RESEARCH

A Randomized Controlled Trial to Assess Pharmacist-Physician Collaborative Practice in the Management of Metabolic Syndrome in a University Medical Clinic in Jordan

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ABSTRACT

BACKGROUND: The prevalence of metabolic syndrome is increasing worldwide, and patients with metabolic syndrome have increased risk of developing cardiovascular disease and type 2 diabetes. Although specific criteria vary, the National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATP III) criteria (2002) defined metabolic syndrome as the presence of 3 or more of the following 5 components: waist circumference more than 102 centimeters (cm) for men or more than 88 cm for women; triglycerides 150 milligrams per deciliter (mg per dL) or more; high-density lipoprotein cholesterol (HDL-C) less than 40 mg per dL for men or less than 50 mg per dL for women; blood pressure (BP) 130/85 millimeters mercury (mm Hg) or more; and fasting blood glucose 110 mg per dL or more.

OBJECTIVE: To evaluate the effect of a pharmacist-physician collaborative practice compared with usual care in the management of patients with metabolic syndrome as defined by the NCEP/ATP III criteria.

METHODS: A prospective, randomized controlled trial conducted in family medicine outpatient clinics in Jordan enrolled 199 patients who met the NCEP/ATP III criteria for metabolic syndrome during an enrollment period from March 15, 2009, through May 10, 2009. Patients were randomized into 2 groups, with 110 in the intervention group (pharmacist-physician collaborative practice) and 89 in usual care (physician only). The patients in the intervention group were provided with pharmacist recommendations and pharmaceutical care counseling. Outcome measures included metabolic syndrome status (binomial) and changes in mean values for each metabolic syndrome component (waist circumference, triglycerides, HDL-C, fasting blood glucose, and systolic and diastolic BP) and for body weight. A 2 × 2 contingency table with a Pearson chi-square test was used to assess by-group differences in metabolic syndrome status after 6 months of follow-up. In difference-in-difference analyses, t-tests (Mann-Whitney U tests when appropriate) were used to assess by-group differences in changes in the individual metabolic syndrome components and body weight.

RESULTS: From baseline to follow-up, 39.1% (n = 43) of intervention group patients versus 24.7% (n = 22) of usual care patients were successfully shifted from a status of metabolic syndrome to no metabolic syndrome ($P = 0.032$). Three of 7 outcome measures were improved more in the intervention group compared with the usual care group. Mean (SD) triglyceride (mg per dL) declined by 30.9 (54.4) from 189.3 (79.6) to 158.4 (77.3) in the intervention group and by 14.5 (50.7) from 202.5 (88.0) to 188.5 (89.0) in the usual care group ($P = 0.029$). For the intervention and usual care groups, mean baseline systolic BPs were 134.7 (16.2) mm Hg and 134.6 (12.2) mm Hg, respectively, declining after 6 months follow-up by 12.1 (20.1) mm Hg in the intervention group versus 6.9 (14.6) mm Hg in the usual care group ($P = 0.018$). Mean baseline diastolic BPs were 83.6 (10.7) mm Hg and 83.6 (7.9) mm Hg, respectively, declining by 7.2 (12.6) mm Hg in the intervention group versus 4.9 (8.1) mm Hg in the usual care group ($P = 0.049$).

CONCLUSIONS: Compared with usual care provided by physicians only, pharmacist involvement in the clinical management of patients with metabolic syndrome increased the proportion of patients who no longer met criteria for the syndrome after 6 months follow-up and improved control of BP and triglycerides.

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What is already known about this subject

- Metabolic syndrome is a secondary target of risk reduction in patients with coronary heart disease after the primary targets of low-density lipoprotein cholesterol and blood pressure (BP). In addition, metabolic syndrome predicts the development of type 2 diabetes mellitus and cardiovascular disease (CVD).
- Clinical pharmacist interventions have been studied for several chronic diseases, such as hypertension, diabetes, and dyslipidemia. A randomized controlled trial by Carter et al. (2009), conducted in a sample of patients with uncontrolled hypertension treated in community medical practices, found BP control rates of 63.9% in patients receiving collaborative pharmacist-physician care versus 29.9% in a control group receiving usual care. In a pooled analysis of 2 randomized controlled trials conducted in outpatients with CVD, Murray et al. (2009) found that the risk of adverse drug events and medication errors was reduced by approximately 34% in patients who received monitoring and instruction from pharmacists compared with those receiving routine dispensing alone.
- The role of pharmacists in managing metabolic syndrome has not been evaluated extensively. Two cross-sectional studies have studied the benefits of pharmacist care on metabolic syndrome screening in community pharmacy patrons and in patients receiving antipsychotics in an outpatient psychiatry clinic.

What this study adds

- The current study is the first randomized controlled trial to evaluate physician-pharmacist collaborative practice in clinical management of metabolic syndrome by combining lifestyle changes and drug therapy.
- Compared with usual physician care, pharmacist-physician collaboration resulted in greater improvements in metabolic syndrome status: 39.1% in the intervention group versus 24.7% in usual care ($P = 0.032$).
- Pharmacist-physician collaboration resulted in improvements in BP and triglycerides but did not have a significant effect on body weight, waist circumference, high-density lipoprotein cholesterol, or fasting blood sugar.

Many patients have a constellation of lifestyle risk factors that constitute a condition known as metabolic syndrome, also called insulin resistance or syndrome X.[1-3] Various definitions for metabolic syndrome have been proposed. The World Health Organization (WHO) first defined metabolic syndrome in 1998 based on impaired glucose tolerance, diabetes, or insulin resistance combined with 2 or more of the following: obesity, dyslipidemia, hypertension, and microalbuminuria.[3] In 1999, the European Group for the Study of Insulin Resistance (EGIR) proposed several modifications to the WHO definition, including deletion of microalbuminuria as a criterion,[4] and the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) revised the definition in 2002. A definition closely based on that of the NCEP/ATP III was adopted by the American Heart Association (AHA) and the National Heart Lung and Blood Institute (NHLBI) in 2005.[5] In 2005, the International Diabetes Foundation (IDF) published new criteria for metabolic syndrome in an attempt to reduce "confusion" caused by "contrasting views on pathogenic mechanisms and the need for clinical usefulness"; however, that definition relied in part on ethnicity-specific waist circumference criteria for obesity.[6]

The present study adopted the NCEP/ATP III (2002) definition of metabolic syndrome because it (a) incorporates the key features of hyperglycemia/insulin resistance, visceral obesity, atherogenic dyslipidemia, and hypertension and (b) uses measurements and laboratory results that are readily available to physicians or other health providers. NCEP/ATP III defined metabolic syndrome as the presence of 3 or more of the following 5 components: waist circumference more than 102 centimeters (cm) for men or more than 88 cm for women; triglycerides 150 milligrams per deciliter (mg per dL) or more; high-density lipoprotein cholesterol (HDL-C) less than 40 mg per dL for men or less than 50 mg per dL for women; blood pressure (BP) 130/85 millimeters mercury (mm Hg) or more; and fasting blood glucose 110 mg per dL or more.[2] The NCEP/ATP III definition differs slightly from that of the AHA/NHLBI, in which the fasting blood glucose criterion is 100 mg per dL or more.[5]

The National Health and Nutrition Examination Survey (NHANES) 2003-2006 found that approximately one-third of adults in the United States met the NCEP/ATP III diagnostic criteria for metabolic syndrome. The prevalence increased with age and body mass index (BMI), and varied by race or ethnicity and gender.[7] In a study from Jordan (2005), the prevalence of metabolic syndrome was 36.3% overall, 28.7% among men and 40.9% among women, and increased significantly with age in both men and women.[8] Similar prevalences were found in other countries in the Middle East.[9-12]

Metabolic syndrome is recognized as a secondary target of coronary heart disease (CHD) risk reduction therapy after the primary target of low-density lipoprotein cholesterol (LDL-C) reduction is achieved.[2] It is well established that metabolic syndrome predicts the development of type 2 diabetes mellitus and cardiovascular disease (CVD).[13-16] Although each individual component of the metabolic syndrome increases the risk of CVD, this risk is even more pronounced when the components are combined in metabolic syndrome. Additionally, increases in the number of metabolic syndrome components presented by a patient are associated with a higher cardiovascular mortality rate.[13-16]

The role of clinical pharmacists in improving treatment outcomes; achieving therapeutic goals; lowering adverse reactions or undesirable effects; and reducing medication costs in many chronic medical conditions, such as hypertension, diabetes mellitus, heart failure, and dyslipidemia, has been demonstrated by many studies using different designs.[17-22] However, studies of the pharmacist's role in the management of metabolic syndrome have been limited to screening for metabolic syndrome in community pharmacy patrons without CHD and in patients receiving antipsychotics.[23,24] In the present study, a pharmaceutical care program was developed, allowing 1 clinical pharmacist to work at a physician's practice site to assess and manage the components of metabolic syndrome. The pharmaceutical care program included interventions and patient counseling to address medication, diet, and physical activity. The aim of the present study was to describe the clinical benefits of a physician-clinical pharmacist collaboration in achieving better glycemic control and better lipid and BP measurements in patients with metabolic syndrome as defined by NCEP/ATP III guidelines.

Methods

Patient Enrollment

This randomized controlled clinical trial was conducted over 9 months in 6 family medicine clinics involving 13 physicians at Jordan University Hospital (JUH), a major teaching hospital in Amman, Jordan. Family medicine clinics at JUH serve approximately 100 patients daily. Of those, approximately one-third are followed up on a monthly basis for management of hypertension, diabetes, dyslipidemia, and other chronic diseases.

This study was approved by the Institutional Review Board (IRB) at JUH. Study enrollment took place during an 8-week time period from March 15, 2009, through May 10, 2009. The pharmacist reviewed paper medical records prior to each visit to identify patients with suspected metabolic syndrome. Patients were asked to participate in the study if they met the NCEP/ATP III criteria for the diagnosis of metabolic syndrome at the time of enrollment.[2] Patients with any of the following conditions documented in the medical record were excluded: pregnancy, renal or hepatic diseases, and dementia or cognitive impairment. Patients who were unable to provide informed written consent were also excluded. Written informed consent

was obtained from all study participants in both study arms. During the process of obtaining patient consent, the patients were informed that they would be assigned to either the intervention group (physician-pharmacist collaborative practice) or control (usual care) group (physician-only team). At the time of recruitment, patients were randomized into the intervention arm (n = 112) and the control arm (n = 90) using a coin-toss method.

Patients remained in the same randomized study arm throughout the duration of the study period. Both study groups were followed for 6 months by the same physician team, which consisted of 2 fellows (post-residency specialists), 6 fourth-year residents, 3 third-year residents, 3 second-year residents, and 1 consultant (at least 2 years in residency subspecialty). The pharmacist team consisted of a master's degree pharmacy student (Hammad) and a faculty pharmacist (Albsoul-Younes).

Data Collection

All patients who agreed to take part in the study were interviewed to collect demographics and clinical values for fasting blood glucose, total cholesterol, triglycerides, HDL-C, and LDL-C. All laboratory measurements were performed in the laboratory of the teaching hospital. Tests were reported as baseline values if they were performed within the last 3 months prior to or on the date of study enrollment (i.e., no baseline values were used that were older than 3 months prior to the date of enrollment). Follow-up testing was performed during the course of the study to assess clinical progress. The last follow-up measurements were collected from both study arms at the sixth scheduled visit and compared with baseline values. The data collection period extended for 9 months (March through November 2009) to ensure at least 6 months of data for all enrolled patients.

Data on age, gender, weight, height, BMI, abdominal circumference, family history of cardiovascular disease and diabetes mellitus, smoking, alcohol consumption, dietary habits, and physical activity were also collected. Physical activity was defined as regular practice of any type of activity 3 to 4 times per week for duration of 30 minutes or more, such as brisk walking, jogging, cycling, or swimming.[4] A current smoker was defined as one who smoked 1 or more cigarettes per day. Waist circumference was measured using a steel measuring tape, with the measurement made halfway between the lower border of the rib and the iliac crest in a horizontal plane. Two independent measurements of waist circumference to the nearest 0.5 cm were recorded at the time of enrollment, 1 by a pharmacist and the other by a physician; the mean of the 2 measurements was recorded and reported as the baseline value.

BP levels were measured monthly by assistant nurses who were blinded to the patient's study arm assignment and recorded the BP measures in the patients' medical records. Patients were instructed to abstain from smoking or caffeine consumption within 30 minutes of the measurement. BP measurements were taken in the right arm with a standard mercury sphygmomanometer after the patient had been seated quietly for at least 5 minutes.

Description of the Intervention Versus Usual Care

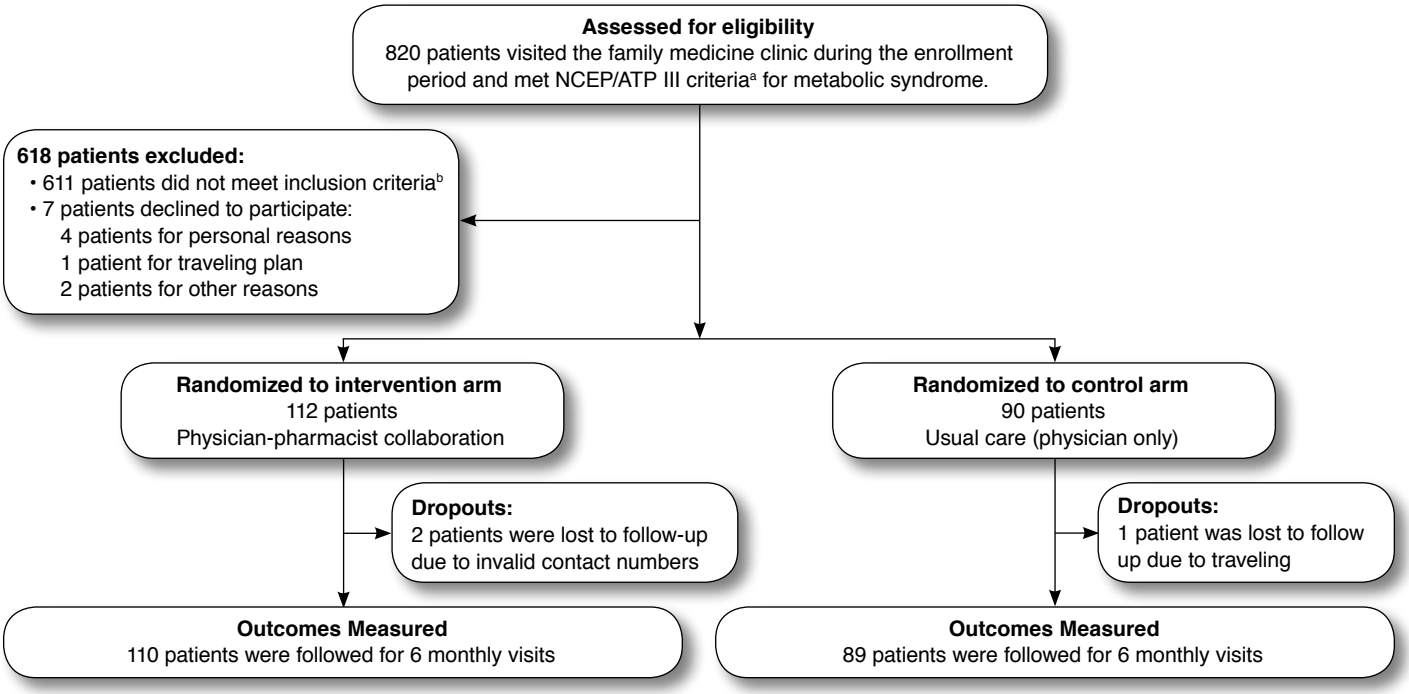
Prior to randomization, the pharmacist initially interviewed patients in both study groups to collect information about medications, medical conditions, and lifestyle (e.g., diet, smoking). At each monthly visit, patients in the intervention group met with a clinical pharmacist for 30 minutes before seeing the physician. In the intervention group, metabolic components were assessed and managed collaboratively by focused care plans designed by the clinical pharmacist and approved by the physician. Pharmacists provided medication counseling, answered questions asked by patients or physicians, encouraged compliance, offered instructions on self-monitoring BP, and advised patients on healthy lifestyle choices (e.g., tobacco cessation and adhering to a healthy diet). Educational materials were also distributed to patients in the intervention group, including brochures on metabolic syndrome, increased risk of cardiovascular disease, and type 2 diabetes mellitus. Pamphlets were provided to patients with information on the recommended dietary approaches to stop hypertension (DASH),[25,26] dyslipidemia, and diabetes mellitus, which were translated into Arabic and tailored to the food habits and recipes of the Jordanian community. Patients in the intervention group were counseled on the components of metabolic syndrome, including cut-off points and goals. An emphasis was put on optimizing adherence to pharmacological and nonpharmacological therapy to reduce the risk for cardiovascular and renal disease and to prevent the development of type 2 diabetes mellitus and the risks associated with individual components of metabolic syndrome.

The pharmacist emphasized lifestyle changes, particularly weight loss and physical activity, as a first-line therapy for at least 3 months. Patients were started on drug therapy as recommended by clinical guidelines.[2] The pharmacists' interventions and proposed patient care plans were discussed with the physicians, who specified whether to accept or reject them as part of each patient's individualized treatment plan.

In the control group, patients received usual care provided by physician teams. For the usual care group, the clinical pharmacist did not provide any recommendations and did not offer educational materials or counseling.

For patients in both study arms, Framingham scores were calculated, and 10-year CHD risk was determined.[3] Based on the CHD risk category, therapeutic choices (low-dose aspirin, therapeutic life changes, lipid-lowering therapy) were recommended by the pharmacist to the treating physician in the intervention arm only.

FIGURE 1 Patient Selection Flowchart



[a]*NCEP/ATP III criterion for metabolic syndrome: at least 3 of the following 5 criteria:*

1. *Abdominal circumference more than 102 centimeters for males or more than 88 centimeters for females.*
2. *HDL-C less than 40 mg per dL for males or less than 50 mg per dL for females.*
3. *Triglycerides 150 mg per dL or more.*
4. *Blood pressure 130/85 mm Hg or more, or receiving hypertension treatment.*
5. *Fasting blood glucose 110 mg per dL or more.*

[b]*611 patients were excluded for the following reasons: pregnancy, renal or hepatic disease, and dementia or cognitive impairment.*

HDL-C = high-density lipoprotein cholesterol; mg per dL = milligrams per deciliter; mm Hg = millimeters mercury; NCEP/ATP = National Cholesterol Education Program/ Adult Treatment Panel.

Patient Follow-Up

Patients in both study arms provided valid phone numbers, which the clinical pharmacist used to call patients and set up appointments during their regular, monthly follow-up visits to the clinic. The pharmacist contacted patients 1 week and 1 day prior to each upcoming appointment to remind and confirm the scheduled visit.

Outcome Measurements

The primary outcomes measured the improvement in metabolic syndrome status over the course of the study period and absolute mean improvement in individual metabolic syndrome components. At baseline and follow-up, metabolic syndrome status was assessed according to the NCEP/ATP III definition (at least 3 of 5 components: abdominal obesity measured by waist circumference, elevated triglycerides, low HDL-C, elevated BP, elevated fasting blood glucose). Patients with 2 or fewer components at the 6-month follow-up were defined as improved (i.e., change from metabolic syndrome to no metabolic syndrome). The intervention pharmacist reviewed the medical records to transfer baseline and 6-month values for each patient into a data collection form. In addition to the 5 metabolic syndrome components, body weight was assessed as an outcome measure.

Data Management and Analysis

Contingency tables with Pearson chi-square tests and t-tests were used to evaluate the baseline differences between the arms at the beginning of the study. To make a by-group comparison of the percentage of patients whose metabolic status improved during the study, a 2×2 contingency table (metabolic syndrome vs. no metabolic syndrome for intervention vs. control at 6-month follow-up) with statistical testing by the Pearson chi-square test was used. To make by-group comparisons of the changes (improvements) in the individual metabolic syndrome components and body weight from

TABLE 1 Baseline Characteristics of Patients with Metabolic Syndrome

Patient Characteristics	Intervention n = 110	Usual Care n = 89	*P* Value[a]
Age in years, mean [SD]	56.0 [9.6]	57.4 [11.5]	0.385
Demographic and clinical categories	**n (%)**	**n (%)**	
Female	66 (60.0)	57 (64.0)	0.559
BMI category[b]			0.695
Overweight	68 (61.8)	52 (58.4)	
Obese	38 (34.5)	34 (38.2)	
Morbid obesity	4 (3.6)	3 (3.4)	
Smoking status			0.232
Current smoker	46 (41.8)	50 (56.2)	
Nonsmoker	64 (58.2)	39 (43.8)	
Sedentary lifestyle: less than 30 min. of moderate exercise 4 times per week	106 (96.4)	83 (93.3)	0.476
Past medical history[c]			0.642
Hypertension and diabetes	39 (35.5)	25 (28.1)	
Diabetes	23 (20.9)	18 (20.2)	
Dyslipidemia and diabetes	12 (10.9)	15 (16.9)	
Hypertension, diabetes, and dyslipidemia	27 (24.5)	23 (25.8)	
Hypothyroidism and diabetes	2 (1.8)	4 (4.5)	
Dyslipidemia	7 (6.4)	4 (4.5)	

[a]*P values for Pearson chi-square tests for categorical variables and Student's t test for continuous variables.*

[b]*BMI categories(kg per m^2):[26] overweight = 25-29.9; obese = 30-39.9; morbid obesity = 40 or more.*

[c]*Defined as a past illness treated by family medicine physicians and recorded in patient medical record; past medical history was verified with the patients. P value represents Pearson chi-square test for a 6×2 table.*

BMI = body mass index; kg per m^2 = kilograms per square meter; SD = standard deviation.

TABLE 2 Number of Metabolic Syndrome Components at Baseline and 6 Months

Metabolic Syndrome Components[a]	Baseline		After 6 months	
	Intervention n = 110	Usual Care n = 89	Intervention n = 110	Usual Care n = 89
	n (%)	n (%)	n (%)	n (%)
5	11 (10.0)	7 (7.9)	3 (2.7)	2 (2.2)
4	44 (40.0)	36 (40.4)	12 (10.9)	29 (32.6)
3	55 (50.0)	46 (51.7)	52 (47.3)	36 (40.4)
2 or fewer[b]	0 (0.0)	0 (0.0)	43 (39.1)	22 (24.7)[b]

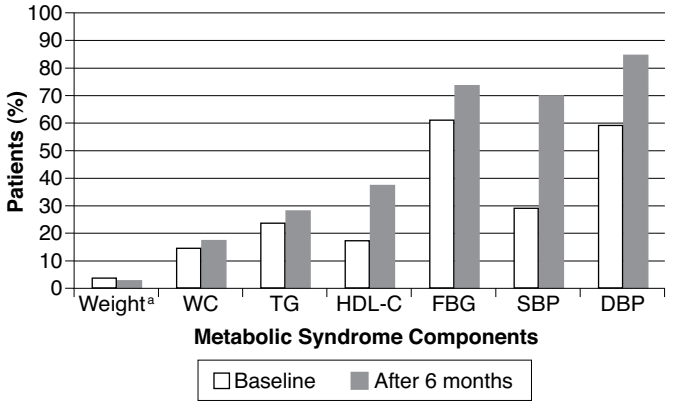
[a]*NCEP/ATP III criterion for metabolic syndrome: at least 3 of the following 5 criteria:*

1. *Abdominal circumference more than 102 centimeters for males or more than 88 centimeters for females.*
2. *HDL-C less than 40 mg per dL for males or less than 50 mg per dL for females.*
3. *Triglycerides 150 mg per dL or more.*
4. *Blood pressure 130/85 mm Hg or more, or receiving hypertension treatment.*
5. *Fasting blood glucose 110 mg per dL or more.*

[b]*Denotes a patient who did not meet criteria for metabolic syndrome. P value of Pearson chi-square test was 0.032.*

HDL-C = high-density lipoprotein cholesterol; mg per dL = milligrams per deciliter; mm Hg = millimeters mercury; NCEP/ATP = National Cholesterol Education Program/Adult Treatment Panel.

FIGURE 2 Percentage of Patients Achieving the Recommended Values of Metabolic Syndrome Criteria in the Intervention Group at Baseline and After 6 Months



[a]*Body weight was included as an outcome measure, although it is not a component of metabolic syndrome as defined by NCEP/ATP III.*

DBP = diastolic blood pressure; FBG = fasting blood glucose; HDL-C = high-density lipoprotein cholesterol; NCEP/ATP = National Cholesterol Education Program/Adult Treatment Panel; SBP = systolic blood pressure; TG = triglycerides; WC = waist circumference.

baseline to 6-month follow-up, a difference-in-difference analysis, which is a commonly used analytic technique for designs with pre-intervention versus post-intervention measures and a control or comparison group, was used.[27,28] First, baseline values were subtracted from 6-month follow-up values to calculate change amounts. Then, the statistical significance levels of by-group differences in the change amounts were calculated using Student's t-tests for variables with normal distributions and Mann-Whitney U tests when normality and equality of variance assumptions were not met.

Normality of mean reduction of systolic and diastolic BP, absolute changes in individual components of metabolic syndrome, and other clinical values or demographics were determined visually by probability plots, quantile-quantile plots, and Kolmogrov-Smirnov-Lilliefors tests. Equality of variances was tested using Levene's test. All data were processed using SPSS version 16 (SPSS Inc., Chicago, IL) and an a priori alpha level of 0.05.

Results

Of the 202 patients who were initially recruited, 199 were randomized into the intervention arm (n = 110) and usual care arm (n = 89; Figure 1). Baseline levels and different demographic characteristics for study samples are shown in Table 1. There were no significant between-group differences in baseline demographics or medical history measures.

TABLE 3 Mean [SD] Outcome Measures at Baseline and 6 Months[a]

	Intervention (n = 110)			Usual Care (n = 89)			
	Baseline	After 6 Months of Follow-Up	Mean Change	Baseline	After 6 Months of Follow-Up	Mean Change	*P* Value[b]
Body weight (kg)[c]	86.7 [12.8]	86.0 [12.8]	-0.69 [1.5]	87.4 [8.5]	87.1 [8.5]	-0.3 [1.16]	0.082
Waist circumference (cm)	103.4 [8.9]	103.3 [8.3]	-0.18 [1.2]	103.2 [8.6]	103.2 [8.1]	-0.1 [0.7]	0.414
Triglycerides (mg per dL)	189.3 [79.6]	158.4 [77.3]	-30.9 [54.4]	202.5 [88.0]	188.5 [89.0]	-14.5 [50.7]	0.029
HDL-C (mg per dL)	39.5 [10.2]	45.5 [11.0]	+4.9 [13.7]	39.2 [7.8]	40.2 [6.9]	+1.8 [12.5]	0.089
FBG (mg per dL)	120.1 [47.6]	106.8 [47.5]	-13.2 [32.3]	121.6 [46.0]	111.6 [43.6]	-5.8 [26.1]	0.082
Systolic BP (mm Hg)	134.7 [16.2]	122.66 [13.2]	-12.1 [20.1]	134.6 [12.2]	127.2 [15.2]	-6.9 [14.6]	0.018
Diastolic BP (mm Hg)	83.6 [10.7]	76.6 [10.7]	-7.2 [12.6]	83.6 [7.9]	78.8 [7.6]	-4.9 [8.1]	0.049

[a]*Baseline values were collected at the initial enrollment visit; the enrollment period was from March 15, 2009, through May 10, 2009. The values for the 6-month follow-up were collected at the last patient visit (i.e., the sixth monthly visit); the follow-up was from March 15, 2009, through November 12, 2009.*

[b]*P values for the between-group comparisons of the baseline-to-follow-up change amounts. For waist circumference, HDL-C, and FBG, Student's t-tests were used; for body weight, systolic BP, and diastolic BP, Mann-Whitney tests were used.*

[c]*Body weight was included as an outcome measure, although it is not a component of metabolic syndrome as defined by NCEP/ATP III.*

BP = blood pressure; cm = centimeters; FBG = fasting blood glucose; HDL-C = high-density lipoprotein cholesterol; kg = kilograms; mg per dL = milligrams per deciliter; mm Hg = millimeters mercury; NCEP/ATP = National Cholesterol Education Program/Adult Treatment Panel; SD = standard deviation.

At baseline, 55 (50.0%) patients in the intervention group had 3 components of metabolic syndrome according to NCEP/ATP III; 44 (40.0%) had 4 components; and 11 (10.0%) had all 5 components (Table 2). The baseline distribution was similar in the control arm: 46 (51.7%) had 3 components; 36 (40.5%) had 4 components; and 7 (7.9%) had 5 components. After 6 months, 43 (39.1%) patients were successfully shifted from metabolic syndrome status to nonmetabolic syndrome status in the intervention arm, compared with 22 (24.7%) patients in the control arm ($P = 0.032$).

From baseline to follow-up, statistically significant differences between the intervention and control arms were observed for triglycerides, systolic BP (SBP), and diastolic BP (DBP; Table 3, Figure 2). Rates of achievement of goals for SBP and DBP at the 6-month follow-up were 70.0% and 84.5%, respectively. This improvement in metabolic status did not appear to be significantly associated with gender ($P = 0.632$), age ($P = 0.651$), or weight ($P = 0.923$; data not shown).

A total of 308 pharmacist interventions were provided during the course of the study, with a mean of 2.8 interventions per patient. Of these, 182 interventions were provided to the physicians, and 126 were provided to the patients, including patient education and adherence counseling (Table 4). Physicians agreed to and implemented 128 (70.3%) of the pharmacist recommendations. For 90 patients, a recommendation to initiate 1 or more new drug therapies was made, including angiotensin-converting enzyme (ACE) inhibitors (n = 23), angiotensin II receptor blockers (ARBs, n = 6), simvastatin (n = 32), atorvastatin (n = 8), gemfibrozil (n = 12), low-dose aspirin (n = 22), and omeprazole (n = 27). Thirteen interventions were recommendations to increase doses, and 27 interventions suggested that patients were at high risk of developing adverse drug reactions and required monitoring or prophylactic therapy. Laboratory monitoring was recommended in 24 interventions, including 9 recommendations for liver enzyme testing (e.g., for patients on statins, particularly in combination with fibrates); 4 for kidney function testing (e.g., for patients on ACE inhibitor and/or planned titration to combination antihypertensive); 5 for thyroid function testing (to exclude secondary causes of high triglycerides); 2 for potassium-level testing; and 4 for testing of creatinine phosphokinase (CPK) levels. Cost-effective interchange was recommended in 19 interventions; drug discontinuation due to adverse reactions or side effects was suggested in 6 interventions; and drug-drug interactions were identified in 3 interventions. We counseled patients on adherence in 13 interventions and on lifestyle modifications in 113 interventions.

Discussion

In family medicine clinics affiliated with a teaching hospital, pharmacist-physician collaboration resulted in a greater rate of success in shifting patients with metabolic syndrome status to nonmetabolic syndrome status compared with usual care, 39.1% versus 24.7%, respectively. Although this study failed to demonstrate significant between-group differences in weight and waist circumference reductions or HDL-C increases, triglycerides were significantly improved in the intervention arm compared with the control arm. Furthermore, both SBP and DBP improved more in the pharmacist care collaborative practice arm than in usual care, and rates of goal achievement in the intervention arm for SBP (less than 85 mm Hg) and DBP (less than 130 mm Hg) at the 6-month follow-up were 70% and 85%, respectively.

The greater success of physician-pharmacist collaboration compared with usual care may have occurred because diagnosis and management of metabolic syndrome are typically not integrated into standard health care protocols. Procedures for metabolic syndrome identification and for making a

TABLE 4 Pharmacist Interventions with Physicians and Patients

Description	Number	Examples
Interventions with physicians		
Initiate drug therapy	90	Simvastatin was initiated for a patient who failed to achieve recommended values for lipid parameters after 4 months of therapeutic lifestyle changes (total cholesterol 245 mg per dL, LDL-C 160 mg per dL). Metformin was initiated for an obese patient presenting with fasting blood glucose more than 126 mg per dL.
Monitor or administer prophylactic therapy for potential adverse drug reactions	27	Omeprazole 20 mg daily before breakfast was recommended for gastro-protection for patient prescribed NSAID.
Laboratory monitoring	24	Potassium-level monitoring was recommended for a patient presenting with elevated levels of potassium. Liver function testing was recommended for a patient who was prescribed simvastatin and gemfibrozil for the treatment of mixed dyslipidemia.
Cost-effective interchange	19	An ACE inhibitor was recommended instead of the initial physician choice of an ARB for a patient with diabetes; the patient had no history of cough or other therapeutic contraindications.
Increase doses of existing drug therapy	13	Increase daily dose of amlodipine from 5 mg to 10 mg for a patient whose blood pressure readings exceeded recommended goals. Increase simvastatin dose to attain recommended lipid parameters.
Drug discontinuation	6	Patient developed dry cough a few weeks after lisinopril was started. Chest examination excluded other causes, and discontinuation of lisinopril was recommended.
Identification of drug-drug interaction	3	Atenolol was discontinued when patient was started on trandolapril/verapamil single-pill combination therapy to avoid additive risk of cardiac suppression.
Interventions with patients		
Adherence counseling	13	Patient reported that she didn't take the diuretic pill to avoid increased frequency of urination. She was advised to take it early in the morning.
Lifestyle recommendations	113	Patients were encouraged to adapt healthier lifestyles, such as brisk walking for 30 minutes daily, swimming, or cycling. A fruit- and vegetable-rich diet was emphasized. A maximum teaspoon of salt daily and aspartame-based sweetener use were stressed.

ACE = angiotensin-converting enzyme; ARB = angiotensin-II receptor blocker; dL = deciliter; LDL-C = low-density lipoprotein cholesterol; mg = milligrams; NSAID = nonsteroidal anti-inflammatory drug.

well-established diagnosis in real clinical settings are critical. Furthermore, implementing clinical pharmacist services in evaluating metabolic syndrome components, monitoring, and educating patients might provide an effective and applicable tool to identify patients who are at high risk of developing atherosclerotic CVD and type 2 diabetes because of the associations of metabolic syndrome and its components with CVD risk.[13-16]

The effectiveness of pharmacist-physician collaboration is consistent with previous published investigations of the role of pharmacists in the treatment of dyslipidemia, diabetes, and hypertension.[17-19,21,22] In a randomized controlled trial by Carter et al. (2009) that evaluated pharmacist-physician collaboration in the treatment of hypertension in community-based medical offices, a greater mean reduction in SBP over a 6-month follow-up was reported for intervention group versus control group patients; BP was controlled in 63.9% of intervention group patients compared with 29.9% of patients in the control group.[19] A randomized trial by McLean et al. (2008) of combined community pharmacist and nurse care in patients with diabetes found that SBP reduction was a mean 5.6 mm Hg greater in intervention than control group patients after 6 months of follow-up.[22] In a pooled analysis of 2 randomized controlled trials conducted in outpatients with CVD (heart failure or hypertension), Murray et al. (2009) found that the risk of adverse drug events and medication errors was reduced by approximately 34% in patients who received monitoring and instruction from pharmacists compared with those receiving routine dispensing alone.[20] In a study by Ramser et al. (2008), triglycerides were reduced by a mean 43.2 mg per dL, from 150.7 mg per dL to 107.5 mg per dL, in patients with diabetes who were resistant to usual care and received a collaborative pharmacist-physician intervention. This study was not controlled and primarily targeted diabetes clinical indicators, and no significant reductions in DBP or SBP were observed.[17] The present study is the first to evaluate a physician-pharmacist collaborative practice addressing lifestyle changes and drug therapy in patients with metabolic syndrome using a randomized controlled trial design.

Limitations

First, the study's 6-month follow-up period may not have been long enough to measure improvements in weight reduction and waist circumference, which may require longer and extensively focused health education programs. A study with longer follow-up is also needed to assess effects on cardiovascular events and

development of type 2 diabetes mellitus. It is also possible that the effects observed in this study diminished over time.

Second, the physician team was the same for both study arms. Physicians worked with the clinical pharmacist for 9 months (full study period) and were aware of recommendations and educational materials given to patients in the intervention arm, which may have produced a cross-over effect and biased the results in the usual care group. Moreover, usual care patients received phone calls from the pharmacist encouraging their attendance for monthly appointments. They were questioned about drug therapy adherence and/or lifestyle habits and were aware of the various components of metabolic syndrome. The combined effects of physicians and pharmacists on the control group may have contributed to improved outcomes in the usual care group and reduced the observed differences in outcomes between the 2 study groups.

Third, physicians were also aware of their roles in the study. Thus, it is possible that they were more cooperative in accepting pharmacist interventions than they would be in routine day-to-day practice settings.

Fourth, the study was conducted in a single teaching hospital in Jordan, and its intervention methods and results may not generalize to other health systems and cultural settings. However, the study's findings are consistent with those of prior research documenting favorable effects of physician-pharmacist collaboration on patients with chronic disease.[17-22]

Conclusions

Compared with usual care provided by physicians only, physician-pharmacist collaboration improved 6-month outcomes in a sample of patients with metabolic syndrome attending family medicine clinics in a teaching hospital in the Middle East. The effects of careful periodic pharmacological and dietary screening, education, and monitoring of metabolic syndrome should be assessed in routine health care provided in a variety of health care system settings.

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DISCLOSURES

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Concept and design were performed by all authors. Data were collected by Hammad with the assistance of Albsoul-Younes. Data interpretation and writing of the manuscript were performed by Albsoul-Younes and Hammad. The manuscript was revised by Albsoul-Younes and Hammad with the assistance of Tahaineh and Yasein.

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