.33 (0.99)	2.24 (0.69)	2.33 (0.60)	2.28 (0.52)	2.28 (0.64)	0.8391
ktv_dp_renal	0.52 (0.48)	0.59 (0.52)	0.75 (0.47)	0.74 (0.41)	0.68 (0.49)	0.0911
ktv_dp_peritoneal	1.81 (0.77)	1.65 (0.49)	1.57 (0.40)	1.53 (0.43)	1.60 (0.46)	0.3141

Adequacy parameters

Concerning Kt/V, all groups presented values >1.7 during the first 4 years of follow-up (Table 2).

Clinical outcomes

Peritonitis episodes were reported at a rate of 0.25 during first 3 years of PD treatment. We did not find any difference related to BMI in patients who developed peritonitis during the first 3 years of follow-up (Table 3).

KT was not reduced in obese incident patients on PD. The probability of undergoing KT was significantly lower in underweight patients, diabetic nephropathy, patients with history of CVD and the elderly population (Table 3 and Figure 1).

Concerning the probability of being transferred to HD, we found a higher incidence of transfers to HD in obese patients (23.73%) compared with patients with normal weight (19.65%, $P < 0.05$), but these differences disappeared when we adjusted the analysis by age (Table 3). Thus, in the multivariate analysis, the risk factors associated with transfer to HD were age [≥ 65 years sub-hazard ratio (SHR) = 1.86, $P = 0.000$] and diabetic nephropathy (SHR = 1.54, $P = 0.002$; Figure 2). To further analyse the survival of the PD technique, we performed an analysis including transfer to HD and death of patient and considering KT a competitive risk. In the univariate analysis, we found a reduced technique survival in the obese population ($P = 0.015$), but these differences disappeared in the multivariate analysis (Figure 3).

In terms of mortality in PD patients, we did not find differences in probability of death between the different BMI groups (Table 3). Patients who started PD in the period from 2007 to 2015 had a lower risk of death than patients starting PD from 2002 to 2006. Other risk factors for death were age, history of CVD and diabetic nephropathy (Figure 4). In the sub-analysis, which included grade of obesity, we found lower risk of death in obesity Grades II and III and a tendency to lower risk of death in obese Grade I compared with non-obese patients. It is important

Table 3. Summary of outcomes related to BMI group

Outcomes	Normal weight			
	Underweight	Overweight	Obesity	
Risk of peritonitis ^a				
Adjusted HR	1	0.77	1.03	1.06
95% CI	–	0.35–1.72	0.81–1.30	0.80–1.40
P-value	–	0.529	0.834	0.687
Undergoing KT ^b				
Adjusted HR	1	0.65	1.14	1.13
95% CI	–	0.44–0.97	0.95–1.36	0.90–1.42
P-value	–	0.034	0.165	0.287
Transfer to HD ^c				
Adjusted HR	1	1.12	0.98	1.12
95% CI	–	0.57–2.22	0.78–1.23	0.86–1.45
P-value	–	0.741	0.864	0.408
Mortality on PD ^d				
Adjusted HR	1	1.42	0.76	0.8
95% CI	–	0.62–3.25	0.57–1.02	0.55–1.16
P-value	–	0.405	0.071	0.241
Patient survival ^e				
Adjusted HR	1	1.76	0.78	0.81
95% CI	–	0.97–3.19	0.62–0.98	0.61–1.07
P-value	–	0.061	0.033	0.141

^aAdjusted by type of PD and age.

^bAdjusted by age, some CVD and primary kidney disease.

^cAdjusted by age and primary renal disease.

^dAdjusted by period, age, some CVD and primary kidney disease.

^ePatient survival until death, or time until the end of observation period.

Adjusted by period, type of PD, age, some CVD and primary kidney disease.

CI, confidence interval; HR, hazard ratio.

to note that only 75 patients were included in this group (Figure 5). In the intention-to-treat analysis, we evaluated how the initial BMI group affected PD incident patient survival even if they changed to TR or HD. Underweight patients presented worse patient survival (Figure 6).

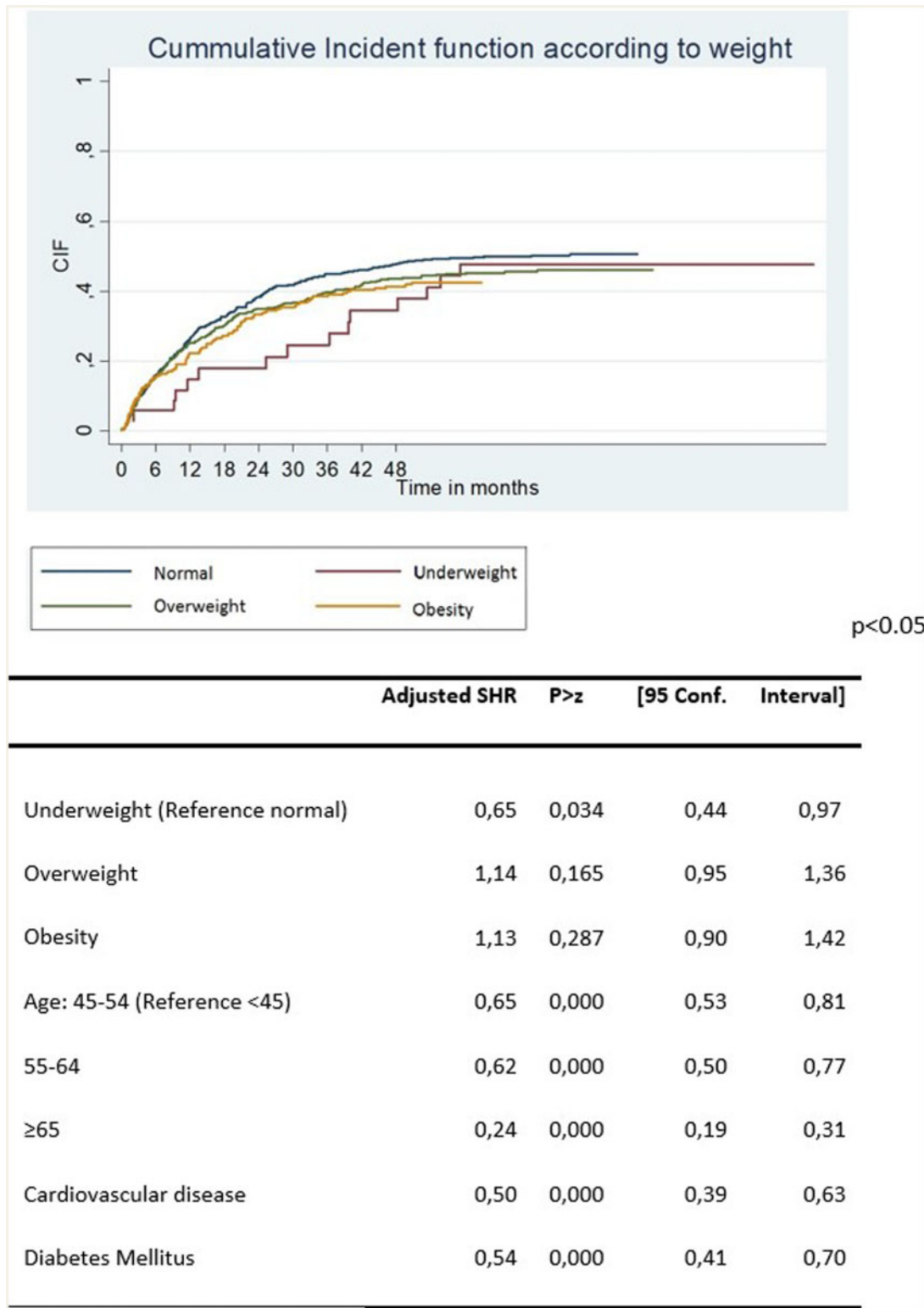


FIGURE 1: Probability of undergoing KT.

Finally, we analysed the probability of death in relation to BMI variations during the follow-up (Table 4). Interestingly, variations of BMI did not modify patient survival in the obesity group (Figure 7). However, in normal-weight patients, an increase of $\geq 7\%$ in respect to the basal weight was found to be protective (Figure 8 and Table 4).

DISCUSSION

Obesity is one of the principal modifiable CVRF in the general population [2, 3] and its protective effect in HD patients is well described [4, 6]. Nevertheless, the effect of obesity in PD population is unclear, and in Catalonia, there is not a standardized

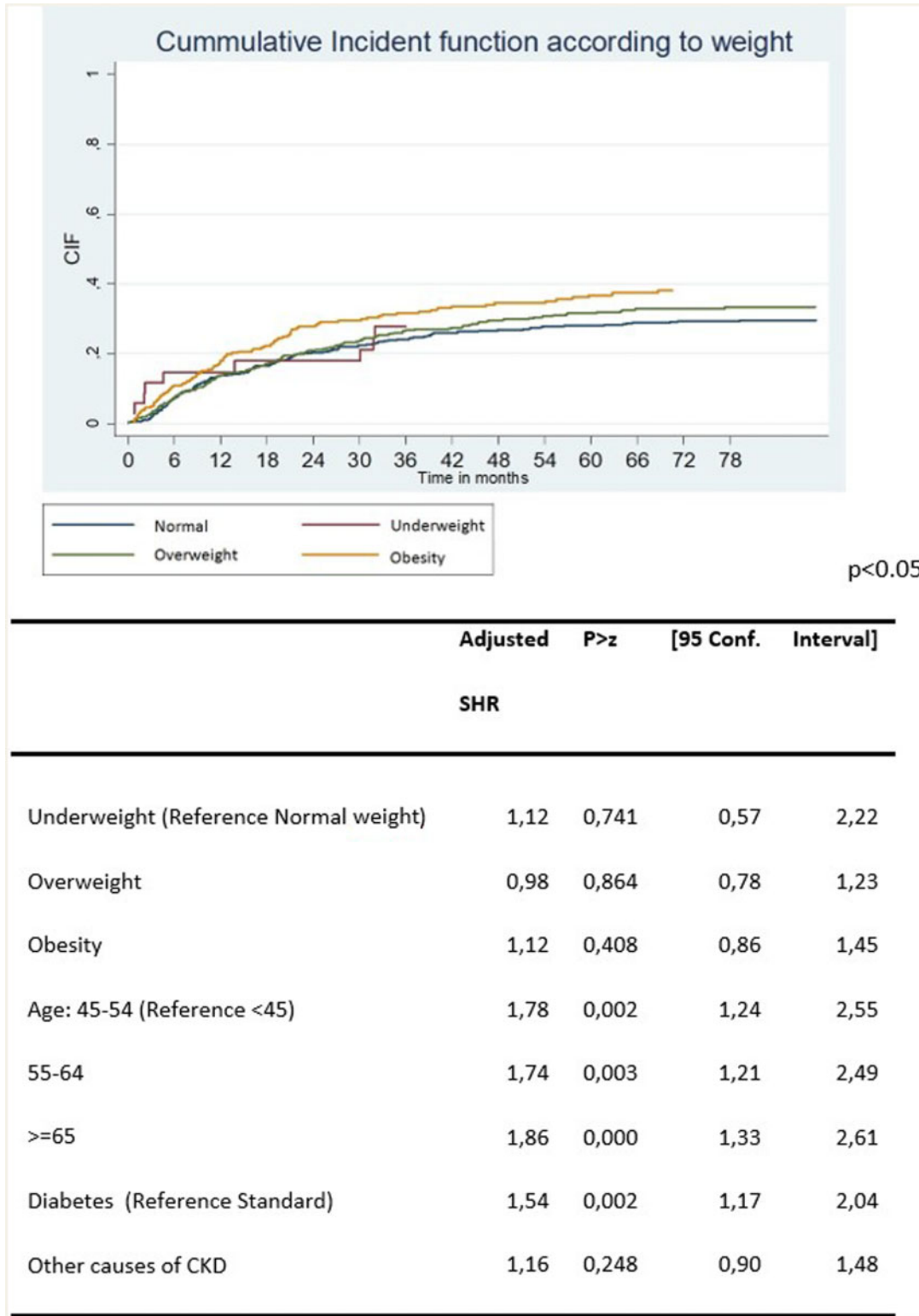
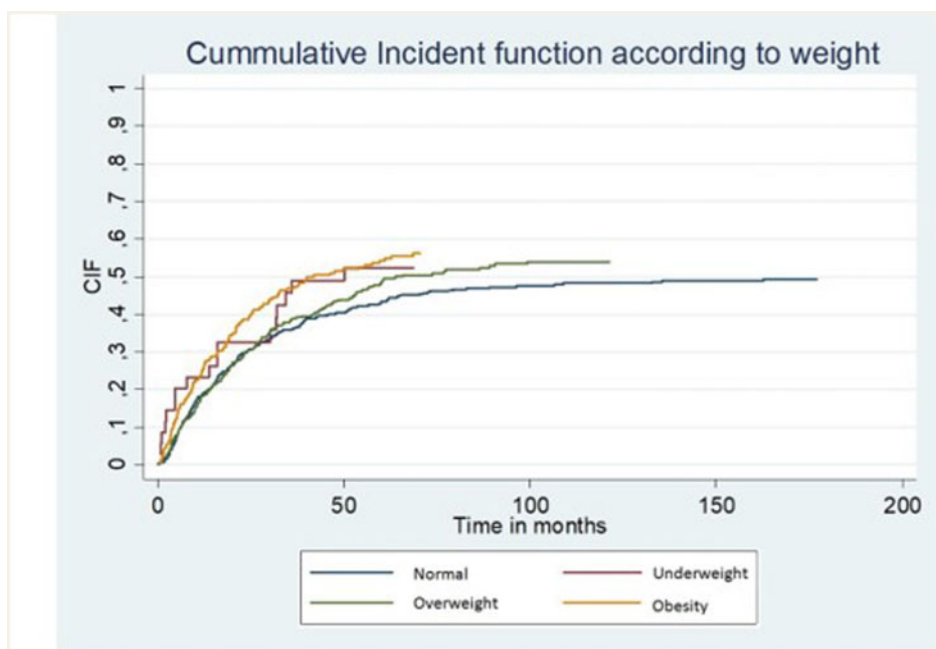


FIGURE 2: Multivariate analysis risk factors to transfer to HD.

exclusion criterion with regards to obesity and PD inclusion. The main objective of our study was to analyse the relation between obesity and BMI variation with technique and patient survival in PD patients in Catalonia.

In the general population, there has been an increase of obesity in the CKD community during the last decades, affecting nearly 30% of incident patients on dialysis in the year 2002 in the USA [15]. Pliakogiannis et al. [16] published dates from the



	Adjusted SHR	P>z	[95 Conf.	Interval]
2007-2015 (reference 2002-2006)	0,69	0,000	0,59	0,80
Underweight	1,43	0,120	0,91	2,25
(Reference Normal weight)				
Overweight	0,86	0,085	0,72	1,02
Obesity	1,02	0,870	0,83	1,25
Age: 45-54 (Reference <45)	2,13	0,000	1,52	2,97
55-64	2,18	0,000	1,57	3,03
>=65	3,34	0,000	2,45	4,55
Any cardiovascular disease	1,54	0,000	1,31	1,81
Diabetic nephropathy (Reference standard)	1,86	0,000	1,47	2,36
Other causes CKD	1,39	0,002	1,12	1,72

FIGURE 3: Multivariate analysis risk factors to technique survival (transfer to HD and death of patient).

Canadian Registry highlighting a prevalence of 13.5% of obesity in PD from 1994 to 1998; Gilbertson et al. [17] observed that 22% of the PD population in the USA were obese from 1995 to 2000, McDonald et al. [18] described 17% of PD patients were obese in

Australia and New Zealand from 1991 to 2002, and Qureshi et al. [19] illustrated a prevalence of 12% in Brazil from 2004 to 2007. In our cohort, obesity affected 20% of incident PD patients (307) from 2002 to 2015, and it is remarkable that the majority of

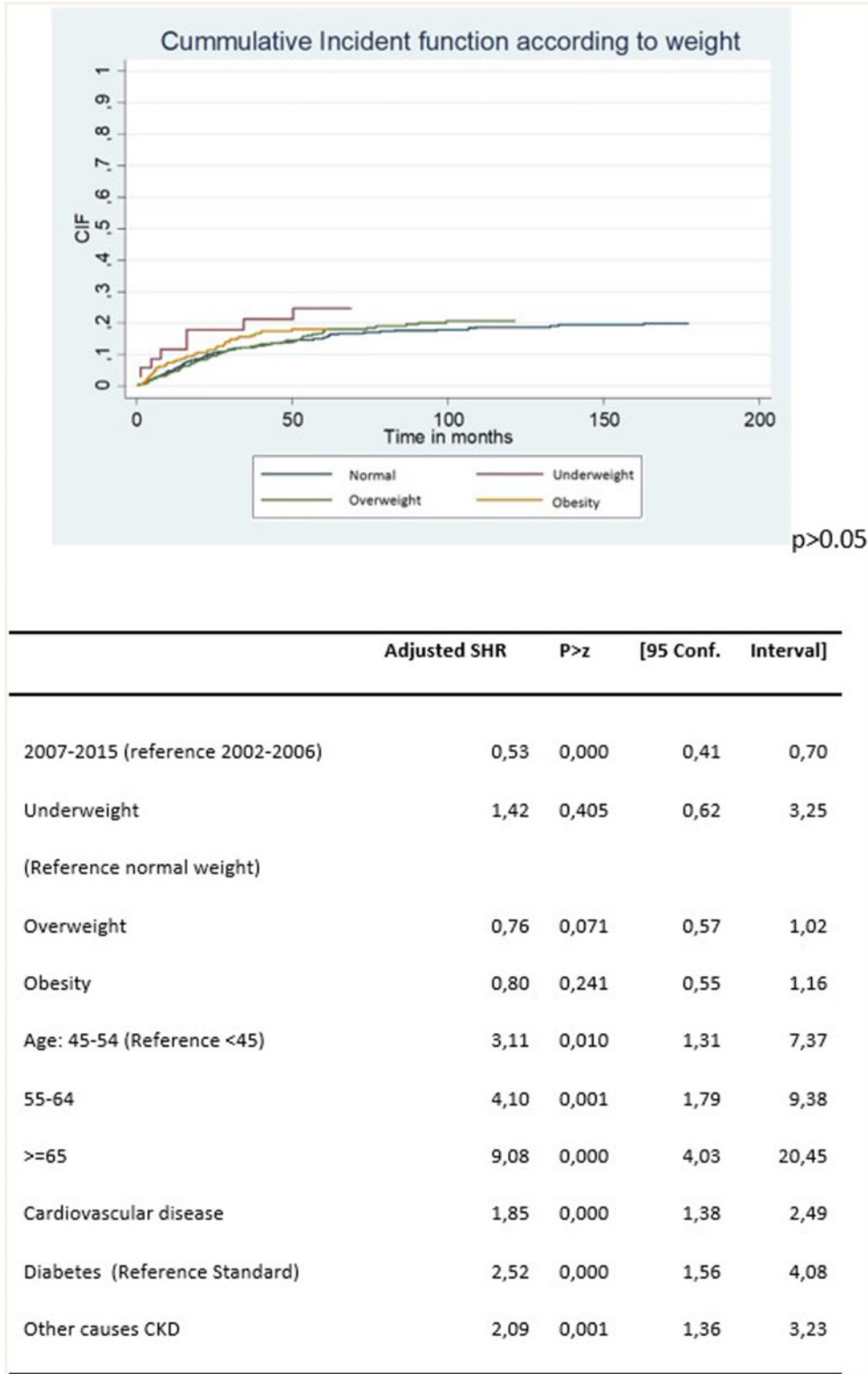


FIGURE 4: Multivariate analysis of mortality.

cases started PD after 2007 compared with the period between 2002 and 2006 (82.7% of obese cases started PD after the year 2007) (P = 0.000).

As per the general population and as per data published by McDonald et al. [18] from the ANZDATA Registry, in our cohort of

PD obese patients, we observed a higher prevalence of DM II and CVD (47.9% obese compared with 25.1% non-obese and 41.7% in obese compared with 31.5%, respectively) than in the non-obese population. On the other hand, despite finding more DM II in obese patients, Obi et al. [20] did not find more hypertension or

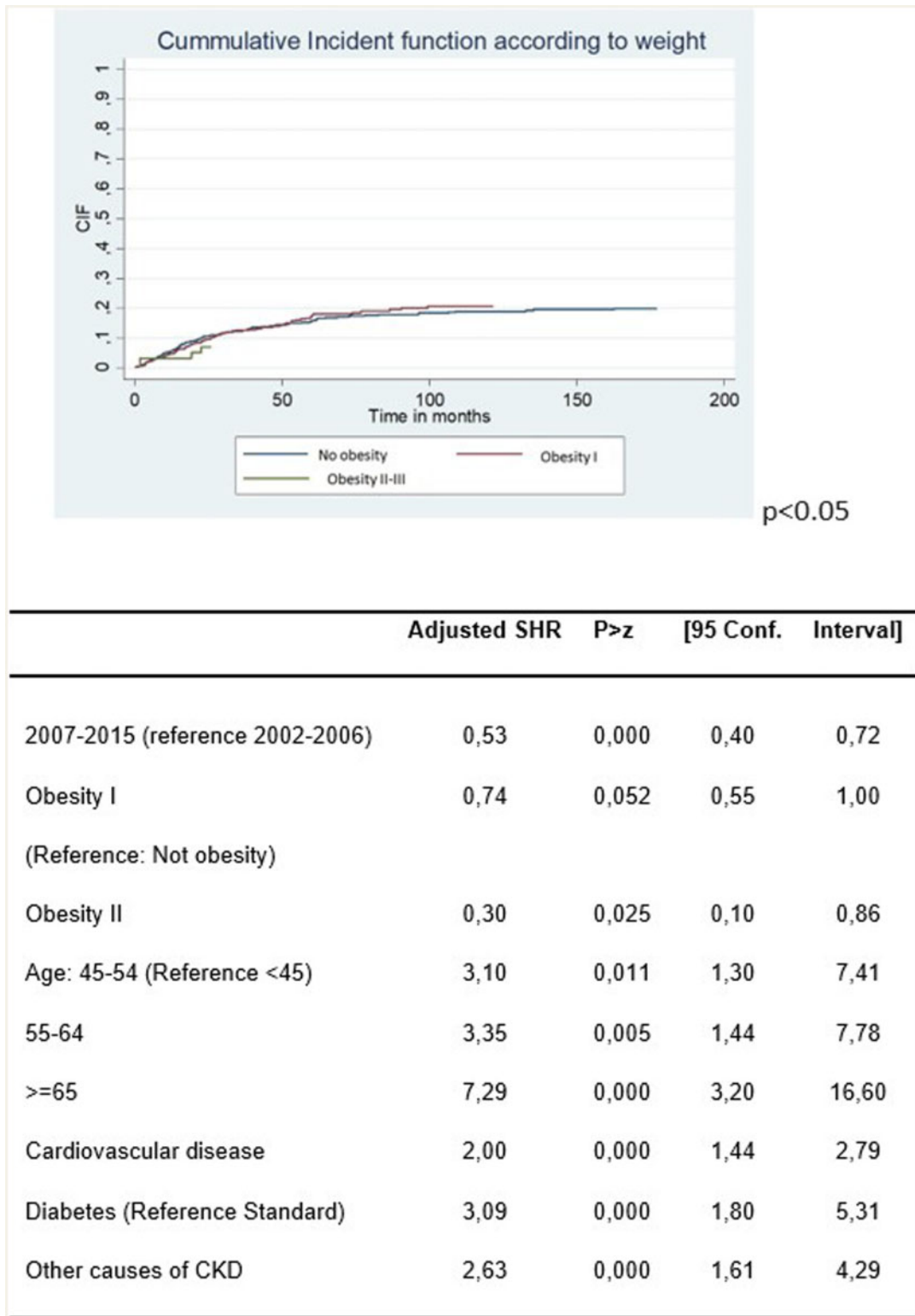


FIGURE 5: Multivariate analysis of risk of mortality. Sub-analysis stratifying by types of obesity.

risk of myocardial infarction, or other cardiac diseases, in the obese group compared with the normal weight one.

There are very few studies analysing PD adequacy in the obese PD population, and the results are conflicting. In 2002, Aslam et al. [21] did not find differences in the initial Kt/V of 104

patients with a high BMI (>27 kg/m²) compared with the control group of 104 patients with normal BMI [20–27] who were matched for age, gender, presence of DM and Charlson Comorbidity Index.

More recently, another group in the USA [22] published a single-centre experience in a small group of obese patients,

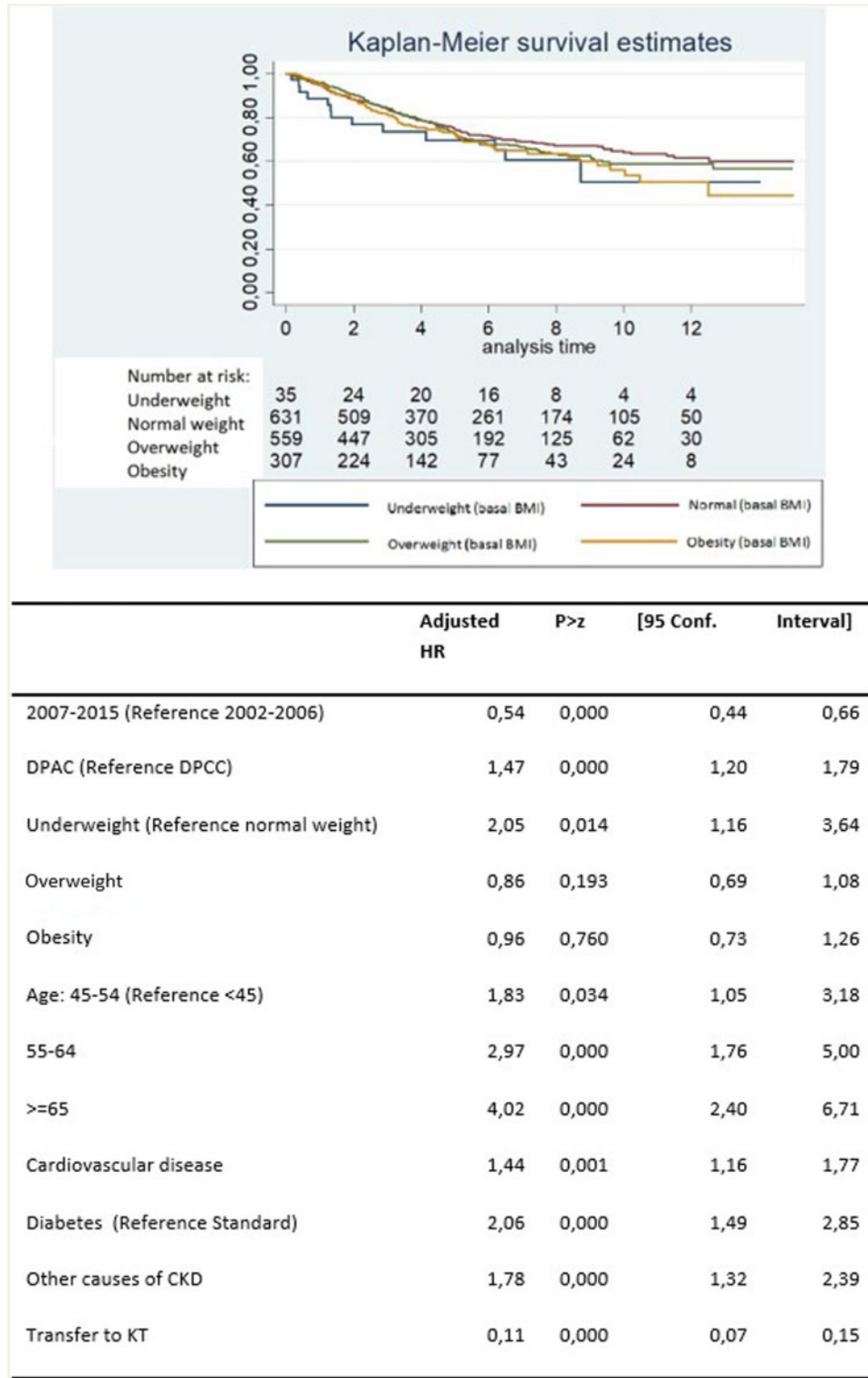


FIGURE 6: Intention-to-treat analysis of patient survival depending of BMI. DPAC, continuous ambulatory PD; DPCC, continuous cycling PD.

including obesity Class III, and did not find any differences. In our study, we have analysed a large cohort of >1500 patients, 20% of them obese, and we did not observe differences between groups during the first and fourth year of follow-up, highlighting only a better Kt/V during the second and third year in the underweight group. It is important to analyse these data with caution, because this group was very small in our population, composed

of only 28 and 23 patients during the second and third years of follow-up, respectively. One possible explanation for better Kt/V in underweight patients could be that this group of patients has a low body volume, and body volume is in the denominator in the Watson formula. As Akula et al. [22] published, one possible explanation for this is the fact that obese patients potentially present a larger abdominal surface participating in solid and

Table 4. Summary of multivariate models of mortality and patient survival in relation to change in BMI

Changes in BMI	Same BMI	Loss 1–4	Loss >4	Gain 1–7	Gain >7
Probability of dying in obese ^a					
Adjusted HR	1	1.12	0.45	1.16	0.78
95% CI	–	0.38–3.32	0.14–1.49	0.41–3.24	0.2–3.0
P-value	–	0.833	0.192	0.779	0.715
Probability of dying in non-obese (normal + overweight + underweight) ^b					
Adjusted HR	1	0.59	0.57	0.59	0.64
95% CI	–	0.30–1.14	0.31–1.04	0.33–1.05	0.36–1.14
P-value	–	0.118	0.065	0.074	0.133
Survival in PD for intention-to-treat in obese ^c					
Adjusted HR	1	1.35	1.00	1.27	0.40
95% CI	–	0.54–3.35	0.41–2.45	0.54–3.01	0.11–1.40
P-value	–	0.524	0.997	0.583	0.152
Survival in PD for intention-to-treat in non-obese (normal + overweight + underweight) ^d					
Adjusted HR	1	1.00	0.97	0.76	0.59
95% CI	–	0.61–1.62	0.62–1.54	0.48–1.20	0.37–0.94
P-value	–	0.976	0.911	0.240	0.027

^aAdjusted by age.

^bAdjusted by period, age, CVD and CKD.

^cAdjusted for period, age, CKD and change of PD to HD or KT.

^dAdjusted for period, type of initial PD, age, CVD and change from PD to HD or KT. CI, confidence interval; HR, hazard ratio.

fluid exchange, and that the fat tissue is not producing many uraemic toxins or participating in urea distribution volume.

Concerning peritonitis, McDonald *et al.* [23] analysed data from the ANZDATA Registry, including a large cohort of >10 000 patients who received PD, and recorded time to first develop peritonitis and episodes of peritonitis per patient-year over a 12-year period. In our study, we did not find differences between BMI groups but, in contrast, they found that higher BMI was associated with a shorter time to develop a first peritonitis episode, independent of other risk factors.

Obi *et al.* [20] studied peritonitis-related and non-peritonitis-related hospitalization and they detected higher incidence of peritonitis-related hospitalization across higher BMI categories in all adjustment models. In contrast, we did not find differences in time to develop a first peritonitis episode, even after stratifying patients into obesity Grades I–III.

Regarding KT, in contrast to the data published by Obi *et al.* [20], Lievense *et al.* [24] described that obese incident PD patients had the same likelihood of undergoing KT as the entire PD cohort. In that line, we did not observe differences in the probability of receiving a KT in obesity group.

In relation to technique survival, the obese group did not show more incidence of transfer to HD in the multivariate analysis as described by some authors previously in prospective observational [25] and multicentre studies [21]. In contrast to our results, data published in a meta-analysis [14] and some cohort studies [17, 18, 20, 26] showed more technique failure in obese patients. One possible explanation for our results showing better technique survival in the obese population could be our peritonitis rate, as peritonitis is one of the most important causes of technique failure. Most studies described obesity as a risk factor for peritonitis episodes and in our population, we did not find differences between BMI groups.

Ahmadi *et al.* [14] published a meta-analysis to analyse the association of BMI and mortality in PD patients. After excluding overlap data, they only included four papers and concluded that underweight patients were associated with higher 1-year

mortality and being overweight with lower 1-year mortality. They also explained that although the association of obese patients with first-year mortality was not significant, both meta-analysed studies [17, 19] showed that being obese at baseline was associated with lower 1-year mortality. These differences in relation to mortality are not maintained over time. In our cohort, we did not find differences in probability of death between the four groups of BMI, but when we performed the sub-analysis comparing non-obese, obese Grade I and obese Grades II and III, we found less risk of death in obese Grades II and III (SHR = 0.30, $P=0.025$) and a tendency of less risk of death in obese Grade I (SHR = 0.74, $P=0.052$). It is important to note that there were only 75 patients included in this last group.

We also analysed the probability of death in relation to BMI variations during the follow-up and we did not find any difference. Qureshi *et al.* [19] also evaluated changes of BMI over time, and they observed a significantly higher mortality in normalized weight with a decrease $\geq 3.1\%$. In that line, in the intention-to-treat analysis, we found that underweight patients presented worse survival (SHR = 2.05, $P=0.014$). Regarding variations in BMI, we did not observe any difference in the obese population; however, an increase of $\geq 7\%$ respect to the basal weight represented a protective factor in non-obese patients on PD (adjusted hazard ratio = 0.59, $P=0.027$).

It is important to note that obese patients had more DM and CVDs, and both entities related to higher mortality.

Our study has several strengths and limitations. The main limitation is that it was a retrospective study based on registry data; we do not have data about the type of dialysis fluid used (use of icodextrin and biocompatible or bioincompatible fluids), and as in most epidemiological studies, we only used BMI as an indicator of obesity. Although BMI has been accepted as one of the most reliable anthropometric indices for obesity, it has a limited ability to differ between muscle mass, adiposity and water. Many PD patients could be overhydrated, especially at the beginning of the treatment, and changes in water component could be related to changes in body weight. Despite the

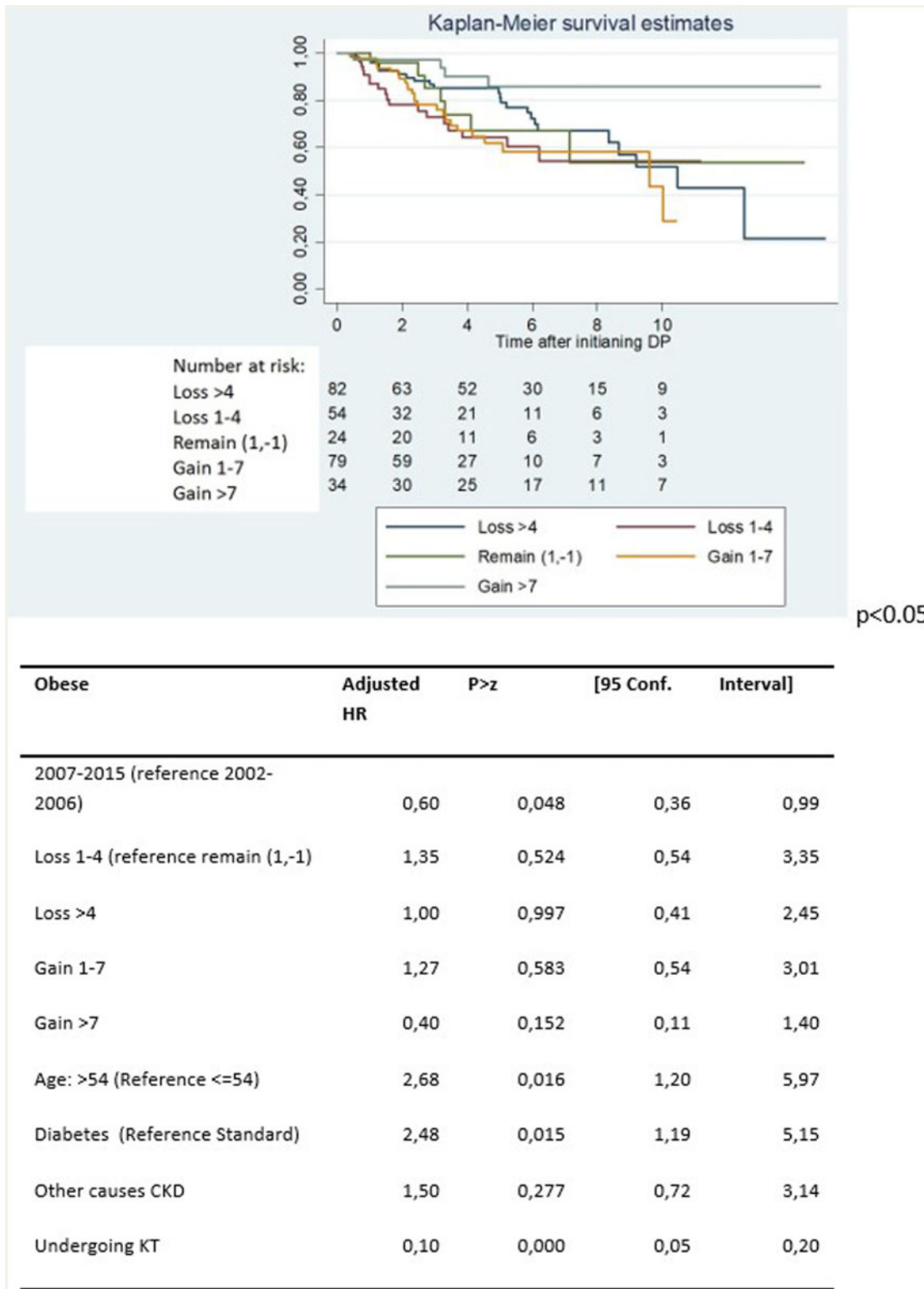


FIGURE 7: Intention-to-treat analysis of patient survival depending of BMI variations in obese patients.

fact that most PD units use clinical criteria and bioimpedance in clinical practice to analyse the state of hydration, this article used retrospective cohort data, and these data are not available.

The main strength is that a large population of incident PD subjects was studied, and our results are in concordance with

other published epidemiological studies; therefore, these results could be extrapolated.

In conclusion, we observed that the prevalence of obese PD patients is growing, and this entity is not related to worst outcomes. The obese PD population presented more prevalence of DM and CVD, but they did not have differences in adequacy

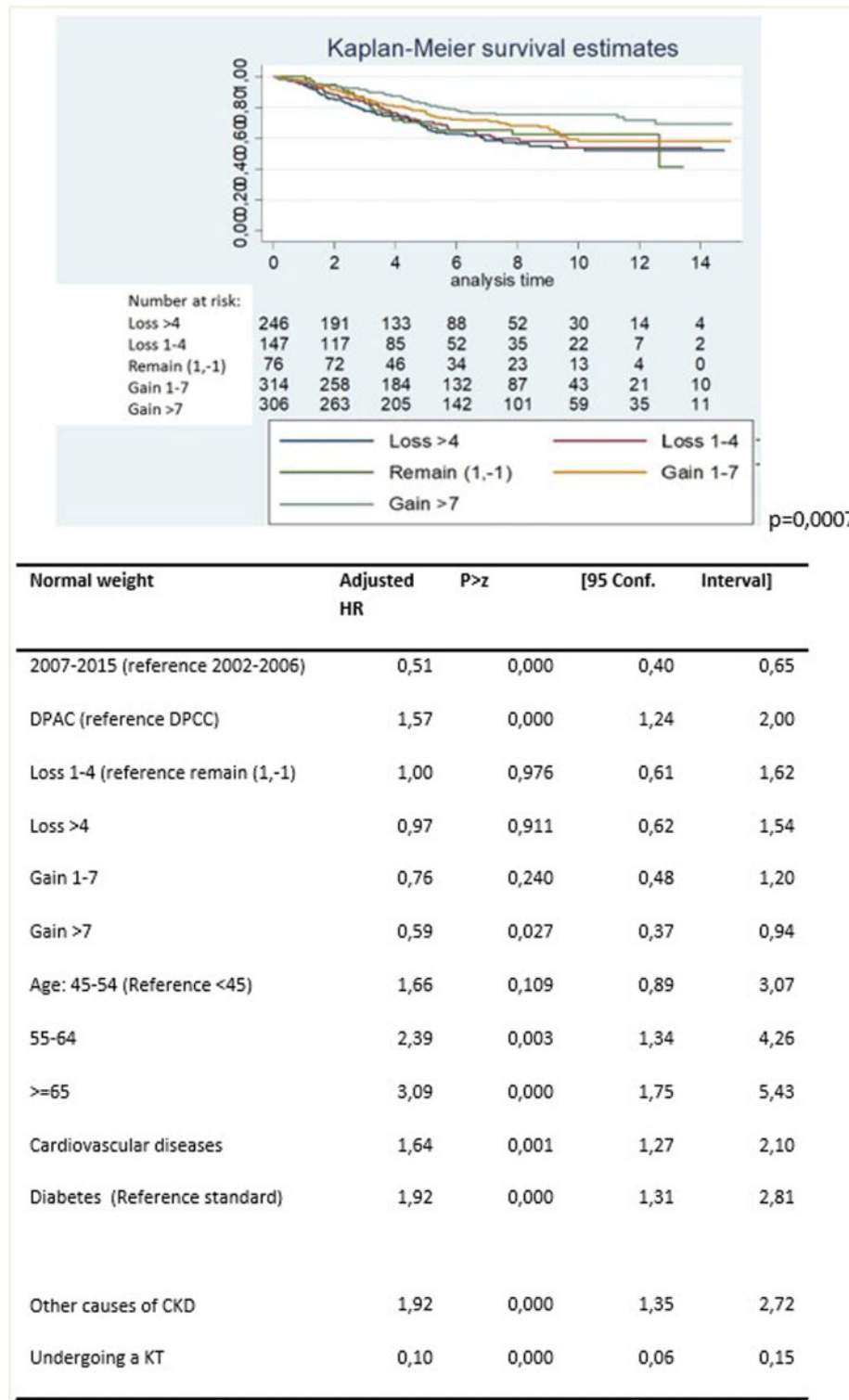


FIGURE 8: Intention-to-treat analysis of patient survival depending of BMI variations in normal weight patients. DPAC, continuous ambulatory PD; DPCC, continuous cycling PD.

parameters, risk of peritonitis, technique failure and probability of undergoing KT in terms of either mortality or patient survival. In addition, variations of BMI are not related to changes in mortality rate or patient survival in the obese population, but an increase of >7% in BMI in non-obese patients is supposed to be a protective factor.

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AUTHORS' CONTRIBUTIONS

M.Q. and I.R. interpreted the data, drafted the manuscript and revised the article critically. N.M. and M.H. analysed and interpreted the data and drafted the article. E.A. and J.C. performed the acquisition of data, analysed data, drafted the article and revised the article critically. D.S. and P.C.-B. revised the article critically. J.M.C. designed the study, interpreted the data and revised the article critically.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

REFERENCES

- GBD. Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med* 2017; 377: 13–27
- Singh GM, Danaei G, Farzadfar F et al.; Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group; Asia-Pacific Cohort Studies Collaboration (APCSC). The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: A pooled analysis. *PLoS One* 2013; 8: e65174
- Lauby-Secretan B, Scoccianti C, Loomis D et al. Special report body fatness and cancer. *N Engl J Med* 2016; 375: 794–798
- Kalantar-Zadeh K, Block G, Humphreys MH et al. Reverse epidemiology of cardiovascular risk factors in maintenance dialysis patients. *Kidney Int* 2003; 63: 793–808
- Registre de malalts renals de Catalunya Informe Estadístic 2016, Vol. 29. Departament de Salut de la Generalitat de Catalunya, 2018, 1–170
- Wolfe RA, Ashby VB, Daugirdas JT et al. Body size, dose of hemodialysis, and mortality. *Am J Kidney Dis* 2000; 35: 80–88
- Kalantar-Zadeh K, Kopple JD, Kilpatrick RD et al. Association of morbid obesity and weight change over time with cardiovascular survival in hemodialysis population. *Am J Kidney Dis* 2005; 46: 489–500
- Jing J, Dukkipati R, Molnar MZ et al. Mortality predictability of body size and muscle mass surrogates in Asian vs White and African American hemodialysis patients. *Mayo Clin Proc* 2013; 88: 479–486
- WHO. WHO Obesity. 2015. http://www.who.int/gho/ncd/risk_factors/obesity_text/en/ (2 July 2017, date last accessed)
- Ricks J, Molnar MZ, Kovesdy CP et al. Racial and ethnic differences in the association of body mass index and survival in maintenance hemodialysis patients. *Am J Kidney Dis* 2011; 58: 574–582
- Del Peso G, Bajo MA, Costero O, et al. Risk factors for abdominal wall complications in peritoneal dialysis patients. *Perit Dial Int* 2003; 23: 249–254
- Johnson DW, Mudge DW, Sturtevant JM et al. Predictors of decline of residual renal function. *Perit Dial Int* 2003; 23: 276–283
- Ong LM, Ahmad G, Mushahar L et al. Risk of peritoneal dialysis-related peritonitis in a multi-racial asian population. *Perit Dial Int* 2017; 37: 35–43
- Ahmadi SF, Zahmatkesh G, Streja E et al. Association of body mass index with mortality in peritoneal dialysis patients: a systematic review and meta-analysis. *Perit Dial Int* 2016; 36: 315–325
- Friedman AN. Obesity in patients undergoing dialysis and kidney transplantation. *Adv Chronic Kidney Dis* 2013; 20: 128–134
- Pliakogiannis T, Trpeski L, Taskapan H et al. Reverse epidemiology in peritoneal dialysis patients: the Canadian experience and review of the literature. *Int Urol Nephrol* 2007; 39: 281–288
- Gilbertson DT, Vonesh EF, Foley RN et al. Body size and outcomes on peritoneal dialysis in the United States. *Kidney Int* 2003; 64: 1838–1844
- McDonald SP, Collins JF, Johnson DW. Obesity is associated with worse peritoneal dialysis outcomes in the Australia and New Zealand patient populations. *J Am Soc Nephrol* 2003; 14: 2894–2901
- Qureshi A, Fernandes N, Franco M et al. Body size and longitudinal body weight changes do not increase mortality in incident peritoneal dialysis patients of the Brazilian peritoneal dialysis multicenter study. *Clinics* 2013; 68: 51–58
- Obi Y, Streja E, Mehrotra R et al. Impact of obesity on modality longevity, residual kidney function, peritonitis, and survival among incident peritoneal dialysis patients. *Am J Kidney Dis* 2018; 71: 802–813
- Aslam N, Bernardini J, Fried L et al. Large body mass index does not predict short-term materials and methods. *Perit Dial Int* 2002; 22: 191–196
- Akula YV, Fülöp T, Dixit MP. Peritoneal dialysis in class 2-3 obesity—a single-center experience. *Am J Med Sci* 2017; 353: 70–75
- McDonald SP, Collins JF, Rumpfeld M et al. Obesity is a risk factor for peritonitis in the Australian and New Zealand Peritoneal Dialysis Patient populations. *Perit Dial Int* 2004; 24: 340–346
- Lievense H, Kalantar-Zadeh K, Lukowsky LR et al. Relationship of body size and initial dialysis modality on subsequent transplantation, mortality and weight gain of ESRD patients. *Nephrol Dial Transplant* 2012; 27: 3631–3638
- Prasad N, Sinha A, Gupta A et al. Effect of body mass index on outcomes of peritoneal dialysis patients in India. *Perit Dial Int* 2014; 34: 399–408
- Badve SV, Brown FG, Mudge DW et al. Automated and continuous ambulatory peritoneal dialysis have similar outcomes. *Kidney Int* 2008; 73: 480–488
- Kalantar-Zadeh K, Kilpatrick RD, Kuwae N et al. Reverse epidemiology: a spurious hypothesis or a hardcore reality? *Blood Purif* 2005; 23: 57–63