Published in final edited form as:
Am Heart J. 2008 September ; 156(3): 528–536.e5. doi:10.1016/j.ahj.2008.05.015.

Baseline Characteristics of Patients with Diabetes and Coronary Artery Disease Enrolled in the BARI 2D Trial

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Abstract

Background—The Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) was undertaken to determine whether early revascularization intervention is superior to deferred intervention in the presence of aggressive medical therapy and whether antidiabetes regimens targeting insulin sensitivity are more or less effective than regimens targeting insulin provision in reducing cardiovascular events among patients with type 2 diabetes mellitus and stable coronary artery disease (CAD).

Methods—BARI 2D is an NIH-sponsored randomized clinical trial with a 2×2 factorial design. Between 2001 and 2005, 49 clinical sites in North America, South America and Europe randomized 2,368 patients. At baseline, the trial collected data on clinical history, symptoms and medications along with centralized evaluations of angiograms, electrocardiograms, and blood and urine specimens.

Results—The majority of BARI 2D patients were referred from the cardiac catheterization laboratory (54%) or cardiology clinic (27%). Of the randomized participants, 30% were women, 34% were minorities, 61% had angina, and 67% had multi-region CAD. Moreover, 29% had been treated with insulin, 58% had HbA1c > 7.0%, 41% LDL cholesterol ≥ 100 mg/dl, 52% blood pressure > 130/80 mmHg, and 56% BMI ≥ 30 kg/m^2.

Conclusions—Baseline characteristics in BARI 2D are well-balanced between the randomized treatment groups, and the clinical profile of the study cohort is representative of the target population. As a result, the BARI 2D clinical trial is in an excellent position to evaluate alternative treatment approaches for diabetes and CAD.

Introduction

The Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) is a randomized clinical trial initiated to evaluate treatment strategies for diabetes and coronary artery disease (CAD) in patients with both of these conditions. In 1996, post-hoc analyses of the original Bypass Angioplasty Revascularization Investigation (BARI) randomized trial demonstrated that multivessel coronary disease patients with type 2 diabetes mellitus had lower survival relative to those without diabetes regardless of the form of revascularization and that

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*BARI 2D Sites and Investigators listed in Appendix

CABG was associated with better survival than PTCA without stents in patients with diabetes.[1] Since most BARI patients had unstable angina and all required revascularization, the optimal treatment approach was unknown for patients with stable coronary disease whose symptoms did not require urgent revascularization. BARI 2D was designed to answer this question by comparing an initial strategy of coronary revascularization coupled with intensive medical therapy versus an initial strategy of intensive medical therapy alone. At the time the trial was designed, data were emerging that suggested that metformin and thiazolidinedione (TZD) drugs might have beneficial effects on cardiovascular disease independent of their blood glucose lowering actions.[2-3] Thus, the second aim of BARI 2D was to evaluate whether managing glycemia with insulin sensitizing medications could improve cardiovascular outcomes compared with insulin-providing medications (insulin or insulin secretagogues).

Patients with type 2 diabetes and established coronary disease are at high risk of cardiovascular events.[4] Yet, few studies include sizable cohorts of diabetes patients presenting at a clinical stage when revascularization is acceptable but not mandatory according to evidence based AHA/ACC Class 1 indications.[5-6] The BARI 2D trial enrolled 2368 such patients. Baseline data provide an opportunity to determine how the trial participants relate to broader patient populations with diabetes, coronary disease or both and to observe associations among risk factors in this population.

Methods

Trial Design

BARI 2D was designed to compare treatment strategies for diabetes and established coronary artery disease in the setting of standardized glycemic control and intensive management of dyslipidemia, hypertension, smoking, and obesity. The trial protocol and rationale have been described in detail.[7-10] Using a 2×2 factorial design, patients were assigned at random to a diabetes treatment and to a cardiovascular treatment. The diabetes component compares an insulin sensitizing strategy of glycemic control versus an insulin providing strategy. The cardiovascular component compares a strategy of intensive medical therapy and initial coronary revascularization versus a strategy of intensive medical therapy alone with revascularization deferred until mandated by symptoms according to clinical guidelines. Eligible patients underwent angiography to document CAD and to determine suitability for elective revascularization. Randomization was stratified by physician-declared *intended revascularization strategy* (PCI or CABG) and by clinical site.

Patients were eligible for BARI 2D if they were at least 25 years old with a diagnosis of type 2 diabetes mellitus, documented ischemia, and angiographically documented CAD with at least one significant lesion (≥ 50% stenosis) suitable for elective revascularization. Those with classic exertional angina but without a pre-procedure stress test were eligible if they had a lesion with ≥ 70% stenosis. Patients were not eligible if they required immediate coronary revascularization or if they had undergone revascularization within twelve months prior to study entry. Other exclusion criteria include: New York Heart Association functional class III or IV congestive heart failure, need for concurrent major vascular surgery, stenosis ≥ 50% of the left main coronary artery, hemoglobin A1c (HbA1c) >13%, serum creatinine >2.0 mg/dl, and hepatic disease. The protocol was approved by Institutional Review Boards at all participating institutions, and patients signed written informed consent.

A total of 2,368 patients were enrolled at 49 clinical centers throughout North America, South America and Europe between January 1, 2001 and March 31, 2005. One additional site was withdrawn from BARI 2D, and data from this site (n=14 patients, no deaths reported at the time of site termination) were excluded from the analyses. Under the protocol, risk factors are managed to aim for target levels HbA1c <7.0%, blood pressure ≤ 130/80 mmHg and LDL

cholesterol <100 mg/dl. The BARI 2D patient treatment phase ends November 30, 2008. The primary endpoint is all-cause mortality, and the principal secondary endpoint is the composite of death, myocardial infarction and stroke. Patient safety and treatment efficacy are assessed by an independent Data and Safety Monitoring Board.

BARI 2D is coordinated at the University of Pittsburgh. The trial is funded as a cooperative agreement by the National Heart, Lung and Blood Institute (NHLBI) and receives additional funding from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Several pharmaceutical companies provide supplemental funding and/or donate medications or supplies. The corporate sponsors played no part in the design, conduct or analysis of the study.

Baseline Data

BARI 2D collected demographic, clinical history, clinical measurements and medication data. Core laboratories provided centralized evaluations of angiographic anatomy, electrocardiograms (ECG), HbA1c, serum lipid levels, urine albumin and creatinine, and fibrinolytic factors. Missing core HbA1c and lipid values were imputed based on local site laboratory values.

Definitions

A *significant lesion* is defined as a luminal narrowing ≥ 50% in an anatomically relevant coronary artery segment of size ≥ 1.5 mm. The *number of diseased myocardial regions* is the number of territories (anterior, lateral or posterolateral) with at least one significant lesion. *Myocardial jeopardy index* is the ratio of jeopardized and anatomically relevant segments downstream of significant lesions relative to all viable left ventricular segments, reflecting the extent of anatomic CAD.[11]

Michigan Neuropathy Screening Instrument (MNSI) *clinical* score is based on physical examination of ankle reflexes, toe vibration sensation and designated abnormalities; values >2 provide clinical evidence of neuropathy. *MNSI screening* score is a count of patient-identified sensory symptoms; values ≥ 7 are consistent with neuropathy.[12]

Statistical Analysis

Descriptive statistics include means +/- standard deviations and proportions; medians are presented for highly skewed data. Variables were compared between the two randomized cardiac treatment groups and two randomized diabetes treatment groups. Selected variables were compared among groups defined by age, gender, race/ethnicity and region. T-tests, Wilcoxon non-parametric tests and chi-square tests were used, and p-values < 0.01 were considered statistically significant due to the multiple comparisons in this manuscript.

Results

Patient Origin

A total of 4623 patients consented to be screened for the BARI 2D trial. A majority were identified in the cardiac catheterization laboratory or cardiology clinic (Figure 1) and generally consented prior to the qualifying angiogram. Approximately half of screened patients were eligible for enrollment (N=2436), and 97% consented to randomization. The reason for ineligibility was not collected before July 15, 2002. Among 1545 ineligible patients with reason for exclusion available, 51% were excluded for insufficient CAD, 10% for CAD that was inappropriate for revascularization, and 28% for severe CAD where revascularization was considered necessary.

Demographic Characteristics and Physical Examination

The typical patient in BARI 2D was white, male and 62 years old; however, 30% of patients were women and 34% were minorities (Figure 2). The majority of participants (63%) were enrolled from the United States, but substantial numbers were enrolled from Canada (15%) and Brazil (15%), with the remaining 7% from Mexico, the Czech Republic, and Austria. The mean body mass index (BMI) was 31.7 +/- 5.9 kg/m^2 and the mean systolic and diastolic blood pressures were 131.7 +/- 20.0 and 74.5 +/- 11.2 mmHg respectively (Table 1).

Clinical History

The frequency of cardiac risk factor combinations in BARI 2D are shown in Figure 3. By design, all participants had type 2 diabetes. Over 80% had a history of hypertension, and 45% had the triad of smoking, hypertension and hyperlipidemia. Almost a third had prior myocardial infarction, but few had congestive heart failure (7%). In addition, 24% had coronary revascularization prior to randomization, 61% had classic angina, and 24% had evidence of atherosclerosis in vascular beds beyond coronary disease. The average duration of type 2 diabetes mellitus was 10.4 +/- 8.7 years. Clinical manifestations and complications of diabetes were relatively common: 23% of patients reported hypoglycemic episodes, and 50% had clinical evidence of neuropathy.

Laboratory Evaluations

At baseline, the mean HbA1c level was 7.7 +/- 1.6%, and 33% of patients had microalbuminuria or macroalbuminuria. The median total cholesterol level was 164 mg/dl, median triglycerides 148 mg/dl, median HDL 37 mg/dl, and median LDL cholesterol 92 mg/dl; notably, 21% of patients had LDL < 70 mg/dl. The median PAI concentration and activity levels were 23.0 ng/ml and 16.0 au/ml respectively, and the median TPA antigen was 9.7 ng/ml.[13] Fifty five percent of BARI 2D patients had abnormal ECG findings (Table 2), and 18% had left ventricular ejection fraction below 50%. Based on angiographic core laboratory data, two-thirds of participants had CAD involving multiple myocardial regions.

After coronary angiography and before randomization, 1605 patients (68%) had PCI designated as the intended revascularization (half of whom were then assigned to initial revascularization and half to initial medical therapy) and 763 (32%) had CABG designated. The intended mode of revascularization correlated to the extent and severity of coronary artery disease. In the PCI-intended stratum, the mean number of significant lesions was 2.3 and 10% of the patients had proximal LAD disease, while in the CABG-intended stratum, the mean number of significant lesions was 3.5 and 19% of patients had proximal LAD disease. The myocardial jeopardy index was significantly higher in the intended CABG stratum (Figure 4).

Risk Factor Status

A comparison of risk factor control in BARI 2D and the latest National Health and Nutrition Examination Surveys (NHANES) cohort of patients with diabetes is shown in Figure 5.[14] At baseline, 12% of BARI 2D patients were at the pre-specified protocol targets for the four major risk factors (HbA1c, LDL, blood pressure, and smoking).

Medications

BARI 2D participants were taking an average of 1.6 diabetes drugs, 2.2 drugs for angina, hypertension or heart failure, and 0.9 lipid drugs (Table 2). Of note, 19% of patients were receiving a thiazolodinedione, 28% insulin, and 75% a statin; however, 9% were not taking any diabetes drugs and 15% were not taking any anti-anginal drugs (beta-blockers, calcium blockers and long-acting nitrates). At baseline, 37% of patients were receiving aspirin, ACE-

inhibitor, statin, and beta-blockers, the standard AHA/ACC evidence-based recommended medications for diabetes and CAD.

Baseline Comparisons

Comparing all baseline characteristics displayed in Tables 1 and 2 among the randomized treatment groups indicated that the initial revascularization group had worse angina symptoms than the medical therapy group (Stable CCS Class 3 or 4 or unstable angina: 22% vs 15%, p=0.002). No other imbalances were detected at the p<0.01 level among the randomized treatment groups.

In contrast, characteristics varied significantly among subgroups defined by age, gender, race/ethnicity and region (Table 3). Younger patients had higher mean HbA1c and lipid levels. Females had higher mean HbA1c, SBP and LDL values but fewer diseased myocardial regions than males. Relative to other groups, Black patients had significantly higher mean blood pressure and LDL cholesterol. The proportion of females and Black participants receiving insulin was higher and metformin was lower compared with their counterparts. Patients from the United States had larger body mass, more frequently had abnormal LV function and prior revascularization, and more often received insulin and TZD than non-US patients. Those outside the US and Canada had worse risk factor control and more extensive myocardial disease.

Discussion

The patients enrolled in the BARI 2D clinical trial represent a large segment of the population of patients with diabetes and coronary disease. Evidence based guidelines for the optimal treatment of both of these conditions are lacking. BARI 2D has the potential to address the impact of alternative diabetes and CAD treatments on cardiovascular outcomes, the major cause of mortality in this population.

Patient Recruitment

BARI 2D required a close collaboration between cardiologists and endocrinologists to formulate the hypotheses and to determine the characteristics of patients for whom the optimal treatments had not yet been resolved. Eligibility criteria were defined to assure that study participants were similar to those in the community to facilitate the generalization of trial results and to provide data for future updates of clinical guidelines to practitioners. Several requirements made the implementation of the glycemic trial protocol more difficult. For example, the exclusion criterion serum creatinine > 2.0 mg/dl (rather than >1.5 mg/dl) meant that metformin could not be used in all insulin sensitizing subjects. Similarly, enrolling patients who already received insulin broadened the trial population but added complexity to the glycemic treatment protocol.

BARI 2D Population

There were few statistically significant and no clinically important baseline differences between the randomized treatment groups. A higher proportion of patients with relatively severe angina symptoms were assigned to initial revascularization. Since the two randomization groups have substantial overlap in symptom status, this factor can be addressed with subsequent analyses.

BARI 2D will evaluate early revascularization intervention versus revascularization deferred until mandated by symptoms. It is not a trial comparing CABG and PCI. The revascularization strategy was physician determined and based upon the patients' coronary anatomy rather than random assignment. By design, those with the most extensive coronary disease were more

frequently physician-selected for the 'CABG intended' stratum. With the stratified randomization, BARI 2D can compare PCI versus medical therapy in a group of PCI-intended patients, and CABG versus medical therapy among CABG-intended patients. Randomized comparisons of PCI versus CABG for patients with diabetes will be performed in other trials such as NHLBI FREEDOM,[15] VA Coronary Artery Revascularization in Diabetes (VA CARD),[16] and Coronary Artery Revascularisation in Diabetes (CARDia).[17]

BARI 2D successfully enrolled a patient group appropriate for the design of the trial. Glycemic and cardiovascular risk factor control was consistent with current guidelines for some participants but inadequate for many others. Establishing a partnership between cardiologists and endocrinologists was an important aspect of BARI 2D. When the final results of BARI 2D are available, the trial will demonstrate the feasibility and potential utility of a combined approach to management of diabetes and CAD.

Comparison with Established Cohorts

In the most recent NHANES cohort with diabetes,[14,18] 48% of the participants were female, 53% were less than 60 years old, 76% were White Non-Hispanic, 18% were Black Non-Hispanic, 7% were Hispanic, and average BMI was 33.0 kg/m^2. The BARI 2D participants were similar to this cohort regarding race/ethnicity, duration of diabetes and body mass but were slightly older and more likely to be male. It is somewhat surprising that only 30% of the BARI 2D population is female given that after menopause, women and men with diabetes have comparable rates of cardiovascular disease.[19] A positive feature of BARI 2D is the inclusion of 17% Blacks and 13% Hispanics since these groups suffer disproportionately from type 2 diabetes. Although hypertension was equally common in BARI 2D and NHANES, high cholesterol was less prevalent in BARI 2D possibly due to the pervasive use of statins among trial participants.

The BARI 2D cohort is also comparable to populations enrolled in clinical trials with related study aims. [20-22] The Prospective Pioglitazone Clinical Trial in Macrovascular Events (PROactive)[20] randomized pioglitazone versus placebo among patients with diabetes and a history of macrovascular disease. By eligibility requirements, 100% of BARI 2D participants had angiographically documented CAD compared to 48% of PROactive patients; however, a larger proportion of PROactive patients had a history of cardiovascular events including MI (47%), stroke (19%), and prior revascularization (31%). The two trials are comparable with respect to age, sex, duration of diabetes and insulin use, but BARI 2D enrolled a greater percentage of minorities (34% vs 1.5%). The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial[21], conducted by the Department of Veterans Affairs, randomized intensive medical therapy with PCI versus without PCI; all COURAGE patients had coronary disease, but only 32% had diabetes. As expected, BARI 2D enrolled a larger proportion of females than COURAGE, and BARI 2D patients were less likely to be current smokers or to have classic angina (61% versus 88%). The Action in Diabetes and Vascular Disease (ADVANCE) trial is a factorial designed trial evaluating blood pressure therapy and intensive glucose control[22] among diabetes patients from 20 countries. Compared to ADVANCE, BARI 2D patients were younger and had higher BMI. Although BARI 2D participants more frequently had history of hypertension (82% versus 69%), they had lower blood pressure (132/75 versus 145/81 mmHg). Insulin use was more common in BARI 2D (28% versus 1%) while metformin and sulfolnylurea use were more common in ADVANCE; HbA1c was similar.

The NHLBI is concurrently sponsoring the Action to Control Cardiovascular Risk in Diabetes (ACCORD).[23] This large randomized trial tests whether intensive treatment aimed at lowering HbA1c to < 6.0% reduces cardiovascular risk compared with standard treatment aimed at maintaining HbA1c in the range of 7.0 to 7.9%. BARI 2D and ACCORD are complementary

trials, the former determining the optimum glucose lowering strategy and the latter the optimal glycemic target for minimizing cardiovascular events and mortality in diabetes. The randomized cohorts are comparable in age, duration of diabetes, minority representation, BMI, HbA1c, and proportions treated with insulin prior to entry. Finally, both trials have similar 5-year follow-up, ideal for the long-term evaluation of treatment strategies.

Conclusion

The baseline data presented in this paper confirm that the BARI 2D clinical trial participants comprise an appropriate patient population for assessing the risks and benefits of the selected interventions. With systematic monitoring of glycemic control, blood pressure and lipids to ensure proper control of cardiovascular risk factors, the BARI 2D study is in an excellent position to evaluate alternative modes of treatment for CAD and to determine whether the mode of diabetes treatment influences cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease.

Acknowledgments

BARI 2D is funded by the National Heart, Lung and Blood Institute and the National Institute of Diabetes and Digestive and Kidney Diseases (U01 HL061744, U01 HL061746, U01 HL061748, U01 HL063804).

BARI 2D receives significant supplemental funding from GlaxoSmithKline, Bristol-Myers Squibb Medical Imaging, Inc., Astellas Pharma US, Inc., Merck & Co., Inc, Abbott Laboratories, Inc., and Pfizer, Inc and generous support from Abbott Laboratories Ltd., MediSense Products, Bayer Diagnostics, Becton, Dickinson and Company, J. R. Carlson Laboratories, Inc., Centocor, Inc., Eli Lilly and Company, LipoScience, Inc., Merck Sante, Novartis Pharmaceuticals Corporation, Novo Nordisk, Inc.

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Investigators:	Warren Laskey, MD
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† Deceased

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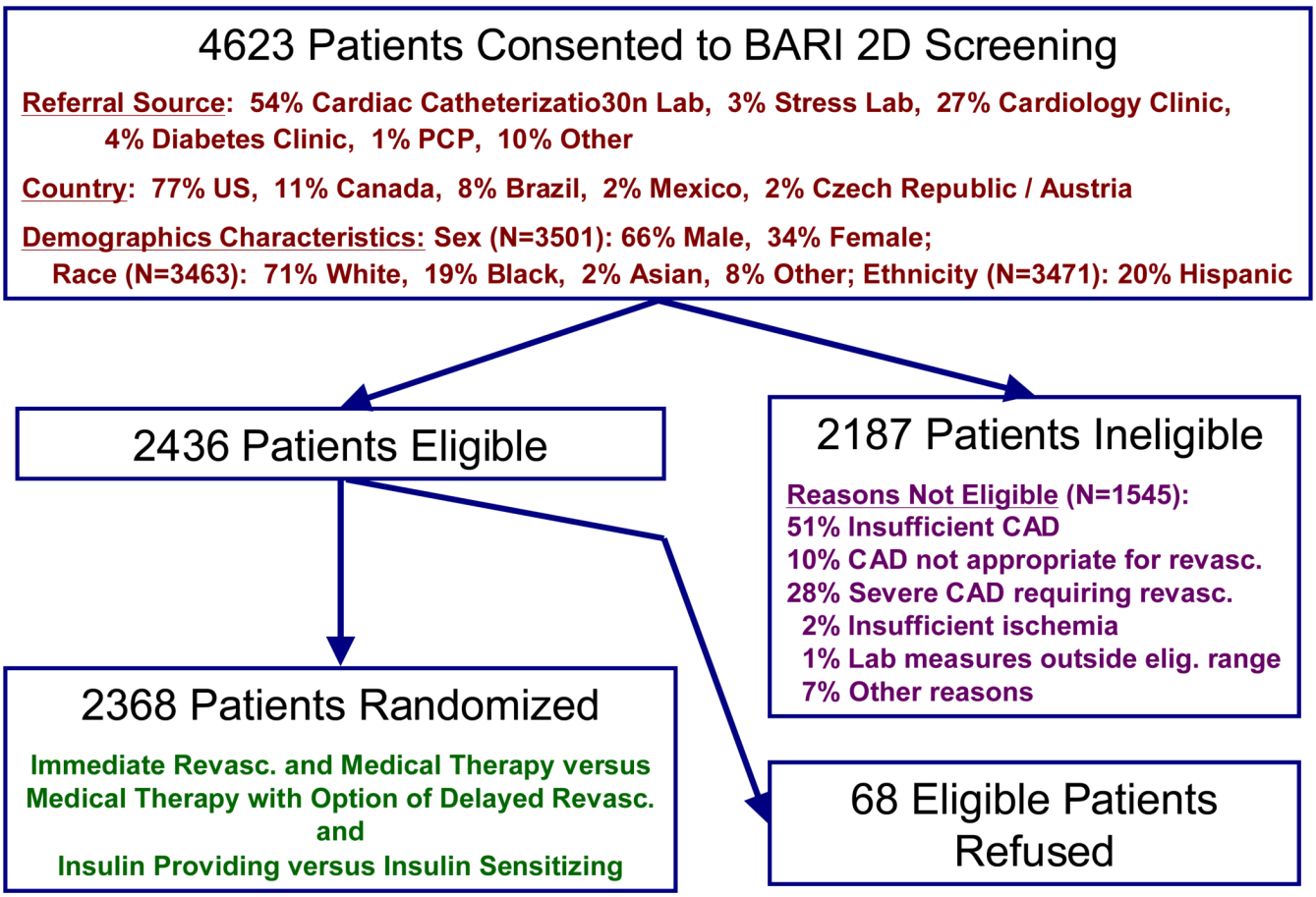

Figure 1.
Flow chart of the enrollment process in the BARI 2D clinical trial.

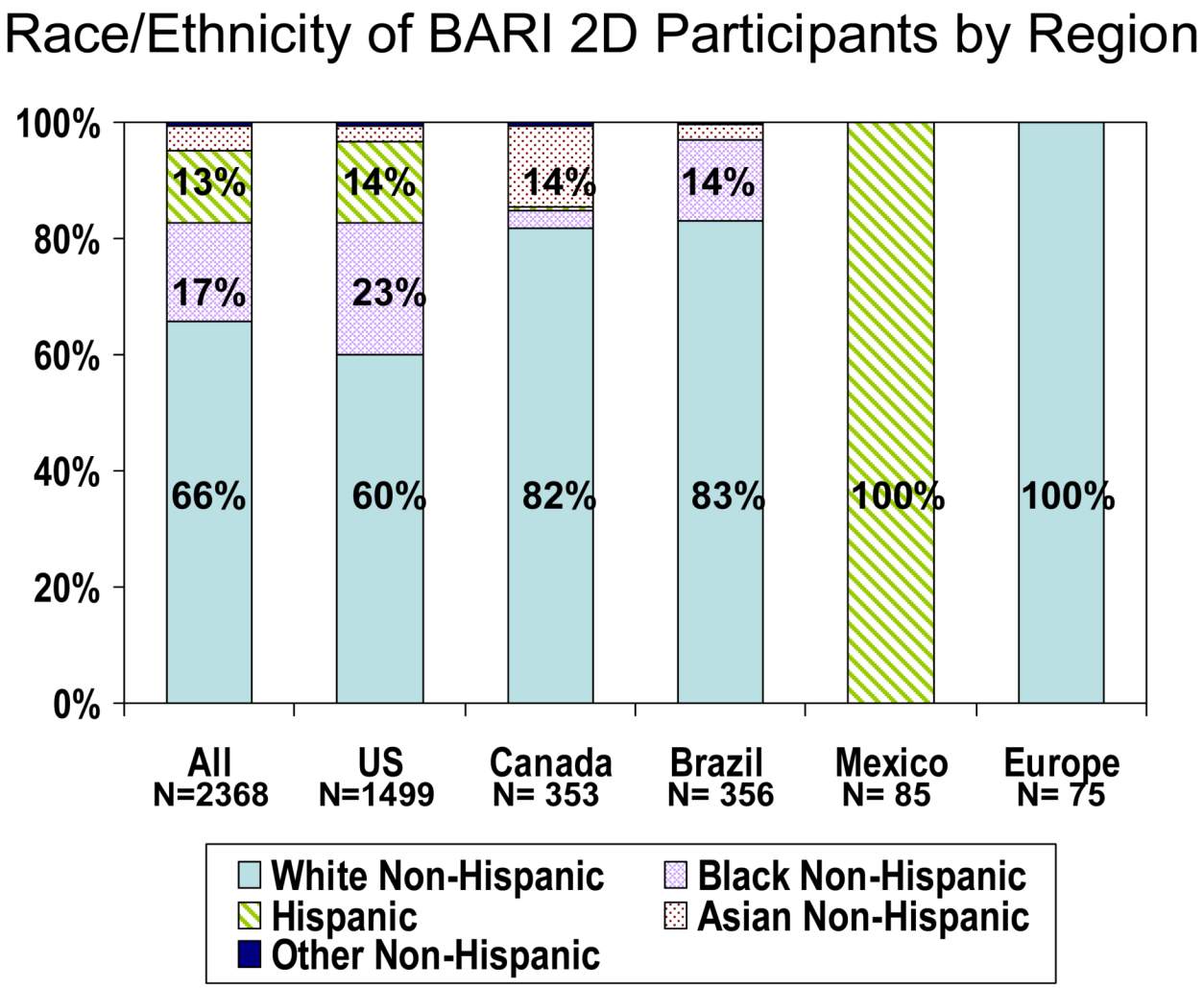

Figure 2.
The BARI 2D population categorized by race/ethnicity overall and stratified by region.

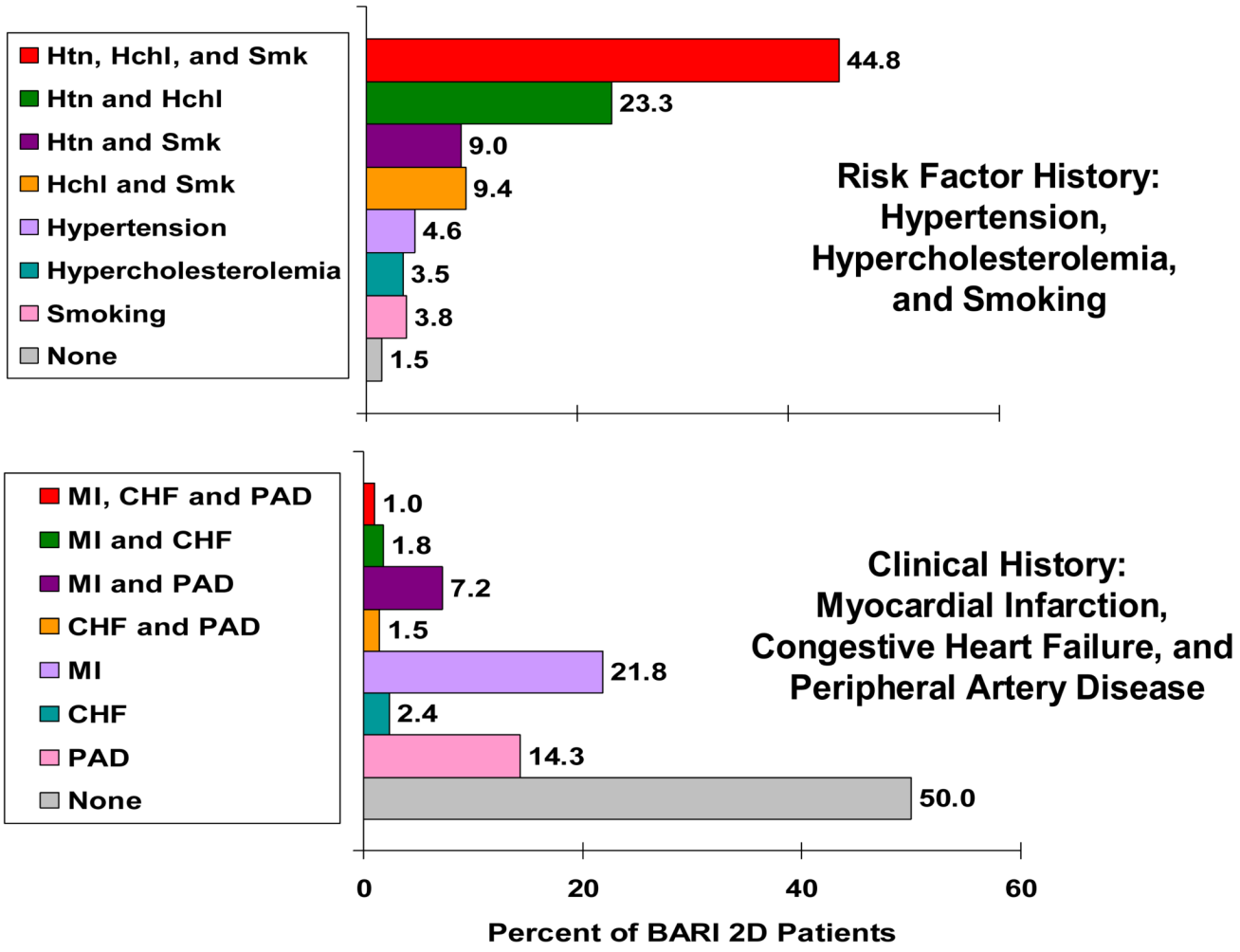

Figure 3.
Observed combinations of cardiac risk factors and clinical history in the BARI 2D population.

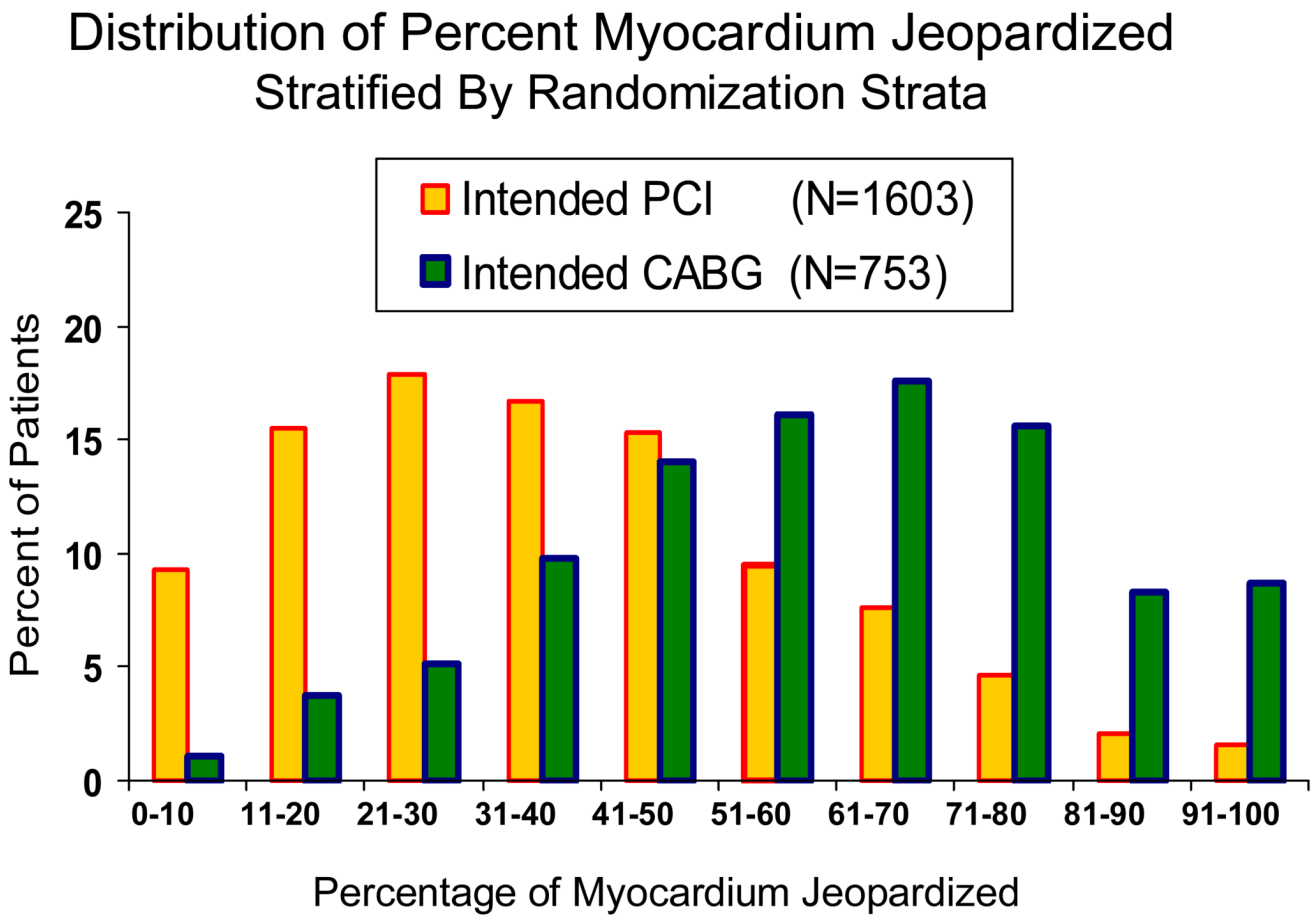

Figure 4.
Distribution of myocardial jeopardy index in the PCI stratum (yellow bars) and CABG stratum (green bars).

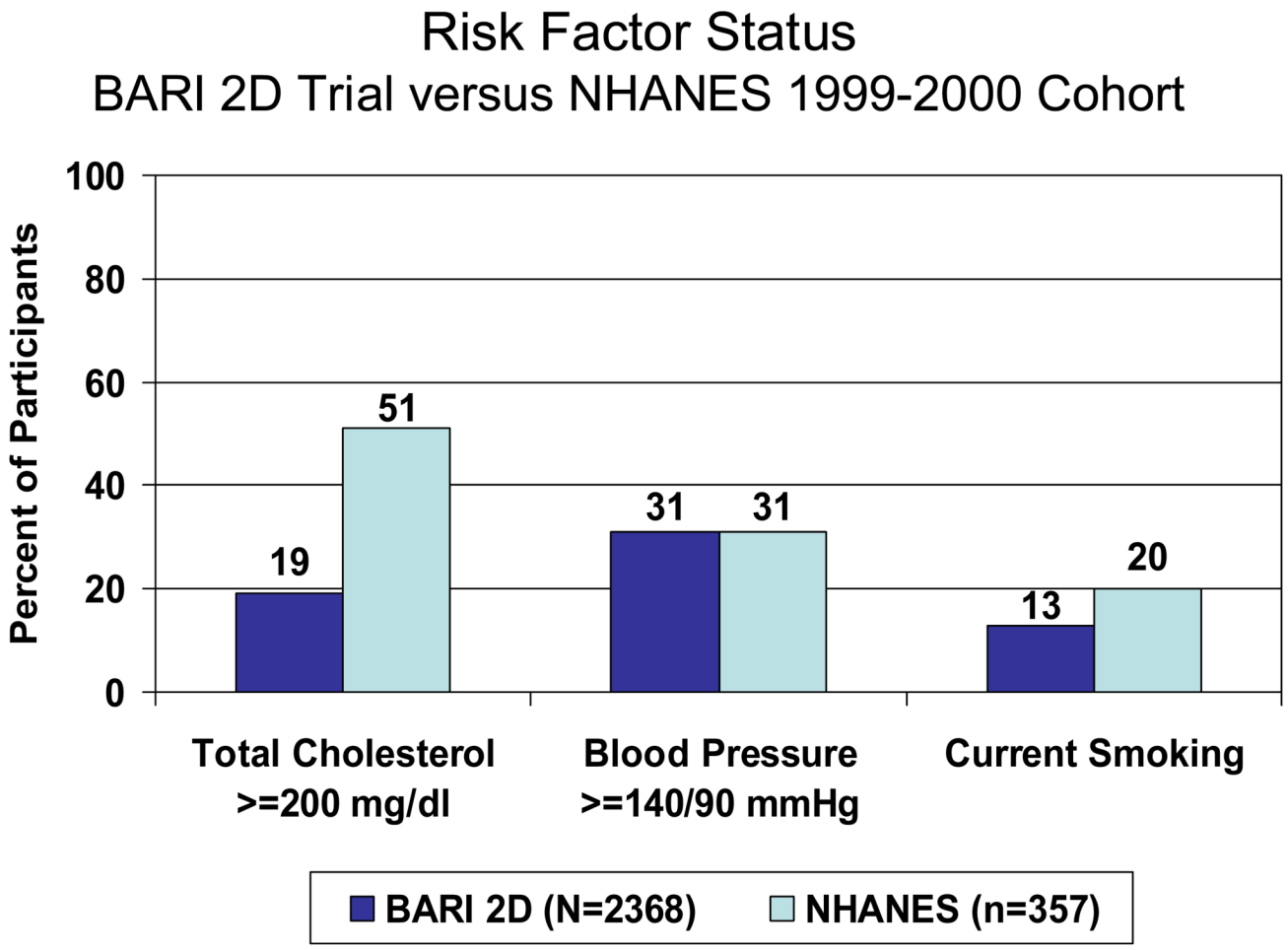

Figure 5.
Frequency of total cholesterol ≥ 200 mg/dl, blood pressure ≥ 140/90 mmHg and current smoking in BARI 2D at baseline and in the NHANES 1999-2000 cohort.[14]

Table 1

Baseline characteristics of BARI 2D population (N=2368)

Demographic and Physical Characteristics		**Cardiac History**		**Diabetes Status and Lipids**	
Age, mean, SD	62.4, 8.9	Hypertension, %	82.5	Duration of diabetes, **%**	
Male, %	70.4	Hypercholesterolemia, %	81.9	< 5 years	33.3
Race, **%**		Cigarette smoking, **%**		5 - < 10 years	23.5
White	70.4	Current	12.5	10 - <20 years	29.2
Black	17.0	Former	54.4	≥ 20 years	14.1
Asian	4.2	Never	33.1	History of insulin, %	29.3
Indian/Native American	4.3	Myocardial Infarction, %	32.0	Glycemia, **%**	
Other	4.1	Congestive Heart Failure, %	6.6	HbA1c ≤ 7.0%	41.7
Hispanic ethnicity, %	12.5	Non-coronary artery disease, %	23.7	7.0 < HbA1c ≤ 8.0%	25.3
Region, **%**		Stroke or TIA, %	9.8	HbA1c > 8.0%	33.0
USA	63.3	Any prior revascularization, %	23.6	Microalbuminuria (30<ACR≤ 300)	22.9
Canada	14.9	Prior PCI, %	19.6	Macroalbuminuria (ACR>300)	9.7
Brazil	15.0	Prior Stent, %	13.4	Hypoglycemic episode, %	22.8
Mexico	3.6	Prior CABG, %	6.4	Laser therapy for retinopathy or macular edema, %	3.1
Czech Republic/Austria	3.2	Angina status, %			
BMI (kg/m^2), %		None	17.9	Lower extremity amputation, %	0.8
Normal or underweight, < 25	9.7	Angina Equivalents Only	21.4	MNSI Screening Neuropathy Score ≥ 7, %	15.9
Overweight, 25 to < 30	34.0	Stable CCS 1	14.3	MNSI Clinical Neuropathy Score > 2, %	50.3
Class 1 Obese, 30 to < 35	32.1	Stable CCS 2	28.8	Total cholesterol ≥ 200 mg/dl, %	19.0
Class 2 Obese, 35 to < 40	15.3	Stable CCS 3	7.5	Triglycerides ≥ 200 mg/dl, %	31.0
Class 3 Obese, ≥ 40	9.0	Stable CCS 4	1.2	HDL<40 male <50 female mg/dl, %	72.4
Blood pressure > 130/80 mmHg,%	52.4	Unstable Angina	9.5	LDL ≥ 100 mg/dl, %	40.5
Ankle Brachial Index ≤ 0.9	20.1				

Table 2

Baseline characteristics of BARI 2D population (N=2368)

ECG and Angiographic Characteristics		Current Medications	
Abnormal Q-wave, %	18.7	Metformin, %	54.1
Major Q-wave, %	8.1	Thiazolodinedione (TZD), %	18.9
ST depression > 0.5 mm, %	15.6	Sulfonylurea, %	53.3
T wave inversion > 1 mm, %	19.5	Insulin, %	27.9
Left bundle branch block, %	2.5	Not taking any diabetes drugs, %	8.7
Abnormal LV function (LVEF < 50%), %	17.5	HMG-CoA reductase (statin),%	74.9
Number of lesions, mean, SD	4.7, 2.3	Fibrate, %	8.6
Number of significant lesions, mean, SD	2.7, 1.8	Beta blocker, %	73.0
Diseased myocardial regions, **%**		Calcium channel blockers, %	31.4
Only non-significant lesions	3.6	Long-acting nitrate, %	31.4
1	29.8	ACE inhibitor, %	64.6
2	35.9	Angiotensin receptor blocker, %	14.4
3	30.7	Diuretic, %	38.6
Myocardial Jeopardy Index, mean, SD	44.5, 24.2	Aspirin, %	88.0
Proximal LAD stenosis ≥ 50%, %	13.2		
Total occlusion(s)	41.0		

Table 3

Baseline characteristics of BARI 2D by subgroups

	Age			Gender			Race / Ethnicity					Region			
Characteristic	**Age<65 N=1439**	**Age≥ 65 N=929**	**p**	**Male N=1666**	**Female N=702**	**P**	**White nH N=1560**	**Black nH N=398**	**Hispanic N=297**	**Other N=113**	**p**	**USA N=1499**	**Canada N=353**	**Other N=516**	**p**
Age, mean, SD	--	--		62.2, 8.7	62.9, 9.3	NS	63.2, 8.7	61.1, 9.6	60.6, 8.7	60.4, 9.2	*	62.9, 9.1	61.9, 8.5	61.3, 8.5	†
Female, %	28.4	31.6	NS	--	--	--	25.1	48.7	30.0	23.9	*	31.8	15.0	33.5	*
BMI, mean, SD	32.4, 6.4	30.7, 5.0	*	31.3, 5.5	32.8, 6.8	*	32.0, 5.7	32.6, 6.9	30.3, 5.3	28.7, 5.6	*	32.8, 6.2	31.1, 5.3	29.1, 4.6	*
HbA1c, mean, SD	7.9, 1.7	7.3, 1.4	*	7.5, 1.6	8.0, 1.7	*	7.5, 1.5	8.0, 1.7	8.0, 1.8	7.9, 1.5	*	7.6, 1.6	7.5, 1.4	8.0, 1.8	*
Systolic Blood Pressure, mean, SD	129.9, 19.8	134.5, 20.0	*	130.4, 18.7	134.8, 22.6	*	130.9, 19.3	137.7, 22.2	128.4, 20.2	130.8, 17.6	*	130.7, 19.0	131.0, 17.8	135.2, 23.7	*
Diastolic Blood Pressure, mean, SD	76.1, 11.1	72.0, 10.9	*	74.8, 10.6	73.8, 12.5	NS	73.7, 11.1	78.0, 12.2	74.5, 10.1	74.0, 9.8	*	72.4, 10.4	74.2, 10.3	80.7, 11.8	*
LDL Cholesterol, mean, SD	98.4, 34.6	93.0, 30.4	*	93.3, 32.0	103.2, 34.5	*	94.1, 32.0	105.8, 37.4	96.0, 30.0	93.5, 33.4	*	94.5, 33.2	92.0, 31.6	104.2, 32.7	*
Triglycerides, mean, SD	193.2, 151.2	162.8, 111.7	*	183.7, 142.6	175.6, 125.9	NS	192.8, 146.3	133.6, 91.7	187.7, 115.5	173.0, 170.0	*	176.0, 136.9	178.1, 144.7	198.9, 134.7	†
Insulin, %	28.9	26.2	NS	24.3	36.4	*	25.3	38.8	26.6	28.3	*	33.2	17.6	19.4	*
Sulfonylurea, %	52.1	55.2	NS	55.8	47.3	*	53.1	49.9	58.2	55.4	NS	51.2	55.8	57.6	‡
TZD, %	19.6	17.7	NS	19.8	16.6	NS	18.9	17.1	20.2	21.4	NS	25.6	16.5	1.0	*
Metformin, %	56.4	50.5	†	55.7	50.1	‡	55.4	46.9	53.5	62.5	†	51.6	69.8	50.4	*
Number of hypertension drugs, mean, SD	2.2, 1.0	2.3, 1.0	‡	2.2, 1.0	2.4, 1.0	*	2.2, 1.0	2.5, 1.0	1.9, 1.0	2.3, 1.0	*	2.3, 1.0	2.2, 1.0	1.9, 1.0	*
Statin, %	74.5	75.6	NS	75.8	72.9	NS	75.2	77.8	70.3	72.6	NS	77.4	77.7	65.8	*
Prior CABG, %	6.2	6.8	NS	7.3	4.4	†	6.6	5.3	7.7	4.4	NS	8.9	3.4	1.2	*
Prior PCI, %	19.1	20.5	NS	19.4	20.2	NS	20.6	19.1	16.5	15.9	NS	23.2	12.2	14.3	*
Diseased myocardial regions, %			NS			*					NS				*
1 or none	34.8	31.3		30.8	39.5		32.2	38.0	36.0	28.4		38.9	26.9	22.1	
2	35.6	36.4		35.6	36.5		35.9	34.2	36.4	40.7		34.3	37.4	39.3	
3	29.6	32.4		33.5	24.0		32.0	27.9	27.6	31.0		26.8	35.7	38.6	
LVEF<50%, %	17.8	17.0	NS	19.7	12.0	*	15.7	22.9	20.0	15.7	†	20.8	19.6	6.6	*

* p<0.001;

† 0.001≤ p<0.01;

‡ 0.01≤ p<0.05;

NS: Not significant (p≥ 0.05).