

Effect of Exercise Therapy on Lipid Parameters in Patients with End-Stage Renal Disease on Hemodialysis

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ABSTRACT

Background: Dyslipidemia has been established as a well-known traditional risk factor for cardiovascular disease in chronic kidney disease patients.

Aim: This study investigated the impact of Hatha yoga exercise on lipid parameters in patients with end-stage renal disease (ESRD) on hemodialysis.

Materials and Methods: This prospective randomized study consisted of 33 ESRD patients in the *Hatha yoga* exercise group that was matched with 35 ESRD patients in the control group. Serum total cholesterol, triglycerides, low-density lipoprotein (LDL)-cholesterol, and high-density lipoprotein (HDL)-cholesterol were determined at baseline (0 month) and after 4 months.

Results: Comparing values after 4 months versus baseline in the prehemodialysis Hatha yoga exercise group, there was found a significant decrease in total cholesterol from 5.126 ± 0.092 mmol/l to 4.891 ± 0.072 mmol/l (-4.58%; $P = 0.0001$), triglycerides from 2.699 ± 0.078 mmol/l to 2.530 ± 0.063 mmol/l (-6.26%; $P = 0.0001$), LDL-cholesterol from 2.729 ± 0.083 mmol/l to 2.420 ± 0.066 mmol/l (-11.32%; $P = 0.0001$), and total cholesterol/HDL-cholesterol ratio from 5.593 ± 0.119 mmol/l to 4.907 ± 0.116 mmol/l (-12.26%; $P = 0.047$). For patients in the Hatha yoga exercise group, 51.5% had normal total cholesterol at 0 month while 70.0% had normal total cholesterol ($P < 0.05$) after 4 four months and 54.5% of patients had normal LDL-cholesterol at 0 month while 84.9% had normal LDL-cholesterol after 4 months ($P < 0.05$).

Conclusion: These findings suggest that *Hatha yoga* exercise has preventive and beneficial effects and may be a safe therapeutic modality in ESRD patients.

Keywords: Cardiovascular, end-stage renal disease, hatha yoga exercise, total cholesterol

INTRODUCTION

Cardiovascular disease (CVD) is a major cause of morbidity and mortality in patients with chronic kidney disease (CKD),^[1,2] and is the leading cause of death in hemodialysis patients accounting

for almost 50 percent of deaths.^[3] The number of patients with CKD is increasing due to premature CVD that manifests itself as a coronary heart disease (CHD).^[4] Premature atherosclerotic CHD is driven by multiple risk factors, including dyslipidemia and oxidative stress, and there is evidence that end-stage renal disease (ESRD) patients on hemodialysis have atherogenic lipid abnormalities.^[5]

The incidence of CVD is high in patients on hemodialysis and approximately two-thirds of all patients with ESRD suffer from dyslipidemia.^[6] Dyslipidemia has been established as a well-known traditional risk factor for CVD in CKD patients on

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maintenance hemodialysis and contributes to the high cardiovascular morbidity and mortality in these patients.^[17] Further, dyslipidemia is highly prevalent in patients on maintenance hemodialysis, with predominance of the atherogenic triad, i.e., hypertriglyceridemia, elevated very low-density lipoprotein (VLDL) and reduced high-density lipoprotein (HDL).^[18] Hemodialysis patients also display elevated concentration of lipoprotein-a (LP-a), and total and low-density lipoprotein (LDL)-cholesterol levels usually remain within normal limits.^[19] The kidney dialysis outcome quality initiative guidelines state that patients on maintenance hemodialysis with fasting triglycerides >5.65 mmol/l, LDL-cholesterol >2.59 mmol/l, and non-HDL-cholesterol >3.36 mmol/l, should be considered for treatment to reduce the cardiovascular complications in these patients.^[10]

Patients with CKD are inactive and are characterized by severe functional limitations.^[11,12] Although renal replacement treatment options, such as hemodialysis or peritoneal dialysis, reduce morbidity and mortality, ESRD patients still experience significantly low physical fitness and poor quality of life.^[13,14] Their cardio-respiratory capacity is reported to be dramatically low.^[15] The maximum oxygen consumption (VO_2 max) in ESRD patients on hemodialysis is reported to be from 15.0 to 21.0 ml/kg/min, values that are half of those reported for healthy sedentary subjects, which range from 35.0 to 40.0 ml/kg/min.^[16,17] Aerobic exercise interventions have been shown to increase VO_2 max in selected patients.^[18] Aerobic exercise training in patients with advanced CKD also reduced VLDL and triglyceride levels, and increase HDL-cholesterol levels.^[19] It also improved arterial stiffness, an effect that had reversed by 1 month after training had ceased.^[20]

Hatha yoga is becoming increasingly popular in western culture particularly as a tool for stress reduction and improving physical fitness. In eastern cultures, *yoga* has traditionally been a part of life, and practitioners of *yoga* are thought to be able to achieve high states of relaxation and self-regulation of stress. *Hatha yoga* uses a combination of *asanas* (postures), *pranayamas* (breathing), and *dhyana* (meditation). Although the exact mechanism is unknown, evidence suggests that the combination of these behaviors are most beneficial when utilized together.^[21] *Hatha yoga* is one form of physical activity that, based upon previous research, may show promise for improving the health of caregivers.^[22,23] Studies carried out on medium or long-term effect of *yoga* exercise on lipid parameters in ESRD patients are sparse and there is only one reported study in the literature that examined the effect of a modified

yoga-based exercise program on lipid parameters in hemodialysis patients.^[24] This study investigated the impact of *Hatha yoga* exercise on lipid parameters in patients with ESRD on hemodialysis.

MATERIALS AND METHODS

Selection of subjects

The study was conducted between January 2009 and April 2009. There were two groups in the study. All the participants were recruited from the hemodialysis unit at the university hospital of the West Indies. The *yoga* group consisted of patients, who participated in 30 minutes of guided *Hatha Yoga* exercise and additional thirty minutes of instructed and unsupervised home training. The participants in the control group continued their regular lifestyle practice without direct intervention from the personnel of this investigation. The patients in the study were between 20 and 70 years of age, had no associated serious illness or harmful dependence on toxic habits and had signed consent form. The study was conducted in accordance with the Declaration of Helsinki.

Using the sample power statistical software (SPSS), set at type 1 error (α) = 0.05 and power of 90%, the minimum number of participants needed to pick up mean differences from normal was calculated to be five persons per group of interest. The groups of interest include analysis broken down by four age categories, two gender categories, four body mass index categories, and two overall grouping of cases versus controls. Hence a minimum of 66 participants (33 cases in the *Yoga* group and 33 control patients without a guided training program) were needed for this study. Cases and control patients were selected using a random sample from the sample frame of list of patients who attended that hemodialysis unit.

After obtaining informed consent, participants were asked to donate 5 ml of blood sample for lipid parameters measurements. Serum samples were processed and refrigerated within 3 hours of blood draw. The serum samples that were not assayed within 24 hours after collection, were stored at 2-8°C. Specimen held for longer times were stored at -70°C.

Biochemical analysis

Biochemical assays of lipid profile parameters in the serum samples were performed with a multichannel auto analyzer (c8000, Abbott Diagnostics, Abbott Park, USA). Parameters that were determined include total cholesterol

(TC), triglyceride, HDL-cholesterol, and LDL-cholesterol. Total cholesterol was determined by an enzymatic method. The cholesterol esters are hydrolyzed to free cholesterol by cholesterol esterase. The free cholesterol is then oxidized by cholesterol oxidase to cholesten-3-one with the simultaneous production of hydrogen peroxide. The hydrogen peroxide produced couples with 4-aminoantipyrine and phenol, in the presence of peroxidase, to yield a chromogen with maximum absorbance at 505 nm.^[25] HDL-cholesterol was measured by an enzymatic method on the supernatant obtained after selective precipitation of apolipoprotein B-containing lipoproteins with phosphotungstic acid in the presence of magnesium ions and centrifugation.^[26] Triglyceride by an analytical methodology based on the sequence of reaction described by Fossati and colleagues.^[27] In this direct colorimetric procedure, serum triglycerides are hydrolyzed by lipase, and the released glycerol is assayed in a reaction catalyzed by glycerol kinase and L-alpha-glycerol-phosphate oxidase in a system that generates hydrogen peroxide. The hydrogen peroxide is monitored in the presence of horseradish peroxidase with 3,5-dichloro-2-hydroxybenzenesulfonic acid/4-aminophenazone as the chromogenic system. The absorbance of this chromogen system is measured at 510 nm.^[27] The methods adopted by the automated instrument for the determination of the above parameters are according to the manufacturer's instruction, Abbott Laboratories (Abbott Diagnostics, Illinois, USA). Serum LDL-cholesterol was calculated according to computational procedures of Friedewald *et al.*:^[28]

[LDL-cholesterol = total cholesterol - HDL-cholesterol - triglyceride/2.2 (mmol/l)].

Normal values of different parameters in lipid profile were considered as per NCEP ATP III [1] criteria guideline.^[29] Total cholesterol of <5.18 mmol/l considered as normal, 5.18 – 6.19 mmol/l was considered as borderline high, whereas those ≥ 6.20 mmol/l were considered as high. Triglycerides values below 1.70 mmol/l were considered as normal; those 1.70-2.25 mmol/l were considered as border-line high, whereas values 2.26-5.64 mmol/l was considered as high and ≥ 5.65 mmol/l considered very high. Low-density lipoprotein values < 2.59 mmol/l were considered normal, between 2.59 – 3.34 mmol/l near optimal, 3.35 – 4.12 mmol/l were considered border-line high, 4.13 – 4.90 mmol/l was considered high, whereas values > 4.90 mmol/l were considered very high. High-density lipoprotein values below 1.04 mmol/l were considered as low, ≥ 1.54 mmol/l were considered as high, and values 1.04 – 1.53 mmol/l were considered as medium.^[29]

Statistical analysis

Values for the continuous variables were expressed as mean \pm SD. Comparisons of patients with ESRD in both groups were performed using unpaired students t-tests for independent samples, a level of $P < 0.05$ considered as statistically significant. Independent observations were assumed using the Fisher exact test and 0.05 was taken to be the cutoff for acceptability of significance levels. The study parameters showed non-Gaussian distribution and statistical significance was assessed by the Mann-Whitney U test.^[30] Statistics were computed using SPSS 11.5 (SPSS Inc., Chicago, Illinois, United States).

RESULTS

The mean age of the patients in the *Hatha Yoga* exercise group was 38.95 ± 2.84 years while that of the control group was 44.59 ± 2.57 years. The mean BMI of the patients in the control group was 25.74 ± 0.50 kg/m² while that of the *Hatha Yoga* exercise group was 25.550 ± 2.21 kg/m². The patients in the control group were in hemodialysis for 4.45 ± 0.65 years while those in the *Hatha Yoga* exercise group were on hemodialysis for 4.86 ± 0.49 years.

There was a significant reduction in serum total cholesterol, triglycerides, LDL-cholesterol, and total cholesterol/HDL-cholesterol ratio, and a significant increase in HDL-cholesterol after 4 months for patients in the Hatha yoga exercise group. In the prehemodialysis *Hatha Yoga* exercise group there was a significant decrease in total cholesterol from 5.126 ± 0.092 mmol/l to 4.891 ± 0.072 mmol/l (4.58% reduction; $P = 0.0001$), triglycerides from 2.699 ± 0.078 mmol/l to 2.530 ± 0.063 mmol/l (6.26% reduction; $P = 0.0001$), LDL-cholesterol from 2.729 ± 0.083 mmol/l to 2.420 ± 0.066 mmol/l (11.32% reduction $P = 0.0001$), and total cholesterol/HDL-cholesterol ratio from 5.593 ± 0.119 mmol/l to 4.907 ± 0.116 mmol/l (12.26% reduction; $P = 0.047$). Furthermore, there was no significant increase in HDL-cholesterol from 0.931 ± 0.022 mmol/l to 1.017 ± 0.016 mmol/l [8.46% elevation; $P = 0.250$; Table 1].

There was a significant reduction in serum total cholesterol and HDL-cholesterol, and a significant increase in triglycerides and total cholesterol/HDL-cholesterol ratio after 4 months in the control group. In patients in the prehemodialysis control group was a significant reduction in serum total cholesterol from 4.7663 ± 0.050 mmol/l to 4.7657 ± 0.054 mmol/l ($P = 0.0001$) and HDL-cholesterol from 0.898 ± 0.015 mmol/l to 0.872 ± 0.013 mmol/l

(2.90% reduction; $P = 0.0001$). Furthermore, there was a significant increase in triglycerides from 3.243 ± 0.186 mmol/l to 3.450 ± 0.180 mmol/l (6.0% elevation; $P = 0.0001$) and total cholesterol/HDL-cholesterol ratio from 5.348 ± 0.086 to 5.505 ± 0.099 [2.9% elevation; $P = 0.0001$; Table 2].

There was significant correlation between the pre-dialysis lipid parameters of patients in the Hatha yoga exercise group at 0 month and after 4 months for total cholesterol ($r = 0.655$), triglycerides ($r = 0.826$), LDL-cholesterol ($r = 0.572$), and total cholesterol/HDL-cholesterol ratio ($r = 0.354$). Furthermore, there was significant correlation between the predialysis lipid parameters for the controls at 0 month and after 4 months for total cholesterol ($r = 0.592$), triglycerides ($r = 0.872$), HDL-cholesterol ($r = 0.645$), and total cholesterol/HDL-cholesterol ratio ($r = 0.584$).

In examining total cholesterol concentrations of patients in the prehemodialysis Hatha yoga exercise group, 51.5% had normal total cholesterol at 0 month, while at the end of therapy after 4 months 70.0% had normal total cholesterol ($P < 0.05$). The results also showed that while 63.6% of the patients in the prehemodialysis *Hatha Yoga* exercise group had low HDL-cholesterol after 4 months, 81.8% had low HDL-cholesterol at 0 month ($P < 0.05$). Furthermore, while 84.9% of patients in the prehemodialysis *Hatha Yoga* exercise group had normal LDL-cholesterol after 4 months, 54.5% had normal LDL-cholesterol at 0 month [$P < 0.05$; Table 3]. In examining total cholesterol concentrations in the control group, 85.7% and 77.1% of the patients had normal total cholesterol concentrations at 0 month and 4 months respectively. There were no significant differences

Table 1: Lipid parameters of prehemodialysis patients in the Hatha yoga exercise group

Lipid parameters	Pre-HD 0 month Mean \pm S.E.	Pre-HD 4 months Mean \pm S.E.	P value
Total cholesterol (mmol/l)	5.126 \pm 0.092	4.891 \pm 0.072	0.0001*
Triglycerides (mmol/l)	2.699 \pm 0.078	2.530 \pm 0.063	0.0001*
HDL-cholesterol (mmol/l)	0.931 \pm 0.022	1.017 \pm 0.016	0.250
LDL-cholesterol (mmol/l)	2.729 \pm 0.083	2.420 \pm 0.066	0.0001*
TC/HDL-cholesterol ratio	5.593 \pm 0.119	4.907 \pm 0.116	0.047*

Total cholesterol (mmol/l). *Statistical significance with $P < 0.05$.

Table 2: Lipid parameters of prehemodialysis patients in the control group

Lipid parameters	Pre-HD 0 month Mean \pm S.E.	Pre-HD 4 months Mean \pm S.E.	P value
Total cholesterol (mmol/l)	4.7663 \pm 0.050	4.7657 \pm 0.054	0.0001*
Triglycerides (mmol/l)	3.243 \pm 0.186	3.450 \pm 0.180	0.0001*
HDL-cholesterol (mmol/l)	0.898 \pm 0.015	0.872 \pm 0.013	0.0001*
LDL-cholesterol (mmol/l)	2.653 \pm 0.086	2.611 \pm 0.072	0.179
TC/HDL-cholesterol ratio	5.348 \pm 0.086	5.505 \pm 0.099	0.0001*

Total cholesterol (mmol/l). *Statistical significance with $P < 0.05$.

in the normal triglycerides and LDL-cholesterol at 0 month compared with after 4 months in control patients [Table 4].

DISCUSSION

Patients with chronic renal insufficiency and those on chronic hemodialysis treatment are at elevated atherogenic

Table 3: Classification of lipid parameters of patients in the Hatha yoga exercise group (0 month and 4 months) according to NCEP ATP III

Lipid parameters	Number (%)	
	0 month	4 months
Total cholesterol		
Normal <5.18 mmol/l	17 (51.5)	23 (70.0)
Borderline high 5.18–6.19 mmol/l	14 (42.4)	10 (30.0)
High \geq 6.22 mmol/l	2 (6.1)	0 (0.0)
Triglyceride		
Normal <1.70 mmol/l	1 (3.0)	1 (3.0)
Borderline high 1.70–2.25 mmol/l	4 (12.1)	5 (15.2)
High 2.26–5.64 mmol/l	28 (84.9)	27 (81.8)
Very high \geq 5.65 mmol/l	0 (0.0)	0 (0.0)
HDL-cholesterol		
Low <1.04 mmol/l	27 (81.8)	21 (63.6)
Medium 1.04–1.53 mmol/l	6 (18.2)	12 (36.4)
High \geq 1.54 mmol/l	0 (0.0)	0 (0.0)
LDL-cholesterol		
Normal <2.59 mmol/l	18 (54.5)	28 (84.9)
Near optimal/above optimal 2.59–3.34 mmol/l	12 (36.4)	4 (12.1)
Borderline high 3.35–4.12 mmol/l	3 (9.1)	1 (3.0)
High 4.13–4.90 mmol/l	0 (0.0)	0 (0.0)
Very high \geq 4.90 mmol/l	0 (0.0)	0 (0.0)

Table 4: Classification of lipid parameters of patients in the control group (0 month and 4 months) according to NCEP ATP III

Lipid parameters	Number (%)	
	0 month	4 months
Total cholesterol		
Normal <5.18 mmol/l	30 (85.7)	27 (77.1)
Borderline high 5.18–6.19 mmol/l	5 (14.3)	8 (22.9)
High \geq 6.22 mmol/l	0 (0.0)	0 (0.0)
Triglyceride		
Normal <1.70 mmol/l	1 (2.9)	1 (2.9)
Borderline high 1.70–2.25 mmol/l	4 (11.4)	2 (5.7)
High 2.26–5.64 mmol/l	30 (85.7)	32 (91.4)
Very high \geq 5.65 mmol/l	0 (0.0)	0 (0.0)
HDL-cholesterol		
Low <1.04 mmol/l	32 (91.4)	34 (97.1)
Medium 1.04–1.53 mmol/l	3 (8.6)	1 (2.9)
High \geq 1.54 mmol/l	0 (0.0)	0 (0.0)
LDL-cholesterol		
Normal <2.59 mmol/l	19 (54.3)	20 (57.1)
Near optimal/above optimal 2.59–3.34 mmol/l	11 (31.4)	9 (25.7)
Borderline high 3.35–4.12 mmol/l	5 (14.3)	6 (17.2)
High 4.13–4.90 mmol/l	0 (0.0)	0 (0.0)
Very high \geq 4.90 mmol/l	0 (0.0)	0 (0.0)

risk, and dyslipidemia appears to be one of the major risk factors. Our study indicates an abnormal lipoprotein profile in ESRD patients on hemodialysis. The majority of the ESRD patients in both the *Hatha Yoga* exercise and control groups had borderline high or high triglycerides, and low HDL-cholesterol at baseline. Approximately one-tenth of the patients in both groups had high LDL-cholesterol concentrations while approximately one-half of the patients in the *Hatha Yoga* exercise group had borderline high or high total cholesterol. The ESRD patients engaged in *Hatha Yoga* exercise demonstrated significantly lower serum total cholesterol, triglycerides, LDL-cholesterol, and total cholesterol/LDL-cholesterol ratio after 4 months compared with baseline values. The risk factor for coronary artery disease (total cholesterol/HDL-cholesterol ratio) is usually elevated in renal failure patients, especially in those with hypertriglyceridemia.^[31] Conversely, the ESRD patients in the control group had significantly higher triglycerides and total cholesterol/HDL-cholesterol ratio, but lower HDL-cholesterol concentrations after 4 months compared with baseline values. In the only study evaluating the effects of a 12-week yoga-based exercise program on biochemical markers in a randomized controlled trial of hemodialysis patients there was significant improvements in total cholesterol and LDL-cholesterol compared with that in the control group but not so in other lipid profile variables such as HDL-cholesterol and triglyceride concentrations. The authors concluded that the simplified yoga-based rehabilitation program is a complementary, safe, and effective clinical treatment modality in patients with ESRD.^[32]

The results of this study are similar to that of Bijlani *et al*, where yoga significantly decreased serum total cholesterol, LDL-cholesterol, VLDL, triglycerides and total cholesterol/HDL-cholesterol ratio in individuals attending a lifestyle education-based program for 9 days.^[32] Furthermore, there are studies that have investigated the use of yoga exercise as a therapeutic intervention in cardiovascular diseases. In a study by Khare and Rai investigating the lipid profile in postmyocardial infarction subjects following yogi life style intervention, there was significant reduction in total cholesterol and LDL-cholesterol, whereas an increase in HDL-cholesterol was also noted.^[33] Mahajan *et al* reported that yoga intervention caused a decrease in all lipid parameters except HDL-cholesterol in angina patients and normal subjects with risk factors of coronary artery disease.^[34] Yogendra *et al*, reported the beneficial effects of yoga lifestyle on reversibility of ischemic heart disease as at the end of 1 year of yoga training, statistical significant reductions in serum total cholesterol, serum LDL-cholesterol, and regression of

disease. The authors also suggest that yoga-based lifestyle modifications help in regression of coronary lesions and in improving myocardial perfusion which translated into clinical benefits and symptomatic improvement.^[35]

Chronic renal failure is often associated with dyslipidemia. Lipid profile abnormalities have been identified as an independent risk factor for atherosclerosis.^[36,37] ESRD patients typically have either normal or increased LDL-cholesterol, increased VLDL and intermediate-density lipoprotein (IDL), leading to elevated triglyceride levels, and decreased levels of HDL-cholesterol. There are also qualitative changes in dyslipidemia with a shift from an atherogenic LDL particle size toward a small, dense apo-B-rich LDL predominance.^[6] It was reported by Alsarani *et al* that 40-50% of patients with ESRD have high triglycerides, 10-45% have high LDL-cholesterol, and 20-30% have high total cholesterol.^[38] In our study approximately 85% of the patients in both groups had high triglyceride concentrations greater than 2.26 mmol/l. Furthermore, 82-92% of the patients in both groups had low HDL-cholesterol. In the choices for healthy outcomes in caring for ESRD (CHOICE) study, 36% of hemodialysed patients had hypertriglyceridemia^[39] where as Pennell and colleagues found the incidence to be 52%.^[8] But the results of this study are not in agreement with the results of some researchers showing significantly decreased plasma triglyceride concentration in hemodialysis patients^[40] or no change.^[41] Furthermore, the atherogenic potential of dyslipidemia in kidney disease may depend more on the apolipoprotein rather than on lipid abnormalities, and may not always be recognized by measurement of plasma lipids alone,^[42] as suggested by Attman and Alaupovic.^[43]

In this study though there was not a significant increase in the mean value of HDL-cholesterol after 4 months, there was an increase in the number of patients with medium HDL-cholesterol, from 18.2% to 36.4%, with fewer people in the low category level. Some studies evaluating the long-term effect of yoga on lipid profile have demonstrated significant rise in values of HDL-cholesterol.^[44,45] In the present study, there was a significant decrease in total cholesterol and triglyceride concentrations in ESRD patients on hemodialysis. Further, it was observed that some patients with borderline high total cholesterol and triglycerides values achieved normal values, whereas patients with high values achieved borderline high values. There were also some cases with high values that attained normal values. Hence, Hatha yoga intervention resulted in an overall improvement in different parameters of lipid profile and is therefore beneficial in the management of dyslipidemia in ESRD patients.

Many patients with renal failure show abnormalities of lipid metabolism. Hypertriglyceridemia and low levels of HDL-cholesterol are frequent abnormalities in uremic patients. The various disturbances of lipoprotein metabolism in uremia can be summarized as decreased catabolism of lipoproteins with an inappropriate synthesis of VLDL.^[46] There is decreased lipoprotein catabolism, resulting in incompletely cleared intermediate particles and diminished formation of HDL.^[47]

In conclusion, the findings of the study demonstrate the efficacy of *Hatha Yoga* exercise on lipid parameters in ESRD patients. These findings suggest that *Hatha Yoga* exercise has preventive and beneficial effects and may be a safe therapeutic modality in ESRD patients. Optimal management of dyslipidemia in ESRD patients with regimens such as *Hatha Yoga* exercise, particularly reduction of low-density lipoprotein cholesterol, should therefore lead to both cardiovascular and renal benefits.

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