Effect of icodextrin dialysis solution on body weight and fat accumulation over time in CAPD patients

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Abstract

Background. The purpose of this study was to analyse the changes of body composition and the effects of icodextrin dialysis solution over time on peritoneal dialysis (PD) in continuous ambulatory peritoneal dialysis (CAPD) patients.

Methods. Among 183 incident patients, 75 patients finished a complete 36-month protocol. Clinical indices including daily glucose absorption and body composition, by bioelectrical impedance analysis (BIA), were measured in both groups (icodextrin group: 36 patients, non-icodextrin group: 39 patients) at the 1st (baseline), 12th, 24th and 36th months.

Results. There were significant increases in body weight and fat mass during the 36 months after initiation of CAPD. It was found that 78% of 3 years of weight gain occurred during the first year and 88% of weight gain at the end of the first year was fat mass gain. The icodextrin group showed a significantly lower percent of fat mass during the first 36 months ($P < 0.05$) and also less changes in body weight, fat mass, percent (%) fat mass, visceral fat area and waist/hip ratio at 1, 2 and 3 years than the non-icodextrin group. There were no significant changes in total body water (TBW), extra cellular fluid (ECF), oedema index and lean body mass (LBM) through comparable daily and ultrafiltration volume (UFV) between the two groups during the initial 3 years. Factors associated with the higher percent of fat mass gain over time on peritoneal dialysis were age, diabetes, gender (female) and non-icodextrin group (all, $P < 0.01$, generalized estimating equation).

Conclusion. The application of icodextrin solution may be a better option to alleviate excessive fat gain over time for patients on PD.

Keywords: fat accumulation; icodextrin; peritoneal dialysis (PD)

Introduction

Peritoneal dialysis (PD) has been regarded as a very useful renal replacement therapy for end-stage renal disease, most importantly being better preservation of residual renal function and better cardiovascular stability. However, many patients on peritoneal dialysis show marked weight gain and fat mass accumulation after the initiation of peritoneal dialysis [1–3]. Accumulation of fat, especially visceral adipose tissue, is considered an important risk factor for cardiovascular disease [4]. The mechanism of rapid accumulation of fat tissue in many peritoneal dialysis patients has not been clearly defined. The initiation of peritoneal dialysis is associated with an increased continuous intraperitoneal carbohydrate load and it may be one explanation for fat mass accumulation [5]. Glucose is the most commonly used osmotic agent in peritoneal dialysis solutions, but its use has been associated with a variety of metabolic consequences, such as acute hyperglycaemia, hyperinsulinaemia and eventually weight gain and dyslipidaemia [6]. Icodextrin is a polymer of glucose molecules, but is absorbed more slowly from the peritoneal cavity compared to glucose. It has a longer duration of ultrafiltration and a lower carbohydrate load compared to 2.5% and 4.25% dextrose dialysis solutions [7]. Replacement of glucose-based dialysis solutions by icodextrin is expected to result in different metabolic profiles from those observed using glucose-based solutions [6]. We hypothesized that the icodextrin dialysis solution may reduce fat accumulation in peritoneal dialysis patients by a decrease in glucose absorption from dialysate and other mechanisms. The purpose of this study was to analyse the changes in body composition over time on peritoneal dialysis in new continuous ambulatory peritoneal dialysis (CAPD) patients and to evaluate the effects of icodextrin dialysis solution on the changes in body composition over time.

Methods

Patients

A total of 183 new CAPD patients from Yeungnam University Hospital were enrolled from June 2001 to September 2004. All patients gave informed consent to participate in the study. Exclusion criteria included severe systemic disease, such as liver cirrhosis or malignancy. The study protocol was approved by the local ethics committee of Yeungnam University Hospital. A total of 75 patients completed a 36-month protocol. One hundred and eight patients were excluded from the analysis mostly due to protocol violations (extraneal 11, non-extraneal 35), death (extraneal 4, non-extraneal 40), transfer to haemodialysis (extraneal 1, non-extraneal 7), renal transplantation (extraneal 2, non-extraneal 3), or transfer to an alternative dialysis centre (extraneal 2, non-extraneal 3) (Figure 1). Among the
enrolled 183 patients, there was a difference between the icodextrin group and the non-icodextrin group in the number of deaths before completing a 36-month protocol \((P < 0.01)\). Among the 75 patients, 32 (42.7\%) were female and 28 (37.3\%) were diabetic. The mean age at entry was 46.0 ± 13.1 years. None of the patients had any record of peritonitis and/or exit site infection for the 4 weeks prior to annual measurements. The kinds of dialysis solution in 75 patients at the 1st, 12th, 24th and 36th months are shown in Table 1. The icodextrin solution was prescribed once daily to the patients who suffered from inadequate control of oedema and ultrafiltration failure, or who wanted to have a long-term dwell to improve the quality of their lives. Ultrafiltration failure was defined such that the net ultrafiltration volume was below 400 ml after a 4 h 2 l 4.25% glucose dialysate. The icodextrin group was defined as the group of patients who used the icodextrin solution for at least 6 months (6–36 months, mean: 24.8 ± 10.9 months).

**Table 1. Kinds of dialysis solution in 75 patients**

<table>
<thead>
<tr>
<th></th>
<th>1st month</th>
<th>12th month</th>
<th>24th month</th>
<th>36th month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dianeal® (ICO)</td>
<td>42 (9)</td>
<td>36 (18)</td>
<td>25 (16)</td>
<td>20 (16)</td>
</tr>
<tr>
<td>Physioneal® (ICO)</td>
<td>6 (1)</td>
<td>17 (16)</td>
<td>22 (16)</td>
<td></td>
</tr>
<tr>
<td>Stay-safe®</td>
<td>12</td>
<td>12</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Balance®</td>
<td>21</td>
<td>21</td>
<td>30</td>
<td>32</td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
</tbody>
</table>

ICO, the number of patients who used icodextrin.

Calculations of dialysis adequacy and urea kinetics

Weekly Kt/V urea was calculated from a 24-h collection of dialysate and urine. The distribution volume of urea, which is generally assumed to be equal to total body water (TBW), was calculated with V, estimated from the Watson equation [9]. The residual renal function (RRF) was calculated as the average of residual renal creatinine and urea clearances. Dietary protein intake was estimated from the protein equivalent of nitrogen appearance (PNA) using the following equation: \(\text{PNA} = 15.1 + 0.195 \times \text{urea appearance (mmol/24 h)} + \text{protein losses (g/24 h)}\) [10]. Urea appearance rate and protein losses were determined from the measured urea and protein excretion in the dialysate and urine. PNA was normalized for actual body weight to obtain nPNA (g/kg body wt/24 h). The daily (24 h) peritoneal glucose absorption was calculated from the infused dialysate volumes and glucose concentrations during the 24 h time interval minus the directly measured volume and glucose concentration of the daily (24 h) drained dialysate.

Measurement of body composition

The measurement of body composition by BIA, weight, and height were performed in all patients in the 1st month after the initiation of peritoneal dialysis and again in the 12th, 24th and 36th months. BIA measurements were carried out using the segmental multifrequency bioelectrical impedance analyser (Inbody 2.0/4.0, Biospace, Seoul, Korea) with eight skin electrodes on both hands and feet while in the standing position. The analyser measures body impedance with six frequencies ranging from 1 to 1000 kHz. The body weight, total body water (TBW), extracellular fluid (ECF), oedema index (ECF/TBW), fat mass, percent (%) fat mass, waist/hip ratio, visceral fat area and lean body mass were measured after drainage of the dialysate. BIA was always performed after drainage of the peritoneal dialysate after a 4.25\% PET, to avoid the effect of dialysate in the peritoneal cavity on the results.

Statistical analysis

The changes over time were compared using a paired \(t\)-test and the differences between the groups were compared using an independent \(t\)-test, Fisher’s exact test, repeated measures ANOVA (SPSS 12.0, Chicago, IL). Factors affecting dependent variables were assessed by the generalized estimating equations population-averaged model (Stata: Stata Corp LP, College Station, TX, USA). Values were presented as mean ± standard deviation, and \(P\)-values below 0.05 were considered significant.

Results

The serial changes of body compositions and laboratory values over time on CAPD

There was significant body weight gain during the 36 months (3.2 ± 6.0 kg, \(P < 0.01\)) and 78\% (2.5 ± 5.0 kg) of total weight gain during the initial 3 years occurred during the initial year. Similarly, the amount of fat mass (14.5 ± 5.8 kg to 16.7 ± 6.1 kg), \% fat mass (23.2 ± 6.8\% to 25.7 ± 7.5\%), visceral fat area (78.7 ± 32.6 cm\(^2\) to 87.4 ± 32.7 cm\(^2\)) and waist/hip ratio (0.865 ± 0.057 to 0.882 ± 0.062) were most markedly increased during the first year (all \(P < 0.01\), respectively).

There was a difference in pattern of gained lean body mass during initial 3 years. Significant increases in ultrafiltration volume (UFV) \((P < 0.05, P < 0.01, P < 0.01\), respectively) and decreases in oedema index (all \(P < 0.01\), respectively) at the 12th, 24th and 36th months were observed. The proportion of gained fat mass in relation to gained body weight at the 12th, 24th and 36th months was decreased over time on PD (88\%, 70\% and 53\%, all \(P < 0.01\)), whereas the gained lean body mass increased over time.
Effect of icodextrin on fat accumulation in CAPD patients

Table 2. Serial changes of body composition and laboratory values over time on PD

<table>
<thead>
<tr>
<th></th>
<th>1st month (Baseline)</th>
<th>36th month</th>
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<tbody>
<tr>
<td></td>
<td>Icodextrin (n = 36)</td>
<td>Non-icodextrin (n = 39)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>62.9 ± 12.5</td>
<td>60.6 ± 9.1</td>
</tr>
<tr>
<td>TBW (l)</td>
<td>33.9 ± 7.0</td>
<td>31.9 ± 4.9</td>
</tr>
<tr>
<td>ECF (l)</td>
<td>12.2 ± 2.6</td>
<td>11.8 ± 2.3</td>
</tr>
<tr>
<td>Oedema index</td>
<td>0.360 ± 0.027</td>
<td>0.369 ± 0.030</td>
</tr>
<tr>
<td>LBM (kg)</td>
<td>48.4 ± 9.1</td>
<td>46.0 ± 7.0</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>14.4 ± 6.0</td>
<td>14.6 ± 5.6</td>
</tr>
<tr>
<td>% fat mass (%)</td>
<td>22.6 ± 6.5</td>
<td>23.7 ± 7.1</td>
</tr>
<tr>
<td>VFA (cm²)</td>
<td>80.6 ± 29.5</td>
<td>77.3 ± 35.3</td>
</tr>
<tr>
<td>W/H ratio</td>
<td>0.862 ± 0.054</td>
<td>0.867 ± 0.060</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.0 ± 3.6</td>
<td>23.1 ± 3.5</td>
</tr>
<tr>
<td>UVF (ml/day)</td>
<td>237.7 ± 652.7</td>
<td>866.9 ± 567.1</td>
</tr>
<tr>
<td>UV (ml/day)</td>
<td>995.3 ± 569.9</td>
<td>847.7 ± 516.7</td>
</tr>
<tr>
<td>4 h D/P Cr</td>
<td>0.714 ± 0.093</td>
<td>0.693 ± 0.092</td>
</tr>
<tr>
<td>D-Glu abs (g/day)</td>
<td>71.6 ± 28.1</td>
<td>79.4 ± 28.5</td>
</tr>
<tr>
<td>D-Pro loss (g/day)</td>
<td>5.7 ± 2.7</td>
<td>7.1 ± 4.0</td>
</tr>
<tr>
<td>Weekly Kt/V</td>
<td>2.31 ± 0.54</td>
<td>2.51 ± 0.63</td>
</tr>
<tr>
<td>RRF (ml/min)</td>
<td>3.80 ± 2.64</td>
<td>3.61 ± 2.40</td>
</tr>
<tr>
<td>nPCR (g/kg/day)</td>
<td>0.85 ± 0.19</td>
<td>0.96 ± 0.21†</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>10.1 ± 1.0</td>
<td>9.9 ± 1.0</td>
</tr>
<tr>
<td>S-CRP (mg/dl)</td>
<td>0.66 ± 1.16</td>
<td>0.61 ± 2.01</td>
</tr>
<tr>
<td>S-albumin (mg/dl)</td>
<td>3.54 ± 0.58</td>
<td>3.32 ± 0.56</td>
</tr>
<tr>
<td>S-T cho (mg/dl)</td>
<td>177.6 ± 38.1</td>
<td>175.5 ± 37.6</td>
</tr>
</tbody>
</table>

TBW, total body water; ECF, extra cellular fluid; oedema index, ECF/TBW; LBM, lean body mass; % fat mass, percent fat mass; VFA, visceral fat area; W/H ratio, waist/hip ratio; BMI, body mass index; UVF, daily ultrafiltration volume; UV, daily urine volume; 4 h D/P Cr, 4 h dialysate/plasma creatinine ratio; D-Glu abs, daily glucose absorption from the peritoneum; D-Pro loss, daily protein loss from the peritoneum; RRF, residual renal function (mean of creatinine clearance and urea clearance); nPCR, normalized protein catabolic rate; Hb, blood haemoglobin; S-CRP, serum C-reactive protein; S-T cho, serum total cholesterol.

Data are means ± SD. *P < 0.05, **P < 0.01, compared with first month, †P < 0.05, ‡P < 0.01, comparing between icodextrin and non-icodextrin groups.

The comparison between the icodextrin group and the non-icodextrin group

Thirty-six patients (48.0%) were in the icodextrin group and 39 patients (52.0%) were in the non-icodextrin group. There were no differences in sex [female 14/36(39%), 18/39(46%)], age (43.8 ± 12.5 versus 48.0 ± 13.5) and diabetes [11/36(31%) versus 17/39(44%)] between the icodextrin group and the non-icodextrin group. As shown in Table 2, there were no significant differences in parameters except daily ultrafiltration volume and nPCR at the 1st month (baseline) between the two groups.

The differences in the changes of body composition over time between the two groups are summarized in Table 2. Compared with the non-icodextrin group, the icodextrin group showed less changes in body weight, fat mass, % fat mass, visceral fat area and waist/hip ratio during year 1, year 2 and year 3 (Figure 2A–D). The icodextrin group showed higher lean body mass gain at the 36 months (1.8 ± 0.05, Figure 3A) and the non-icodextrin group showed higher fat mass gain at the 12th, 24th and 36th respectively, Figure 3B. The proportion of gained fat mass in relation to gained body weight at the 12th, 24th and 36th months were decreased over time on PD in the icodextrin group (77%, 30% and −6%) and the non-icodextrin group (86%, 80% and 72%) whereas, the gained lean body mass (LBM) increased over time (Figure 3).

In a repeated measures ANOVA, the icodextrin group showed significantly lower % fat mass than the non-icodextrin group during the first 36 months (P < 0.05).

The icodextrin group showed less delta changes of glucose absorption via dialysate than the non-icodextrin group during 2 and 3 years (−24.1 ± 27.3 g/day versus −1.5 ± 24.9 g/day and −12.5 ± 46.9 g/day versus 6.9 ± 31.9 g/day, P < 0.01 and P < 0.05, respectively).

There was a significant decrease in oedema index (ECF/TBW) in both icodextrin group and non-icodextrin group over time on PD (−0.013 ± 0.022, −0.013 ± 0.028, −0.006 ± 0.030 and −0.012 ± 0.020, −0.012 ± 0.023, −0.009 ± 0.025 delta changes during 1, 2 and 3 years, P < 0.01, P < 0.01, P > 0.05 and P < 0.01, P < 0.05, respectively), but there were no significant differences in delta changes of oedema index between the icodextrin and non-icodextrin groups during 1, 2 and 3 years. In spite of lower initial daily ultrafiltration volume in the icodextrin group, application of the icodextrin solution could make up the comparable daily UFV compared with the non-icodextrin groups over time on PD (Table 2). There were no significant differences of TBW, ECF, oedema index and LBM between the icodextrin group and the non-icodextrin group during the initial 3 years (Table 2).

The comparison between the diabetic and non-diabetic groups

Twenty-eight patients (37.3%) were in the diabetes group and 47 patients (62.7%) were in the non-diabetes group.
Fig. 2. Comparison of changes in body composition between the icodextrin group (closed bar, n = 36) and the non-icodextrin group (open bar, n = 39). (A) Changes in body weight, (B) changes in fat mass measured by BIA, (C) changes in % fat mass measured by BIA, (D) changes in visceral fat area by BIA. BIA: bioelectrical impedance analysis, % fat mass: fat mass/body weight, *P < 0.05, **P < 0.01.

There were no significant differences in sex [female 11/28(39%) versus 21/47(45%)] and the usage of icodextrin [11/28(39%) versus 25/47(53%)] between the diabetes group and the non-diabetes group. The mean age (50.0 ± 10.0 years versus 43.6 ± 14.4 years, P < 0.05) and the oedema index (0.385 ± 2.027 versus 0.352 ± 0.023, P < 0.001) in the diabetes group were higher than in the non-diabetes group at the 1st month. The serum albumin in the diabetes group was lower than in the non-diabetes group at the 1st month (3.06 ± 0.59 versus 3.64 ± 0.45, P < 0.001).

There were no significant differences in body weight, fat mass, % fat mass, waist/hip ratio and visceral fat area at the 1st month (baseline) between the two groups. Compared with the non-diabetes group, the diabetes group showed more delta changes in fat mass and waist/hip ratio during 1, 2 and 3 years (Figure 4B, D).

The comparison according to gender

Forty-seven patients (59.5%) were male and 32 patients (40.5%) were female. There were no significant differences in the delta changes of body weight, fat mass, percent (%)...
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Fig. 4. Comparison of changes in body composition between the diabetes group (closed bar, \( n = 28 \)) and the non-diabetes group (open bar, \( n = 47 \)).

(A) Changes in body weight, (B) changes in fat mass measured by BIA, (C) changes in \% fat mass measured by BIA, (D) changes in waist/hip ratio by BIA. BIA: bioelectrical impedance analysis, \% fat mass: fat mass/body weight, \(* P < 0.05\), \(* * P < 0.01\).

 fat mass, waist/hip ratio and visceral fat area during each of the 3 years between the genders.

The factors associated with fat accumulation

According to generalized estimating equation (GEE), factors associated with higher percent (\%) fat mass gain over time while on peritoneal dialysis were age, presence of diabetes, gender (female) and non-icodextrin group (\( P < 0.01\), Table 3).

Discussion

There are several large-scale epidemiologic studies showing that high BMI is associated with improved survival on haemodialysis patients but previous studies reported conflicting results regarding an association between obesity and survival in peritoneal dialysis patients [11–20]. Recently, Mcdonald SP et al. demonstrated that obesity was independently associated with death and technique failure during PD treatment in a large cohort [18].

Many studies have reported that peritoneal dialysis patients show increased fat mass after initiation of peritoneal dialysis [1–3]. Weight gain and fat tissue accumulation are observed with marked variations among peritoneal dialysis patients [2,21,22]. Our results are also consistent with the results of those studies. In particular, there was marked fat accumulation during the first year. Amelioration of uraemic milieu after initiation of PD or other factors might be possible speculation for marked fat accumulation during the initial first year in CAPD patients. The amount of glucose in conventional PD solutions are 10–40 times that of blood glucose (1360 mg/dl to 3860 mg/dl) and a large portion of glucose is rapidly absorbed by diffusion into the circulation following intraperitoneal infusion of glucose-based solutions [6]. During CAPD with glucose solutions, it was estimated that about 100–200 g of glucose is absorbed over 24 h [23,24], and glucose uptake from the dialysis solution represents a significant portion of energy intake [25]. Several studies demonstrated that icodextrin dialysis solutions reduce glucose absorption from the dialysate [26,27]. It is suggested that the lower caloric load associated with the icodextrin solution contributes to a reduction of weight gain compared to glucose-based solutions [27]. A multicentre, randomized, controlled trial demonstrated that the icodextrin group lost weight, total body water and extracellular fluid volume, whereas the control group gained weight [28]. Our study, like prior studies, demonstrated that the icodextrin group had less change than the non-icodextrin group in body weight and fat mass over time. Moreover, we demonstrated that the icodextrin group had lower glucose absorption from the dialysate compared with the non-icodextrin group.

The different types of dialysate which were used in this study varied, with two low-glucose degradation products (GDP) and two high-GDP conventional solutions. The icodextrin solution was used with one low-GDP and one high-GDP solutions. In terms of fat gain, we did not find significant differences between low- and high-GDP solutions (data not shown, GEE).
The mechanism by which many peritoneal dialysis patients rapidly accumulate fat mass is not clear. Our results showed that the diabetic group had higher change of fat mass, % fat mass and waist/hip ratio at 36 months, but there was no difference according to gender. Obesity has been suggested to be prevalent in peritoneal dialysis patients because of excessive peritoneal glucose absorption [29]. However, factors associated with percent (%) fat mass gain over time on peritoneal dialysis were age, diabetes, female gender and non-icodextrin dialysis solution in this study. Among these associating factors, the type of solution (icodextrin) is the only independent variable we can manipulate to alleviate excessive fat gain in CAPD patients. A non-icodextrin solution is a significant associating factor for fat accumulation over time on PD. Our study also demonstrates that the amount of glucose absorption via dialysate was not an associating factor for fat accumulation; this may be due to icodextrin application overlapping with that of less glucose absorption via dialysate.

Recently, a few studies were performed examining a gene influencing fat accumulation in CAPD patients. Wang et al. reported peritoneal dialysis patients with the UCP2 del/del genotype who showed a significant increase in fat mass during the first year of peritoneal dialysis [30]. It has been suggested that there is a possible role for the UCP2 gene during peritoneal dialysis [30]. It has been suggested to be prevalent in peritoneal dialysis patients with the UCP2 del/del genotype who showed a significant increase in fat mass during the first year of peritoneal dialysis. However, factors associated with percent (%) fat mass gain over time on peritoneal dialysis were age, diabetes, female gender and non-icodextrin dialysis solution in this study. Among these associating factors, the type of solution (icodextrin) is the only independent variable we can manipulate to alleviate excessive fat gain in CAPD patients. A non-icodextrin solution is a significant associating factor for fat accumulation over time on PD. Our study also demonstrates that the amount of glucose absorption via dialysate was not an associating factor for fat accumulation; this may be due to icodextrin application overlapping with that of less glucose absorption via dialysate.

Besides the role of icodextrin on less fat gain, the effect of icodextrin on lean body mass and oedema control in CAPD patients was also verified in this study. The icodextrin group showed less glucose absorption via dialysate and less weight and fat gain over 36 months than the non-icodextrin group. Therefore, the application of icodextrin solution may be a better option to alleviate excessive fat gain over time in CAPD patients.

**Conflict of interest statement.** This research was partially supported by the Yeungnam University research grant in 2007(Jun-Young Do).

**References**


Metabolic syndrome and mortality in CAPD patients

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Abstract

Background. Metabolic syndrome is associated with higher morbidity and mortality in the general population, but the corresponding effects in patients on dialysis have not been clearly defined. In this study, we prospectively investigated the effect of metabolic syndrome and its individual components on outcome in non-diabetic peritoneal dialysis (PD) patients.

Method. The study subjects included 106 stable non-diabetic PD patients who had been on PD for >3 months. We measured baseline characteristics, blood pressure, fasting blood glucose, lipid profiles and high-sensitivity CRP (hsCRP), and defined metabolic syndrome using the modified National Cholesterol Education Program (Adult Treatment Panel III) criteria. Mortality, technical failure and hospitalization were evaluated during the follow-up period.

Results. Metabolic syndrome was present in 50 patients (47.2%), and these showed higher baseline hsCRP levels (0.67; 95% CI: 0.50–0.94 versus 1.78 mg/dl; 95% CI: 1.21–2.57; P < 0.001). Patients with metabolic syndrome experienced significantly lower 5-year survival rates than patients without (90% versus 67%; P = 0.02), although these groups did not differ in peritonitis rates, technical failure or hospitalization. A Cox proportional hazards analysis identified the following as predictors of mortality: metabolic syndrome (RR: 3.39; 95% CI: 1.16–9.94; P = 0.02),

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