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Cardiovascular prevention in coronary heart disease patients: guidelines implementation in clinical practice

Prevenção cardiovascular abrangente em pacientes com doença arterial coronária: implementação das diretrizes na prática clínica

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Abstract

Objective: **To demonstrate the utilization of a clinical improvement program in stable coronary artery disease patients to increase the evidence-proven treatment utilization, and to describe the ongoing clinical practice and lifestyle change counseling.**

Methods: **Cross-sectional study followed by a longitudinal component in which the tools utilization to improve clinical practice was assessed by means of additional cross-sectional data collection. 710 consecutive patients were included (Phase 1). After tools implementation, within 6 months period, 705 patients were included (Phase 2) for comparative analysis. Randomly, 318 patients from Phase 1 were selected, 6-12 months after the first evaluation (Phase 3).**

Results: **Phase 1 to Phase 2: there were improvement on smoking cessation (*P*=0.019), dyslipidemia (*P*<0.001), hypertension and physical activity (*P*<0.001). There was significant difference on angiotensin converting enzyme inhibitors – ACEI (67.2% vs. 56.8%, *P*<0.001); angiotensin II receptor blockers – ARB II (25.4% vs. 32.9%, P=0.002) and beta-blocker (88.7% vs. 91.9%, *P*=0.047). Phase 1 to Phase 3: there was both weight (*P*=0.044), and blood pressure reduction (*P*<0.001). There was statistical significant difference on ACEI (64.8% vs. 61.6%, *P*=0.011) and ARB II (27.0% vs. 31.3%, *P*=0.035).**

Conclusion: **There was no significant change on the evidence-based pharmacological treatment utilization between pre and post-intervention phases; there was significant improvement concerning smoking and physical activity in phase 2; substantial improvement on blood pressure levels in both comparisons (Phase 1 to 2 and Phase 1 to 3). The inclusion of a case-manager for the process management was crucial for program efficacy. Comprehensive programs for clinical practice should be pursued for longer follow-up period.**

Descriptors: **Coronary disease. Secondary prevention. Risk factors. Guidelines as topic.**

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Abbreviations, acronyms and symbols	
ASA	acetylsalicylic acid
ARA II	Angiotensin receptor antagonism II
CHAMP	Cardiac Hospitalization Atherosclerosis Management Program
COURAGE	Outcomes Utilizing Revascularization and Aggressive Drug Evaluation
CAD	Coronary Artery Disease
EUROASPIRE	European Action on Secondary Prevention through Intervention to Reduce Events
HDL	High-density lipoprotein
ACE	inhibitors Angiotensin converting enzyme
BMI	Body Mass Index
LDL	Low-density lipoprotein
DBP	Diastolic Blood Pressure
SBP	systolic blood pressure
PURE	Prospective Urban Rural Epidemiological
SPSS	Statistical Package for the Social Sciences
STABILITY	STabilization of Atherosclerotic plaque By Initiation of darapLadIb Therapy

Resumo

Objetivo: **Demonstrar a eficácia de um programa de otimização da prática clínica em pacientes com doença arterial coronária para prescrição de medicamentos e documentar a prática clínica vigente quanto aos medicamentos e medidas para a mudança do estilo de vida.**

Métodos: **Estudo de corte transversal, seguido de componente longitudinal. Foram incluídos 710 pacientes consecutivos (Fase 1). Após aplicação de ferramentas para melhoria da prática clínica, foram incluídos, após seis meses, 705 pacientes com coleta dos mesmos dados (Fase 2). Foram selecionados aleatoriamente, a partir do primeiro grupo, 318 prontuários para comparação desses mesmos pacientes (Fase 3).**

Resultados: **Comparação entre as Fases 1 e 2: melhora em relação a tabagismo (*P*=0,019), dislipidemia (*P*<0,001), hipertensão arterial e atividade física regular (*P*<0,001). Diferença significativa para inibidores da enzima de conversão da angiotensina – IECA (67,2% vs. 56,8%, *P*<0,001); antagonistas do receptor da angiotensina II – ARA II (25,4% vs. 32,9%, *P*=0,002) e betabloqueador (88,7% vs. 91,9%, *P*=0,047). Comparação entre as Fases 1 e 3: houve redução do peso (*P*=0,044) e pressão arterial (*P*<0,001). Em relação à prescrição de medicamentos recomendados, diferença para IECA (64,8% vs. 61,6%, *P*=0,011) e ARA II (27,0% vs. 31,3%, *P*=0,035).**

Conclusão: **Não houve mudança significativa na utilização de medicamentos; entretanto, observou-se melhora significativa em relação ao tabagismo e atividade física na Fase 2; melhora substancial nos níveis de pressão arterial, na comparação tanto entre as Fases 1 e 2 como entre as Fases 1 e 3. A inclusão de enfermeiro treinado para gerenciar o processo foi fundamental. Programas abrangentes de melhoria de qualidade assistencial, provavelmente, devem ser continuados por período de seguimento maior.**

Descritores: **Doença das coronárias. Prevenção secundária. Fatores de risco. Guias como assunto.**

INTRODUCTION

Despite guidelines recommendations on chronic coronary artery disease (CAD) and available scientific evidence to show that the optimal pharmacological treatment, in addition to vigorous intervention on risk factors and lifestyle has benefits in relation to reducing nonfatal cardiovascular events and mortality [1-4], there is a substantial gap between knowledge (availability of data and scientific evidence) and its application in clinical practice, which needs to be filled, due to the secondary prevention therapy is underutilized in clinical practice in patients with CAD.

This fact occurs worldwide, as demonstrated by studies EUROpean Action on Secondary Prevention through Intervention to Reduce Events (EUROASPIRE) I, II and III, which revealed that the prevention of cardiovascular disease in clinical practice is inadequate in European countries [5]. These studies concluded that there is need for more effective management regarding the prescription of drugs with proven efficacy and lifestyle modification, with control of risk factors in patients with CAD [5].

Similarly, the study Prospective Urban Rural Epidemiological (PURE) aimed to assess the use of drugs recommended by the guidelines: antiplatelet agents, statins, angiotensin-converting enzyme inhibitors (ACEI) or antagonists of the angiotensin II receptor (ARB) and beta-blockers in patients with CAD or stroke in high, middle and low income countries, [6]. This study demonstrated that the use of these drugs was far from desirable, even in developed countries [6].

In an attempt to try to reduce the gap between scientific knowledge and the application of it in clinical practice, there were programs that consist of implementing tools and strategies to improve appropriate prescribing of these medications and compliance with them, in order to achieve the aims in relation to the control of risk factors and lifestyle modification.

The Cardiac Hospitalization Atherosclerosis Management Program (CHAMP) assessed patients hospitalized for acute myocardial infarction, unstable angina, cardiac catheterization, for procedures such as coronary artery bypass grafting or percutaneous coronary intervention and ischemic heart failure [7]. The program demonstrated that treatment for secondary prevention, started early, brought

improvement in the prescription of drugs and compliance with them, which resulted in significant reduction of events in one year after discharge [7].

The study Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE), in addition to compare optimal medical therapy alone with optimal medical treatment associated with percutaneous coronary intervention in patients with stable CAD, it included all patients in a program of lifestyle modification life administered by trained nurses to manage processes ("case manager") and demonstrated significant changes in behavior, improving the parameters dependent of change of lifestyle and medication adherence, as well as control of risk factors [8].

Although these studies cited in the international literature, there is lack of information related to this issue, especially in tertiary care hospitals specialize in cardiology in the country.

METHODS

We included patients of both genders, CAD patients with proven coronary angiography showing at least one epicardial coronary artery lesions with ≥ 50%, clinically stable, with or without previous myocardial infarction, pharmacological treatment alone or who underwent revascularization procedures. Patients were identified through the review of medical records of patients seen consecutively in the Medical Section of Coronary Artery Disease, and collected data regarding demographic and anthropometric characteristics, clinical features, risk factors, laboratory tests and treatment used in routine clinical practice.

After this initial collection, the tools used for optimization of clinical practice were:

a) meeting with physicians and health sector, reinforcing the importance of prescription drugs and non-pharmacological measures recommended by guidelines;

b) monthly meeting with residents, instructing and guiding for recommendations;

c) printed posters set in all offices on the drugs recommended for all patients with stable CAD, with their doses and the aims to be achieved regarding the levels of low density lipoprotein (LDL)-cholesterol, systolic (SBP) and diastolic blood pressure (DBP) and the levels of fasting glucose and glycated hemoglobin levels in diabetic patients;

d) process manager ("case manager") to assess the prescription of therapies recommended by spreadsheets distributed daily in the offices to be filled by physicians;

e) guidance to physicians about the need to inform patients about the CAD, which and what are the risk factors and their importance in disease development and progression, how to control them and the benefits of this control;

f) multidisciplinary team consisting of physician responsible for the anti-smoking group, a physical education teacher, dietician and psychologist available for individual interviews and specific guidance in each area, as needed;

g) delivery of booklets with the guidelines of the multidisciplinary team.

Patients included

Phase 1: pre-intervention: consisting of 710 patients who had their medical records assessed for collection of the described data.

Phase 2: post-intervention: consists of 705 consecutive patients who were seen in the section, with the same information collected in phase 1.

Phase 3: consisting of 318 patients selected from the initial sample (Phase 1), randomly, whose medical records were assessed for new data collection, after six to twelve months.

Analysis plan

a) comparison between the data of Phases 1 and 2 (pre- and post-intervention);

b) comparing the data from Phases 1 and 3, with the aim of comparing the same patients between them.

The study design involved cross-section, followed by longitudinal component. The minimum sample size calculation was performed proposing that it would be considered a proper difference of the use of acetylsalicylic acid (ASA) between the two samples, increased from 90% to 95% and the probability of type 1 error $\alpha = 95\%$ and power of Test $1-\beta=0.90$, resulting in 620 patients for each of the samples. Numerical variables were described by their minimum and maximum values, averages, standard deviations and medians and categorical variables were described by absolute and relative frequencies (%). Inferential analysis was performed taking into account the characteristics of the study:

Phases 1 and 2

For numeric variables, we used the nonparametric Mann-Whitney test for comparison of independent groups, and for categorical variables, the chi-square test.

Phases 1 and 3

For numeric variables, we used the nonparametric Wilcoxon test for comparing dependent groups for categorical variables, and the nonparametric McNemar test for comparison of proportion before and after.

The level of significance for the tests was 5% (alpha=0.05) and statistical packages used were SPSS for Windows, version 19.0 (SPSS Inc. Chicago, Illinois) and R software (version 2.15.2).

RESULTS

Comparative results between patients in Phases 1 and 2

The demographic characteristics

Gender, age and ethnicity were comparable between the

two groups. Regarding clinical characteristics, there was a statistically significant difference with respect to stable angina (*P*<0.001), CABG (*P*=0.001) and renal failure (*P*=0.018), more prevalent in Stage 2, and in relation with heart failure (*P*=0.003) and asymptomatic ventricular dysfunction (*P* <0.001) more prevalent in Step 1 (Table 1)

Regarding associated risk factors

Smoking, diabetes, dyslipidemia, LDL >100 mg/dl and/ or high-density lipoprotein (HDL) <40 mg/dl (men) and HDL <45 mg/dl (women), hypertension (BP > 140/90 mmHg) , hypertriglyceridemia (TG>150 mg/dl) and physical activity, there was significant difference compared to nonsmokers (*P*=0.019) and information about smoking more prevalent in Stage 2 (*P*<0.001), a lower proportion of dyslipidemia (*P*<0.001), a lower proportion of hypertensive patients (*P*<0.001) and an increase in the proportion of regular physical activity (*P*<0.001) in Phase 2 (Table 2).

Regarding anthropometric data

For weight, height, body mass index (BMI), waist circumference, SBP and DBP and heart rate, the minimum, maximum, average, standard deviation and median significant difference were calculated regarding the improvement for abdominal circumference between men (*P*=0.022), SBP (*P*<0.001) and DBP (*P*<0.001) in Phase 2 (Table 3). A significant increase in the number of collected information comparing the two phases, demonstrating the efficiency of program service quality with respect to the collection of important data for clinical practice: information on weight were available in 56.5% vs. 93.8% of the time vs. 56%. 94%, on BMI, 55.6% vs. 93% and the abdominal circumference, 5.6% vs. 71.6% respectively for Phases 1 and 2 (*P*<0.001). As to laboratory, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, fasting glucose and glycated hemoglobin, the minimum, maximum, average, standard deviation and median were calculated. For these variables there was no significant difference between the two groups (Table 4).

In addition, we calculated the proportion of patients with laboratory tests within the targets and the results were: LDL <70 mg/dl: 31.6% vs. 34.8% (*P*=0.198), HDL> 40 mg> dL (men): 41.0% vs. 37.0% (*P*=0.118) HDL>45 mg/dl (women) vs 19%. 19% (*P*=0.784), triglycerides <150 mg/dl 67% vs. 68% (*P*=0.847) and among diabetics, fasting glucose <100 mg/dl: 15.4% vs. 19.1% (*P*=0.235), and HbA1c <7.0%: 46% vs. 40.3% (*P*=0.167).

Comparing the prescription of drugs recommended by the guidelines between the pre- and post-intervention, the results showed significant differences, with lower use of ACE inhibitors (*P*<0.001) and greater use of ARBs (*P*=0.002) and beta blockers (*P*=0.047) (Table 5). Assessing the number of patients of whom ACE inhibitor or ARB were prescribed, the results were: 657 (92.5%) in Phase 1 and 627 (89.0%) in Phase 2 (*P*=0.025).

Comparative results between patients in Phases 1 and 3

Whereas patients in Phase 3 are a subset of patients randomly selected from the first group (Phase 1), the demographic data are similar. Likewise, information about the clinical characteristics were similar, but there was a significant difference only for peripheral arterial disease: 31 (9.7%) patients and 42 (13.3%) between Stages 1 and 3, respectively (*P*=0.007).

Regarding risk factors, we considered only modifiable risks: smoking and physical activity. For both smoking and physical activity, the results showed no significant differences between the two phases.

Regarding anthropometric measurements, there was significant differences for weight, with increase from Phase 1 to 3 (*P*=0.044) and reductions in SBP and DBP from Phase 1 to 3 (*P*<0.001) (Table 6).

Table 1. Clinical characteristics

	Phase 1 (N = 710)		Phase 2 (N = 705)		
	N	%	N	%	*P* Value
Stable angina	160	22.5	222	31.5	< 0.001
Myocardial infarction	451	63.5	423	60.1	0.195
Surgical MR	373	52.5	438	62.2	0.001
Percutaneous MR	142	20.0	131	18.6	0.524
Heart failure	129	18.2	88	12.5	0.003
Asymptomatic ventricular dysfunction (EF <50%)	175	24.6	98	13.9	< 0.001
TIA / stroke	38	5.4	43	6.1	0.532
PAD	66	9.3	68	9.7	0.789
CRF (Cr > 2.0mg/dl)	29	4.1	49	7.0	0.018
Chronic AF	7	1.0	13	1.8	0.168

CABG = coronary artery bypass grafting, EF = ejection fraction; TIA = transient ischemic attack, PAD = peripheral arterial disease; CRF = chronic renal failure, Cr = creatinine, AF = atrial fibrillation

Table 2. Associated risk factors.

	Phase 1 (N = 710)		Phase 2 (N = 705)		
	N	%	N	%	*P* Value
Smoking					
Never	122	17.2	175	25.0	0.019
Ex-smoker	388	54.6	409	58.0	0.134
Current	65	9.2	60	8.5	0.289
No information	135	19.0	61	8.5	< 0.001
Diabetes (FPG > 126 mg/dl)	302	42.5	305	43.3	0.729
Dyslipidemia	686/710	96.6	543/705	77.7	
LDL > 100 mg/dl	473/487	97.1	376/495	76.6	< 0.001
HDL < (male) 40 mg/dl					
LDL >100 mg/dl	213/223	95.5	165/205	78.6	
HDL < (fem) 45 mg/dl					
Arterial Hypertension (AP > 140/90 mmHg)	679	95.6	613	87.2	< 0.001
Hypertriglyceridemia (TG > 150 mg/dl)	260	36.6	237	33.6	0.253
Physical activity					
Regular	19	2.7	157	22.4	< 0.001
Sedentary	103	14.5	311	44.4	
No information	588	82.8	232	33.1	< 0.001

FPG = fasting plasma glucose, LDL = low density lipoprotein, HDL = high density lipoprotein, BP = blood pressure, TG = triglycerides

Table 3. Anthropometric measurements.

	Phase 1 (N = 710)					Phase 2 (N = 705)					
	Min	Max	Mean	SD	Median	Min	Max	Mean	SD	Median	*P* Value
Age (years)	32	93	64.9	9.09	65	29	96	65.2	9.9	65	0.390
Weight (kg)	45.0	136	76.2	14.09	75.0	35.0	151.0	74.8	14.08	74.0	0.209
Height (cm)	135	189	164.3	8.75	165	136	193	163.5	8.72	164	0.182
BMI (kg/m²)	16.5	489	28.13	4.40	27.68	14.80	64.5	27.88	4.57	27.40	0.357
WC (cm)											
Male	79	140	105.7	13.61	104.5	61	195	99.76	11.55	99.0	0.022
Female	83	126	100.6	11.80	98.0	63	130	96.88	11.13	97.0	0.414
SAP (mmHg)	80	240	136.3	22.66	130.0	65	210	129.1	18.75	130.0	<0.001
PDAP (mmHg)	50	140	81.54	11.52	80.0	40	120	77.63	10.5	80.0	<0.001
HR (beat/min)	44	120	68.61	10.21	68.0	41	124	68.50	9.35	68.0	0.755

kg = kilogram, cm = cm, BMI = body mass index, m2 = meters squared, WC = waist circumference, SBP = systolic blood pressure, DBP = diastolic blood pressure, HR = heart rate, mmHg = millimeters of mercury, beat/min = beats per minute, Min = minimum, Max = maximum, SD = standard deviation

Table 4. Laboratory exams

	Phase 1 (N = 710)					Phase 2 (N = 705)					
	Min	Max	Mean	SD	Median	Min	Max	Mean	SD	Median	*P* Value
Total Cholesterol (mg/dl)	79	469	162.95	45.17	155.00	64	311	157.78	38.51	152.00	0.139
LDL (mg/dl)	23	255	87.77	34.41	81.00	23	217	84.80	30.15	81.00	0.317
HDL (mg/dl)											
Man	24	77	43.68	9.74	43.00	27	96	43.95	11.10	42.00	0.049
Women	20	113	50.60	13.83	50.00	31	96	50.31	11.64	48.00	0.549
Triglycerides (mg/dl)	34	1111	144.77	100.3	120.00	36	800	138.77	81.67	120.00	0.624
Blood glucose (mg/dl)	50	497	117.87	44.56	106.00	51	316	114.71	38.08	103.00	0.259
Hb A1c (%)	4.8	15.9	6.9	1.59	6.4	4.7	15.0	6.84	1.57	6.3	0.393

LDL = low-density lipoprotein, HDL = high-density lipoprotein, mg/dl = milligrams per deciliter, HbA1c = hemoglobin, A1c, Min = min, Max = maximum, SD = standard deviation

Table 5. Recommended medications.

	Phase 1 (N = 710)		Phase 2 (N = 705)		*P* Value
	N	%	N	%	
Antiplatelet	684	96.3	676	96.4	0.923
AAS	676	95.2	668	94.8	0.846
Clopidogrel	14	2.0	17	2.5	0.572
Ticlopidine	5	0.7	4	0.6	0.716
Statins	699	98.5	686	97.7	0.317
Simvastatin	599	85.7	465	67.8	< 0.001
Atorvastatin	93	13.3	219	31.9	< 0.001
Rosuvastatin	6	0.9	2	0.3	0.288
Ezetimibe	212	29.6	65	9.2	< 0.001
ACEI	477	67.2	398	56.8	< 0.001
Enalapril	403	84.5	363	91.2	0.047
Captopril	66	13.8	32	8.0	< 0.001
Ramipril	6	1.3	2	0.5	0.159
ARA II	180	25.4	229	32.9	0.002
Losartan	177	98.3	221	96.5	0.070
Candesartan	1	0.6	0	0	1.000
Beta-blocker	630	88.7	644	91.9	0.047
Propranolol	8	1.3	4	0.62	0.953
Atenolol	339	53.8	371	57.6	0.067
Carvedilol	240	38.1	223	34.6	0.384
Metoprolol	44	6.9	47	7.3	0.719

ASA = acetylsalicylic acid, ACE inhibitors = Angiotensin converting enzyme, ARA II = antagonist receptor angiotensin II

Table 6. Anthropometric measurements.

	Phase	N	Min	Max	Mean	SD	Median	*P* Value
Weight (kg)	1	73	460	136.0	76.37	16.56	74.0	0.044
	3	73	460	137.0	77.37	16.62	74.0	
BMI (kg/m2)	1	66	17.85	41.89	27.76	4.64	27.68	0.184
	3	66	17.30	41.90	28.15	4.55	28.15	
WC (cm2)	1	6	83.0	117.0	101.0	11.82	102.0	0.255
	3	6	84.0	113.0	103.1	11.27	106.0	
SAP (mmHg)	1	305	90.0	240.0	136.76	23.20	130.0	< 0.001
	3	305	80.0	215.0	131.93	20.54	130.0	
DAP (mmHg)	1	304	60.0	140.0	81.49	12.11	80.0	< 0.001
	3	304	40.0	120.0	78.06	11.05	80.0	
HR (bat/min)	1	280	48.0	113.0	67.93	9.79	67.0	0.255
	3	280	50.0	143.0	69.05	11.64	68.0	

kg = kilogram, BMI = body mass index; m2 = meters squared, cm = centimeter, WC= waist circumference, SBP = systolic blood pressure, DBP = diastolic blood pressure, mmHg = millimeters of mercury, HR = heart rate; beat/min = beats per minute, Min = minimum, Max = maximum, SD = standard deviation

Regarding laboratory tests, the results showed no significant difference (Table 7).

When comparing the proportion of patients in Phases 1 and 3 who had laboratory tests within the targets, the results were: LDL <70 mg/dl: 34.6% and 37.3% (*P*=0.509), HDL> 40 mg/dl (men): 54.3% and 58.8% (*P*=0.073), HDL> 45 mg/dl (women): 62.2% and 60.2% (*P*=0.630), fasting glucose < 100 mg/dl: 13.6% and 21.2% (*P*=0.136), and HbA1c <7.0%: 47.4% and 51.3% (*P*=1.00), respectively. Comparing the prescription of recommended medications, there was a significant difference for lower use of ACE inhibitors (*P*=0.011) and increased use of ARBs (*P*=0.035) - Table 8.

Table 7. Laboratory tests.

	Phase	N	Min	Max	Mean	SD	Median	*P* Value
Total cholesterol (mg/dl)	1	274	93.0	398.0	158.98	43.74	150.0	0.762
	3	274	82.0	323.0	157.15	39.92	151.0	
LDL (mg/dl)	1	276	34.0	255.0	84.41	34.83	81.5	0.762
	3	276	30.5	194.0	82.62	30.47	80.9	
HDL (mg/dl)	1	195	24.0	77.0	44.01	9.66	43.0	0.453
Men	3	195	27.0	96.0	44.02	11.14	42.0	
HDL (mg/dl)	1	82	29.0	113.0	51.96	14.11	50.5	0.276
Women	3	82	31.0	96.0	50.24	11.69	48.0	
TG (mg/dl)	1	276	34.0	1111.0	146.12	99.38	120.5	0.387
	3	276	35.0	827.0	146.76	95.81	125.5	
FG (mg/dl)	1	280	63.0	339.0	115.66	31.36	106.50	0.956
	3	280	63.0	314.0	115.99	39.23	104.00	
HbA1C (%)	1	147	4.8	12.5	6.69	1.39	6.3	0.312
	3	147	5.0	12.8	6.79	1.50	6.3	

mg/dL = milligrams per deciliter, LDL = low density lipoprotein, HDL = high density lipoprotein, TG = triglycerides, FG = fasting glucose, HbA1c = hemoglobin H1c, Min = minimum, Max = maximum, SD = standard deviation

Table 8. Recommended medications

	Phase 1		Phase 3		*P* Value
	N	%	N	%	
Antiplatelet	308	96.9	309	97.2	1.000
AAS	304	98.7	307	99.36	0.453
Clopidogrel	7	2.3	3	0.97	0.289
Ticlopidine	2	0.6	1	0.37	1.000
Statin	314	99.7	315	99.1	1.000
Simvastatin	272	85.5	236	74.2	< 0.001
Atorvastatin	39	12.3	76	23.9	< 0.001
Rosuvastatin	2	0.6	3	0.9	1.000
Ezetimibe	85	26.7	16	5.2	0.011
ACEI	206	64.8	191	61.6	0.011
Enalapril	178	56.0	180	56.6	0.878
Captopril	26	8.2	10	3.1	< 0.001
Ramipril	2	0.6	1	0.3	1.000
ARA II	86	27	99	31.3	0.035
Losartan	86	27	97	30.5	0.080
Candesartan	0	0.0	1	0.3	1.000
Beta-blocker	285	89.6	286	89.9	1.000
Propanolol	4	1.4	3	0.9	1.000
Atenolol	156	54.7	155	54.2	1.000
Carvedilol	103	36.14	111	38.1	0.229
Metoprolol	22	7.7	17	5.9	0.186

ASA = acetylsalicylic acid; ACE inhibitors = Angiotensin converting enzyme; ARA II = antagonist receptor angiotensin II

DISCUSSION

Results of Phases 1 and 2

The demographic characteristics, gender, age and ethnicity, were comparable. Regarding clinical characteristics, there was significant differences related to the higher proportion of stable angina ($P<0.001$), CABG ($P=0.001$) and in relation to the lower proportion of heart failure ($P=0.003$) and asymptomatic ventricular dysfunction ($P<0.001$). Comparing the risk factors, we found the proportion of dyslipidemia and hypertension significantly lower ($P<0.001$ for both variables) in Phase 2. There was improvement in regard to smoking, as the category of never-smokers. For regular physical activity, there was a significant improvement in Phase 2, from 2.7% to 22.4% ($P<0.001$), but the proportion of patients with missing information on this variable was very high in Phase 1: 82.8 % vs. Phase 2 33.1% ($P<0.001$).

Regarding anthropometric measurements between the two populations, the study showed significant improvement compared to waist circumference in men ($P=0.022$), SBP ($P<0.001$) and DBP ($P<0.001$), demonstrating substantial improvement in the last two parameters, which can be attributed to increased adherence to prescribed medications and better understanding about the importance of diet and

physical activity after intervention. With respect to weight, BMI and waist circumference among women, there was a reduction in numbers, but without reaching statistical significance. We note that there was a significant increase in the number of information collected in Phase 2: for the weight from 56.5% to 93.8%, for height from 56% to 94%, for BMI from 55.6% to 93.9% and for waist circumference from 5.6% to 71.6%, all *P*<0.001, demonstrating the effectiveness of the intervention for improving quality of care. The comparison of laboratory tests showed a significant difference for the variable HDL-cholesterol in men (*P*=0.049). As for total cholesterol, LDL-cholesterol, triglycerides, fasting glucose and HbA1c, we found numerical reduction, but without reaching statistical significance. Again, this finding may reflect lack of statistical power to detect difference. The substudy of the COURAGE trial that assessed intensive multifactorial intervention for patients with stable CAD assessing medication adherence and the parameters resulting from the modification of lifestyle through program managed by trained nurses ("case manager") showed: significant reduction of smoking from 23% to 19% (*P*<0.025), increased physical activity of 58% to 66% (*P*<0.001), reduced SBP (*P*<0.001), LDL-cholesterol (*P*<0.0014) , increasing HDL-cholesterol (*P*<0.001) and triglycerides (*P*<0.001).

Among diabetic patients, glycated hemoglobin remained unchanged (*P*=1.0). The BMI increased after 5 years (*P*<0.001). Comparing the results of this clinical study with the present project, we found some similarities and differences. Regarding the blood pressure, there was significant decrease in both. With respect to smoking, there was significant reduction in the COURAGE trial and in the present study, significant reduction of never-smokers. A significant increase of patients who practiced regular physical activity in COURAGE, as in this study. As for LDL-cholesterol, there was a significant reduction in COURAGE, and in this study, only numerical reduction, but without statistical significance. We note that the average LDL-cholesterol pre-randomization was higher in COURAGE: 101 ± 0.83 mg/dl, compared to the average of the present study, even before the intervention: 87.77 ± 34.41 mg/dl, possibly due to the higher level of prescribing in our service, because it is a tertiary and academic hospital. The BMI in the present study showed numerical reduction, but without statistical significance, while there was significant increase in COURAGE. The glycated hemoglobin in diabetic patients remained unchanged in both studies. Additionally, in the present study, we calculated the proportion of patients with laboratory tests within the recommended targets in Phases 1 and 3: LDL <70 mg/dl: 31.6% vs. 34.8% (*P*=0.198), HDL> 40 mg/dl (men) and > 45 mg/dl (women): 41% vs. 37% (*P*=0.118) and 19% vs. 19% (*P*=0.784), respectively; triglycerides <150 mg/dl 67% vs. 68.0% (*P*=0.847) and among diabetics, fasting glucose <100 mg/dl: 15.4% vs. 19.1% (*P*=0.235) and glycated hemoglobin <7%: 46% vs. 40.3% (*P*=0.167). Except triglyceride levels, all other parameters showed ratios below 50% within the targets. We can, in an exploratory way, interpret the absence of differences in these parameters after implementation of the intervention program, as a result of the lack of statistical power to detect differences that may exist, short observation period so that the improvement could be demonstrated and finally the lack of efficacy the tools used in the program.

Comparing the prescription of recommended medications, the results of this study showed antiplatelet: 96.3% vs. 96.4% (*P*=0.923), statins: 98.5% vs. 97.7% (*P*=0.317) and statistically significant lower use of ACE inhibitors: 67.2% vs. 56.8% (*P* <0.001) and greater use of ARBs: 25.4% vs. 32.9% (*P*=0.002) and beta-blockers: 88.7% to 91.9% (*P*=0.047). The use of medication deemed appropriate in the COURAGE trial after five years was higher as antiplatelet agents: from 87% to 96%, statins: 64% to 93%, ACEI or ARB: 46% to 72% and beta-blockers: 69 % to 85% (*P* <0.001). In the present study, the proportion of patients on ACE inhibitors or ARBs, set amidst Phases 1 and 2 was: 92.5% and 89%, respectively (*P*=0.025). The reduction in the use of this class of drugs may be in fact higher proportion of patients with chronic renal failure in Phase 2.

The CHAMP program assessed patients with the characteristics already discussed and demonstrated that preventive treatment initiated early, during admission and before discharge, substantially improved the prescription of drugs and adherence to the same of those which resulted in significant reduction of events one year after discharged in relation to recurrent myocardial infarction, hospitalization and cardiac and total mortality (*P* <0.05 for all events). This program also showed that medication adherence was maintained during the period of six years, 68%, 92%, 91% and 94% for aspirin, 12%, 68%, 72% for beta-blockers in 78%, 4%, 52 %, 64% and 70% for ACEI and 6%, 88%, 89% and 90% for statins in periods respectively the 1992/1993 1994/1995, 1996/1997 and 1998/1999.

Comparing the present study regarding the use of medicines, this study showed similar proportion of use in relation to all drugs after six years of evolution. The CHAMP project was performed twelve years before the present study and, on that date, the use of evidence-based medications was substantially lower, e.g., 12% beta-blockers, statins 6% and 4% of ACE inhibitors. This study was performed in a tertiary and academic hospital, where the use of these therapies is already in reasonable proportions, with lower propensity to increase in use after programs of quality of care improvement.

Recent publication of the preliminary results of the study Stabilization of Atherosclerotic plaque By Initiation of darapLadIb Therapy (STABILITY), involving 15,828 patients in 39 countries with chronic CAD, showed that the proportion of the prescription of recommended therapy for secondary prevention of CAD was adequate: antiplatelet (96%), statins

(97%), ACE inhibitors and ARBs (77%) and beta-blockers (79%). Despite this, many patients did not reach treatment goals for blood pressure (46%), LDL-cholesterol (29%), glycemic control among diabetics and the prevalence of overweight and obesity were high (79% and 36%, respectively) with considerable regional differences. Among diabetic patients, 44% achieved target HbA1c <7% [9].

These results show many similarities with the present study, since the proportion of use of drugs recommended, both during pre- and post-intervention, was quite satisfactory, but the patients who achieved the proposed targets were lagging behind: waist circumference (21.1%), LDL-cholesterol (34.8%), HDL cholesterol (56%) and HbA1c (40.3%). The exception was the control of blood pressure, both systolic and diastolic, whose averages significantly reduced in comparison with the Phase 1 and 2 [9].

Comparing these data with the results of the present study, we consider some differences: a) the setting of a clinical trial is different from what happens in the real world, because the profile of the patients and the inclusion and exclusion criteria are not always the same and, in the present study, patients were included in the outpatient care routine and b) differences in follow-up time: 4.6 years on average for COURAGE, six years in CHAMP and, in this study, between six to twelve months, c) in studies under discussion the same patients in the pre- and post-intervention period were compared, whereas in the present study, the comparison between Phases 1 and 2 were independent populations, and Phases 1 and 3 were dependent groups.

Results of the Phase 1 and Phase 3

The demographic and clinical characteristics were similar except for peripheral arterial disease, whose proportion was 9.7% in Phase 1, and 13.3% in Phase 3 (P=0.007). Regarding risk factors, we consider only the modifiable: smoking and physical activity, and for both variables, there was no significant differences between the two phases. Regarding anthropometric measures, there was a significant increase of the weight (P=0.004) and a significant reduction in SBP (P<0.001) and DBP (P<0.001). For BMI and waist circumference, there was increased number, but without reaching statistical significance. Regarding laboratory tests, there was no significant differences between the two phases, although total cholesterol and LDL-cholesterol showed numerical reduction, but other variables remained in similar levels.

Comparing the proportion of patients' exams within the targets, we observed: LDL cholesterol <70 mg/dl: 34.6% vs. 37.3% (P=0.509), HDL-cholesterol> 40 mg/dl (men): 54.3% vs. 58.8% (P=0.073), HDL-cholesterol> 45 mg/dl (female): 62.2% vs. 60.2% (P=0.630) and among diabetics, fasting glucose <100 mg/dl: 13.6% vs. 21.2% (P=0.136), and HbA1c <7.0%: 47.4% vs. 51.3% (P=1.00). When we compare the prescription of recommended medications, there was a significant difference for lower use of ACE inhibitors (P=0.011) and increased use of ARBs (P=0.035). In Phase 3, different from that observed in Phase 2, there was no increase in the number of collected information, particularly with respect to demographics, making difficult the appropriate methodological data analysis. We can attribute this to the fact of not acting managing process nurse at this stage.

The STABILITY study, which involved patients with a profile similar to the current study aimint the atherosclerotic plaque stabilization in patients with chronic CAD using the suitable standard medication, based on the ACC/AHA guidelines for secondary prevention, established as targets: proportions ≥ 90 % of patients on aspirin, ≥ 80% of patients on statin therapy, ≥ 80% of patients with LDL-cholesterol <100 mg/dL, ≥ 80% of patients with SBP <140 mmHg and DBP <90 mmHg and ≥ 70% of diabetic patients with HbA1c <7%. After four years of follow-up, this study obtained the following proportions of use of medicines: aspirin, 96% and 94.3%, statins, 96.7% and 95%, beta-blockers, 76.3% and 79%, ACEI/ARBs , 82.7% and 86.7%; in relation to the targets: LDL cholesterol <70 mg/dl, 33% and 33.7%, SBP <140 mmHg, 76.3% and 66.4%, DBP < 90 mmHg, 85.5% and 89.3%, HbA1c <7%, 29.8% and 39.3%, respectively [9].

Assessing data related to our center in this clinical study, comparing the initial visit to the last visit, the results showed: use of AAS: 100% and 100%, statins: 94.1% and 100%, beta-blockers: 76.5% and 88.2%, ACEI/ARBs: 70.6% and 76.5%, LDL-cholesterol <70mg/dL: 17.6% and 29.4%, SBP <140 mmHg: 42.9% and 85, 7%, DBP <90 mmHg: 74.4% and 100% and HbA1c <7.0%: 16.7% and 33.3%, respectively. Comparing the results of STABILITY in our center with this study, it was observed proportion of prescription medications comparable, however, regarding some targets, although it deals with an assessment of daily clinical practice in the institution, showed relatively better results than STABILITY, as follows: LDL-cholesterol <70 mg/dl: 37.3% vs. 29.4% and HbA1c: 51.3% vs. 33.3%.

CONCLUSION

There was no significant change in the use of medications with proven efficacy in secondary prevention of CAD between the pre- and post-intervention, both between Phases 1 and 2 and between Phases 1 and 3, considering their proper prescription from pre- intervention. Regarding the parameters related to the modification of lifestyle through non-pharmacological measures, there was a significant improvement in relation to smoking and physical activity in Phase 2 compared to Phase 1, and numerical improvement, but did not reach statistical significance for other parameters such as waist circumference, BMI, LDL-cholesterol, HDL-cholesterol, and in relation to the targets of HbA1c for

diabetics. There was substantial improvement in the levels of SBP and DBP in both comparison between Phases 1 and 2 and between Phases 1 and 3. The inclusion of nurses trained to manage the "case manager" process is critical to the effectiveness of a comprehensive prevention program for patients with CAD. Programs for improving quality of care in tertiary and academic hospitals, should probably be continued by follow-up period exceeding one year.

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