Carvedilol Reduces Aortic Wave Reflection and Improves Left Ventricular/Vascular Coupling: A Comparison With Atenolol (CENTRAL Study)

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Blood pressure (BP) characteristics, such as central aortic pressure and arterial stiffness, independently predict cardiovascular events. The effects of pharmacologically dissimilar β-blockers on these properties have not been fully elucidated. Patients with essential hypertension and without significant concomitant cardiovascular disease were randomly assigned to controlled-release carvedilol, force-titrated to 80 mg (n=22), or atenolol, force-titrated to 100 mg (n=19); each was given once daily for 4 weeks. Baseline characteristics were similar. At the end of week 4, atenolol and carvedilol reduced central and brachial systolic and diastolic BP to a similar extent. Central augmentation index was increased in atenolol-treated patients but not carvedilol-treated patients (atenolol 4.47% vs carvedilol −0.68%; *P*=.04). Mean augmented central aortic pressure increased slightly during atenolol treatment (+1.1 mm Hg) but decreased slightly during carvedilol treatment (−1.1 mm Hg), although the difference in these changes was not statistically significant (*P*=.23). Pulse pressure amplification was reduced more with atenolol at week 4 (atenolol −10.7% vs carvedilol −1.8%; *P*=.02). Therefore, we conclude that carvedilol results in more favorable pulse pressure amplification and augmentation index by increasing arterial compliance and reducing the magnitude of wave reflection, respectively, compared with atenolol. *J Clin Hypertens (Greenwich).* 2011;13:917–924. ©2011 Wiley Periodicals, Inc.

For many years, β-blockers were advocated as first-line therapy for most patients with hypertension. This class flourished during the past 50 years as the mainstay for the prevention and treatment of various cardiovascular disorders such as cardiac arrhythmias, myocardial infarction, and hypertension. Recently, the role of β-blockers in uncomplicated hypertension has been questioned. Indeed, several recently updated guidelines have deemphasized their place in therapy.[2,3] The reasons for this evolution are multifactorial, including publication of several clinical trials and meta-analyses which concluded that β-blockers are less effective than contemporary antihypertensives.[4–7] These observations could be ascribed to multiple factors including the fact that β-blockers exhibit an adverse metabolic profile, are poorly tolerated relative to newer antihypertensives, and have mismatched mechanisms of action with the pathophysiology of hypertension in elderly hypertensive patients.[8–11]

Multiple recent studies suggest that blood pressure (BP) characteristics beyond the brachial cuff, such as central aortic pressure, wave reflection, and arterial stiffness, independently predict cardiovascular events, including all-cause and cardiovascular mortality, fatal and nonfatal coronary events, and fatal strokes in uncomplicated essential hypertension.[12–15] These characteristics cannot be appreciated with conventional clinic BP measurements at the brachial artery. Radial artery tonometry and synthesis of the central aortic pressure waveform provide a more detailed view of arterial function and left ventricular afterload, which appear to have implications for left ventricular workload and oxygen demand, an established determinant of coronary events in both normotensive and hypertensive patients.[16]

Assuming that all β-blockers are created equally neglects clear differences in pharmacology and clinical trial evidence.[6] Nonvasodilating β-blockers, such as atenolol, reduce BP by primarily reducing ventricular contractility and lowering cardiac output, ignoring the role of increased peripheral vascular resistance in the pathophysiology of hypertension. Conversely, vasodilating β-blockers, such as carvedilol or nebivolol, exhibit several unique features that may be more suited to treat hypertension.[3] Vasodilating β-blockers reduce peripheral resistance, augment cardiac output, improve insulin resistance, stabilize lipids, and are better tolerated than nonvasodilating β-blockers.[3,17,18] The extent to which these differentiating characteristics contribute to carvedilol's favorable effects on clinical outcomes is unclear. In light of the recent observations that atenolol does not

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reduce cardiovascular morbidity and mortality as well as other agents and the suggestion that this might be related to its inability to foster favorable central hemodynamic parameters, we randomly assigned hypertensive patients to either controlled-release carvedilol or atenolol to compare central pressure and arterial wave reflection in the aorta.[3,6,7,19]

METHODS

Study Design

Carvedilol Reduces Aortic Wave Reflection and Improves Left Ventricular/Vascular Coupling: A Comparison With Atenolol (CENTRAL) study was a prospective, open-label, comparative, randomized control trial that evaluated brachial and central hemodynamic profiles in patients taking atenolol or controlled-release carvedilol. Patients taking an antihypertensive agent prior to enrollment entered a washout period for a duration equal to at least 5 half-lives of the drug and typically for 2 weeks. In the event that patients were antihypertensive-naive, they proceeded immediately to randomization. Eligible patients were randomly assigned to starting doses of either controlled-release carvedilol 20 mg or atenolol 25 mg once daily in a 1:1 ratio. Forced titration occurred in both carvedilol and atenolol arms to 40 mg and 50 mg, respectively, at week 1, and to 80 mg and 100 mg at week 2. Patients continued on controlled-release carvedilol 80 mg and atenolol 100 mg for the remainder of the study (weeks 2–4) (Figure 1). Titration occurred unless patients had a clinic BP reading $<120/70$ mm Hg or a heart rate <60 beats per minute (bpm). Patient hemodynamic profiles, specifically measurements of central aortic and brachial BP and pulse pressure, pulse pressure amplification, central augmentation index, and central augmentation pressure, were measured during 3 study visits: at baseline and at week 2 and week 4 study visits. BP at weeks 2 and 4 was measured 4 hours after the morning dose of carvedilol or atenolol based on the peak concentrations of atenolol and carvedilol.

Study Population

We recruited adult patients 18 years or older with a formal diagnosis of essential benign hypertension, defined as a systolic BP >140 mm Hg or diastolic BP >90 mm Hg who were treatment-naive or treated with <2 antihypertensive agents. Any of the following parameters resulted in exclusion from the study: secondary forms of hypertension (sleep apnea, Cushing syndrome, primary aldosteronism, pheochromocytoma, aortic coarctation, renovascular disease), treatment with ≥ 2 antihypertensive drugs at baseline, baseline clinic systolic BP >170 mm Hg, other diseases requiring treatment with BP-lowering medications (migraine prophylaxis, glaucoma, essential tremor, anxiety), heart rate <55 bpm (in the absence of β-blocker therapy), known cardiovascular disease (including history of angina pectoris, heart failure, presence of a cardiac pacemaker and defibrillators, history of myocardial infarction or revascularization procedure, or cerebrovascular disease), known diabetes mellitus (type 1 or 2), renal insufficiency defined as a

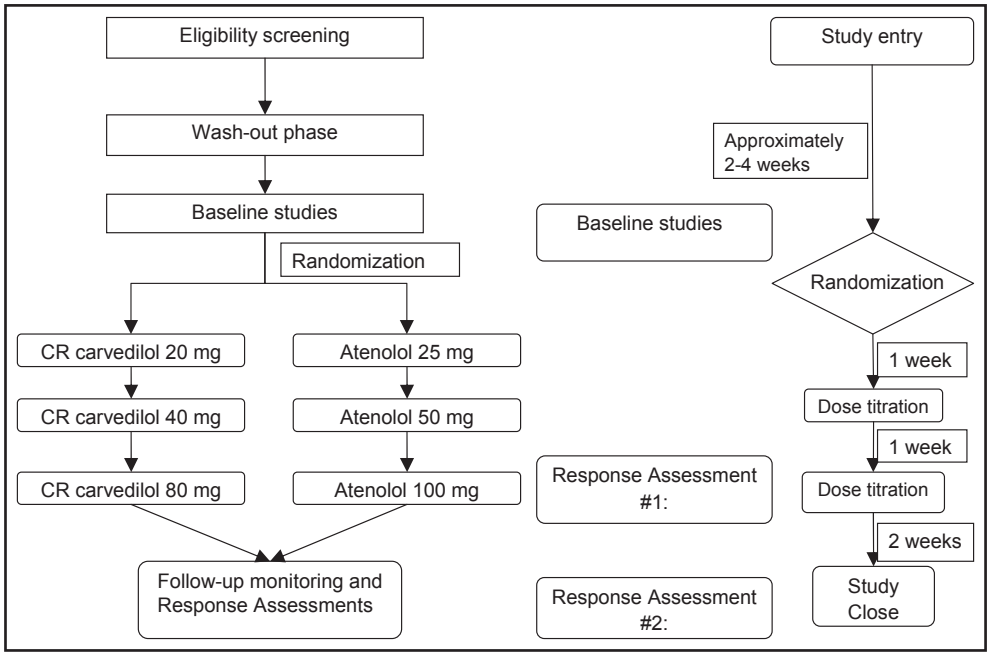

FIGURE 1. Schematic representation of patient enrollment and randomization. CR indicates controlled release.

serum creatinine >1.5 mg/dL in men and 1.4 mg/dL in women, primary renal disease, pregnancy or lactation, or a history of Raynaud syndrome. Women of childbearing age underwent a human chorionic gonadotropin test to exclude administration of drug in the presence of pregnancy. Patients with asthma or chronic obstructive pulmonary disease were included or excluded at the discretion of their physician and the primary investigator. The institutional review board ethics committee approval was obtained and patients who qualified for the study provided written informed consent prior to initiating the study.

Brachial and Central Hemodynamic Measurements

Measurement of brachial cuff BP was performed prior to central hemodynamic assessment. After resting for a period of 5 minutes in the seated position, brachial BP was recorded as a mean of two readings in the nondominant arm using an oscillometric BP monitor (Omron HEM Model 907-XL; Omron, Tokyo, Japan). Assessment of arterial wall properties, wave reflection characteristics, and event timing were performed noninvasively using the SphygmoCor system (AtCor Medical, Sydney, Australia) on the same arm used for brachial BP measurements.[16] Radial artery BP waveforms were recorded using applanation tonometry. After 20 sequential waveforms were acquired and ensemble averaged, a validated generalized mathematic transfer function was used to synthesize the central aortic BP waveform. The radial waveforms were processed with the SphygmoCor device to yield measurements of central aortic systolic pressure, central pulse pressure, incident pressure wave amplitude, reflected pressure wave amplitude (augmentation pressure), and augmentation index (augmentation pressure/central pulse pressure) according to an established protocol.[16] Heart rate was determined from the waveform using cardiac cycle length (period), whereas mean arterial pressure was determined by integration of the pressure waveform. Pulse pressure amplification was calculated as: brachial pulse pressure/central pulse pressure.

Statistical Analysis

Descriptive statistics were used to analyze and report demographic information, baseline BP measurements, and baseline central hemodynamic component measurements. We used the Student *t* test for continuous variables and the chi-square test for categorical variables to compare differences in baseline demographics between the two study groups. We checked the sampling distribution of BP and central hemodynamic measurements using the Kolmogorov–Smirnov test and Q-Q plot. For normally distributed data, we used the Student *t* test to compare differences in the change from baseline within each study group and the differences in change from baseline between study groups. Non-normally distributed data were similarly analyzed using the Wilcoxon signed-rank test.

Statistical significance was defined a priori as a *P* value <.05. All statistical analyses were performed using SAS 9.2 statistical software (SAS Institute Inc, Cary, NC). In order to achieve 80% power for detecting a 3-mm Hg difference in central systolic pressure, assuming a standard deviation of 3 mm Hg, 37 patients were required to ensure significant statistical power.

RESULTS

Baseline Characteristics

At baseline, mean age, weight, and body mass index were similar between treatment groups (Table I); however, patients taking carvedilol were slightly taller compared with those taking atenolol (171 cm vs 165.6 cm, respectively; *P*=.04). Brachial and central systolic and diastolic BPs were not significantly different between groups (*P*>.05). Brachial and central pulse pressures and heart rate did not differ significantly (*P*>.05). All arterial stiffness parameters were

TABLE I. Baseline Characteristics of Untreated Hypertensive Patients Randomly Assigned to Atenolol or Controlled-Release Carvedilol

	Atenolol (n=19)	Carvedilol (n=22)	*P* Value Between Treatment
Age, y	46.1±9.9	47.7±13.1	.65
Height, cm	165.6±8.8	171±7.6	.04
Weight, kg	91.1±f28.4	95.6±27.3	.61
Body mass index, kg/m^2	33.6±11.6	32.7±9.2	.79
Brachial systolic blood pressure, mm Hg	143.1±14.0	145.3±10.4	.56
Brachial diastolic blood pressure, mm Hg	94.8±6.8	92.8±9.6	.45
Brachial pulse pressure, mm Hg	48.2±12.0	52.5±10.9	.24
Central systolic blood pressure, mm Hg	131.2±12.5	133.1±10.6	.6
Central diastolic blood pressure, mm Hg	95.9±6.8	93.8±9.7	.43
Central pulse pressure, mm Hg	35.3±11.0	39.4±10.9	.25
Heart rate, bpm	73.3±10.0	73.4 ±10.7	.98
Pulse pressure amplification, mm Hg	1.39±0.16	1.36±0.17	.52
Central augmentation pressure, mm Hg	8.3±6.2	9.8±7.4	.47
Central augmentation pressure$_{75}$, mm Hg	7.6±5.4	9.0±5.8	.42
Central augmentation index, %	21.4±9.9	22.9±12.3	.69
Central augmentation index$_{75}$, %	20.6±10.3	22.1±10.1	.66

Abbreviations: bpm, beats per minute; central augmentation index$_{75}$, central augmentation index adjusted at a heart rate of 75 bpm; central augmentation pressure$_{75}$, central augmentation pressure adjusted at a heart rate of 75 beats per minute. Values are expressed as mean±standard deviation.

not significantly different at baseline, including pulse pressure amplification (*P*=.52), central augmentation pressure (*P*=.47), central augmentation pressure adjusted at a heart rate of 75 bpm (*P*=.42), central augmentation index (*P*=.69), and central augmentation index adjusted at a heart rate of 75 bpm (*P*=.66). There were no other statistically significant differences in baseline demographics.

Brachial and Central BP, Pulse Pressure, and Heart Rate

At week 2, brachial and central systolic BPs were similar among both groups (Table II). Treatment with atenolol resulted in significantly greater reductions in brachial diastolic BP compared with carvedilol at week 2 (−15.2 mm Hg vs −8.1 mm Hg, respectively; *P*=.02). Atenolol also decreased central diastolic BP more than carvedilol at week 2 (−15.5 mm Hg vs −8.1 mm Hg, respectively; *P*=.02). No significant differences were observed between atenolol and carvedilol at week 4 for these parameters (Table II). Carvedilol reduced brachial pulse pressure to a greater extent than atenolol at week 2 (−6 mm Hg and −0.5 mm Hg, respectively; *P*=.04). After 2 weeks, atenolol increased central pulse pressure (2.4 mm Hg) whereas carvedilol reduced central pulse pressure (−4.2 mm Hg; *P*=.004 for the comparison between changes). Central and brachial pulse pressures did not significantly differ at week 4 (Table II). At week 2, atenolol reduced heart rate to 61.6 bpm while carvedilol reduced heart rate to 64.8 bpm. At week 4, heart rate was reduced to 60.7 bpm and 63.0 bpm in the atenolol and carvedilol groups, respectively. The difference between groups for heart rate was not statistically significant at weeks 2 (*P*=.21) or 4 (*P*=.45).

Augmented Pressure

In patients treated with atenolol, augmented pressure was increased from baseline at weeks 2 and 4 (2.1 and 1.1 mm Hg, respectively). Conversely, carvedilol decreased the augmented pressure at both week 2 and 4 (−1.5 and −1.1 mm Hg, respectively) (Figure 2). The comparison between changes with the two drugs was statistically significant at week 2 (*P*=.0035), but not week 4 (*P*=.23). The change in augmented pressure adjusted at a heart rate of 75 bpm was significantly different for the two study drugs at week 2 (atenolol −0.72 mm Hg vs carvedilol −2.96 mm Hg; *P*=.04) but not at week 4 (atenolol −1.24 mm Hg; carvedilol −3.1 mm Hg; *P*=.18) (Figure 2).

Augmentation Index

The augmentation index (an indicator of wave reflection intensity) increased from baseline with atenolol but not with carvedilol at week 2 (4.44% and 0%, respectively; *P*=.03 for the comparison between changes). Similar results were observed at week 4 (atenolol 4.47% vs carvedilol −0.68%; *P*=.04 for the comparison between changes) (Figure 2). Analysis of the augmentation index adjusted for a heart rate of 75 bpm yielded nonsignificant differences between changes with atenolol and carvedilol at week 2 (−1.28% vs −4.09%, respectively; *P*=.15) and at week 4 (−1.59% vs −5.41%, respectively; *P*=.06) (Figure 2).

Pulse Pressure Amplification

The increase in augmentation pressure was accompanied by a significant reduction in the pulse pressure amplification in atenolol (−8.6%) compared with carvedilol (−2.3%) at week 2 (*P*=.05). Similar results

TABLE II. Drug-Induced Change in Hemodynamic and Wave Reflection Profiles From Baseline in Patients Treated With Atenolol or Controlled-Release Carvedilol at Week 2 and 4

	Week 2			Week 4		
	Atenolol 50 mg (n=18)	Carvedilol 40 mg (n=22)	*P* Value Between Treatment	Atenolol 100 mg (n=17)	Carvedilol 80 mg (n=22)	*P* Value Between Treatment
Brachial systolic blood pressure, mm Hg	−15.7±13.0	−14.1±12	.67	−19.5±17.6	−17.6±11.3	.68
Brachial diastolic blood pressure, mm Hg	−15.2±10.2	−8.1±9.1	.02	−15.1±10.4	−13.1±7.9	.51
Brachial pulse pressure, mm Hg	−0.5±7.2	−6±9.0	.04	−4.4±11.3	−4.5±10.8	.99
Central systolic blood pressure, mm Hg	−13.1±14.3	−12.4±11.2	.87	−16.0±18.7	−16.1±10.4	.98
Central diastolic blood pressure, mm Hg	−15.5±10.2	−8.1±9.3	.02	−15.4±10.1	−13.2±8.1	.46
Central pulse pressure, mm Hg	2.4±6.4	−4.2±7.1	.004	−0.7±11.7	−2.9±9.8	.51
Heart rate, bpm	−11.7±7.8	−8.6 ±7.8	.21	−12.6 ±7.1	−10.4 ±10.0	.45
Pulse pressure amplification, mm Hg	−0.09±0.11	−0.02±0.09	.05	−0.1±0.11	−0.02±0.11	.02
Central augmentation pressure, mm Hg	2.1±4.0	−1.5±3.1	.0035	1.1±6.0	−1.1±5.3	.23
Central augmentation pressure$_{75}$, mm Hg	−0.7±3.8	−3.0±2.8	.04	−1.2 ±4.3	−3.1±4.1	.18
Central augmentation index, %	4.4±6.9	0.0±5.9	.03	4.5±7.7	−0.7±7.4	.04
Central augmentation index$_{75}$, %	−1.3±6.7	−4.1±5.6	.15	−1.6±6.4	−5.4±6.1	.06

Abbreviations: bpm, beats per minute; central augmentation index$_{75}$, central augmentation index adjusted at a heart rate of 75 bpm; central augmentation pressure$_{75}$, central augmentation pressure adjusted at a heart rate of 75 bpm. Values are expressed as mean±standard error of the mean.

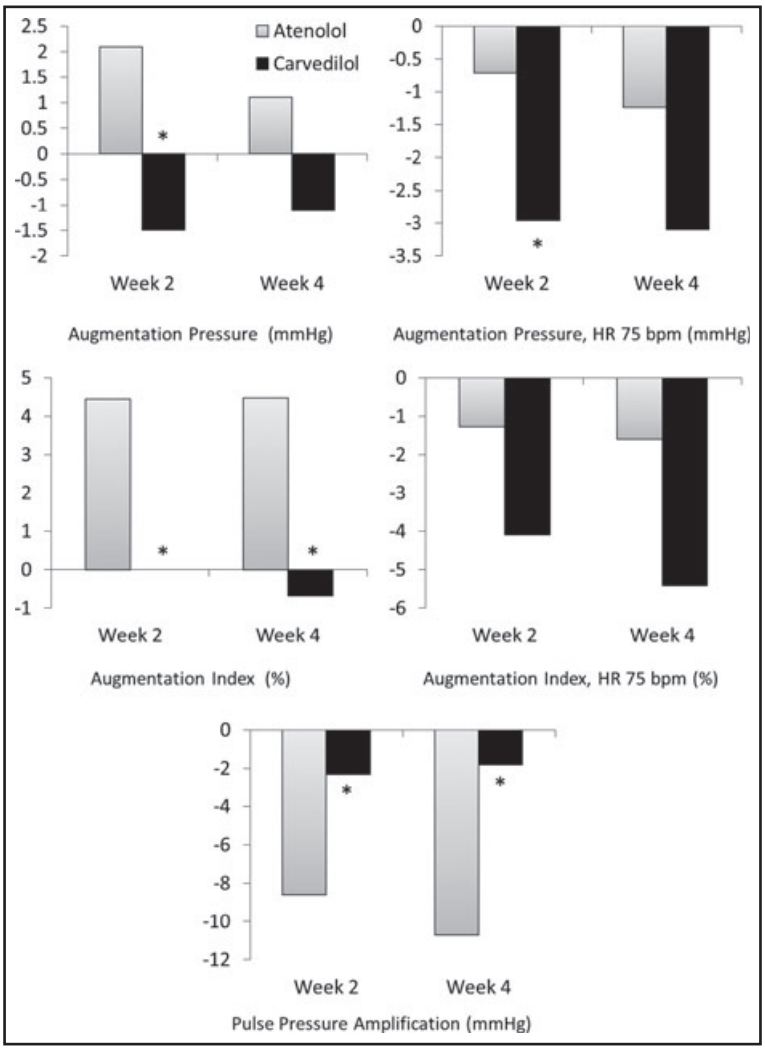

FIGURE 2. Changes in wave reflection properties from baseline to week 2 and 4 in patients taking atenolol 100 mg or extended-release carvedilol 80 mg. bpm indicates beats per minute; HR, heart rate. *$P<.05$.

were observed for atenolol (−10.7%) and carvedilol (−1.8%) at week 4 (P=.02) (Figure 2).

DISCUSSION

In patients with essential hypertension, we found no significant difference in the magnitude of central or brachial BP-lowering after 4 weeks of therapy with controlled-release carvedilol or atenolol; however, differences in wave reflection characteristics (ie, augmentation pressure and augmentation index) were observed. Atenolol increased the augmentation pressure and augmentation index while carvedilol lowered or maintained these parameters. While both treatment arms decreased pulse pressure amplification, it was significantly reduced by atenolol compared with carvedilol (Table II).

In the present study, while atenolol reduced brachial BP effectively as assessed by brachial sphygmomanometry, it does not reduce augmentation pressure or index, a finding that has been observed in other studies.[3,20] In fact, augmentation pressure and augmentation index were increased with atenolol monotherapy in this study (Table II). Recent data from the Conduit Artery Function Evaluation (CAFE) have spotlighted the potential importance of these two parameters in reducing coronary events. In this study, an amlodipine-based regimen conferred a 10% relative risk reduction in combined end points of nonfatal myocardial infarction and fatal coronary heart disease compared with an atenolol-based regimen despite similar reductions in brachial BP.[19] Part of this advantage was ascribed to beneficial effects of the amlodipine-based regimen on central aortic BPs.[4] Because nonvasodilating β-blockers may only slow the pulse rate, there is a subsequent alteration in pulse wave morphology that dictates both the timing and the magnitude of the

reflected wave such that it returns during the end of systole rather than during diastole. This leads to an elevated augmented pressure in the aorta and poor ventricular/arterial coupling.[3,21,22] Furthermore, distal arterial reflection sites are shifted closer to the heart while using nonvasodilating β-blockers, which results in premature return of the arterial wave to the aorta.[23] The directional changes in augmentation pressure and augmentation index in the carvedilol and atenolol arms observed in this study reflect carvedilol's peripheral vasodilatory action compared with atenolol, the latter of which either does not affect peripheral arteries or could paradoxically cause vasoconstriction. At higher doses, atenolol might block vasodilatory β_2 receptors, causing constriction and increased peripheral resistance.

β-Blockers with vasodilatory effects reduce augmentation of central aortic pressures by reducing wave reflection and providing protective effects on the arterial vasculature. For example, carvedilol has been shown to improve coronary flow reserve after 6 months of treatment in patients with hypertensive left ventricular hypertrophy compared with the nonvasodilating β-blocker metoprolol.[24] This is likely due to carvedilol's ancillary α_1-blocking effects, which induce vasodilation of the coronary microcirculation. Additionally, dilevalol, a β-blocker with α-blocking effects, decreases wave reflection and augmentation index through its peripheral vasodilatory actions and also confers a greater reduction of carotid pressure compared with atenolol.[25] Nebivolol also significantly decreases wave reflection compared with atenolol, likely through its positive action on endothelial function and peripheral resistance by increasing nitric oxide levels.[26,27] Another study that applied radial tonometry in patients treated with nebivolol or atenolol reported that both agents reduced brachial and central BP similarly; however, nebivolol yielded a reduction in augmentation pressure and augmentation index but increased pulse pressure amplification.[20] These observations with nebivolol were attributed to potentiation of nitric oxide–mediated vasodilation at the site of the small muscular arteries, which resulted in decreased wave reflection and vasculoprotection.

A recent retrospective study found that patients chronically treated with either carvedilol or nebivolol had greater reductions in central systolic BP and central pulse pressure compared with atenolol.[28] In contrast, our study did not detect a significant reduction in central BP with carvedilol compared with atenolol. One explanation for the similar reductions in central BP between carvedilol and atenolol at the end of the study is that vasodilating β-blockers exert their beneficial effects on central aortic pressure by simultaneously decreasing heart rate and pulse wave velocity. If the reduction in heart rate and delay in return of the arterial waveform offset each other, then the reflected wave may still return during the end of systole, curbing a fraction of the benefit that vasodilating β-blockers have on aortic hemodynamics. An alternative explanation is that atenolol and carvedilol may impart differences on the incident and reflected waveforms. Atenolol may decrease the incident waveform amplitude while simultaneously increasing the wave reflection amplitude, an effect that appears to be opposite with carvedilol.

Pulse pressure amplification, a metric that is inversely correlated with cardiovascular risk factors, was decreased significantly more with atenolol than with carvedilol in this study. [29,30] Reductions in pulse pressure amplification are indicative of decreased arterial distensibility and vascular compliance.[31] As the cardiac workload increases with age, central pulse pressure and peak central systolic BP increase, subsequently reducing pulse pressure amplification.[31] Such changes are thought to encourage a shift from normal cardiac function to cardiac hypertrophy and eventually congestive heart failure.

In addition to vasodilation, carvedilol exhibits a unique pharmacologic profile consisting of vasculoprotective actions and positive effects on central hemodynamics and glucose metabolism; these effects are uncommon within the class.[17,24] Moreover, carvedilol has antioxidant effects that buffer reactive oxygen species by scavenging free radicals, suppressing free-radical generation, and preventing ferric ion-induced oxidation.[32] For example, in one head-to-head study, carvedilol exhibited more pronounced antioxidant effects than atenolol in post–acute myocardial infarction patients.[33] The extent to which these actions translate into the effects observed in this study are unclear. Carvedilol's antioxidant effects have been suggested to contribute to improved outcomes in patients with heart failure and recent myocardial infarction.[34] This antioxidant effect may be attributable to stimulation of endothelial nitric oxide or reduced nitric oxide inactivation.[35]

LIMITATIONS

Several limitations of this study are noteworthy. First, controlled-release carvedilol reaches peak antihypertensive effects between 3 and 7 hours and atenolol reaches peak effects between 2 and 4 hours.[36,37] In the present study, BP assessments were performed 4 hours following dose administration. It is not clear whether measuring the peak effect on BP with carvedilol later would have resulted in more favorable effects on the metrics assessed in this study. Second, the short duration of this study may not have captured the full antihypertensive potential of carvedilol. Extended carvedilol therapy (ie, >4 weeks) results in a significant decrease in plasma renin activity[38]; however, whether plasma renin activity influences central aortic BP and wave reflection effects is unknown. Third, the short duration of this study also fails to clarify whether atenolol and carvedilol impart differences in myocardial structure and function over time, as was

seen in a study comparing nebivolol and metoprolol during a 1-year period. This study demonstrated that left ventricular wall thickness was significantly reduced in patients receiving nebivolol but not metoprolol, and correlated with a reduction in both central systolic BP and central pulse pressure.[39] Finally, patients in our study allocated to atenolol were of a shorter stature compared with those who were given carvedilol (Table I). This short stature has been shown to independently correlate with elevations in pulse pressure in two studies and it is thought to cause the early arrival of reflected waves that increase the efforts of the left ventricle and stiffen the aorta.[40–42] Whether this demographic had a significant influence in our population is unknown.

CONCLUSIONS

The present study is the first to compare carvedilol with a nonvasodilating β-blocker, atenolol, with regard to effects on central aortic hemodynamics. Atenolol has been studied frequently in patients with hypertension, and recent meta-analyses have illustrated the shortcomings of this agent in the management of uncomplicated hypertension. β-Blockers with vasodilating effects, such as carvedilol, have a unique pharmacologic profile that includes reductions in arterial stiffness, blunting of wave reflection, and reduction of augmentation pressure. Such observations, including those seen in this study, should serve as an impetus for future studies with vasodilating β-blockers and to better characterize their role in the treatment of uncomplicated hypertension. Our findings parallel those of other studies examining vasodilating and nonvasodilating β-blockers in that each reduce brachial and central BP, but vasodilatory compounds elicit positive changes in arterial wave properties. Given that augmentation pressure has been shown to independently forecast cardiovascular risk, our findings have potentially important implications for the management of hypertension. Vasodilating β-blockers might be preferred to nonvasodilating agents in patients with hypertension because of their desirable effects on augmentation pressure and augmentation index, arterial wave stiffness, and glucose and lipid metabolism. The extent to which the findings in this study might explain the less-than-ideal outcomes in β-blocker studies to date as well as the extent to which these findings should inform therapy remains a contentious matter. However, it is certain that additional studies must be performed to elucidate the value of central aortic hemodynamic assessment in patients with hypertension as well as to better explain differences among antihypertensive drugs.

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