Section Editor: **Peter S. A. Glass**

The Risk of Hypertension after Preoperative Discontinuation of Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Antagonists in Ambulatory and Same-Day Admission Patients

Rebecca S. Twersky, MD, MPH,* Vasudha Goel, MD,* Preeti Narayan, MD,* and Jeremy Weedon, PhD, MA, BS†

BACKGROUND: The continued use of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II subtype I receptor antagonists (ARBs) medications in the preoperative period has been reported to be associated with intraoperative hypotension that can be unresponsive to pressor drugs. As a result, several investigators suggested discontinuation of these medications before scheduled surgery but did not report on unintended consequences that might result from discontinuation. We conducted a prospective, single-blind, randomized trial to observe the effect of the medications on preoperative arterial blood pressure recordings in patients presenting for ambulatory and same-day surgery.

METHODS: Six hundred forty-four patients presenting for ambulatory and same-day surgery were enrolled prospectively between 2006 and 2011 and randomly assigned to 2 groups based on continuation or discontinuation of ACEIs and ARBs. An intention-to-treat analysis was performed. The primary outcome was presence of hypertension (HTN) immediately before surgery. Secondary outcomes included surgical cancellations due to HTN, prolongation of hospitalization, adverse clinical events, and HTN in the postoperative period.

RESULTS: Data for 526 patients were analyzed. There were 262 patients in the discontinuation group and 264 patients in the continuation group. Discontinuation of ACEIs and ARBs on the day of surgery was not associated with increased prevalence of preoperative HTN ($P = 0.775$). The upper bound of a 95% confidence interval for the difference in prevalence of Stage 1 and 2 HTN between study arms indicates that discontinuation of study medication is unlikely to be associated with an increase in Stage 1 HTN of >4.8 percentage points and in Stage 2 HTN of no >5.8 percentage points. Discontinuation was not associated with an increase in postoperative HTN, with prolongation of hospitalization or with adverse clinical events.

CONCLUSIONS: Discontinuing ACEIs and ARBs in patients on the day of surgery did not result in a substantively increased incidence of pre- or postoperative HTN compared with patients who continued these medications on the day of surgery. The results provide an evidentiary basis for the safety of discontinuing ACEIs and ARBs on the day of surgery without increasing adverse hemodynamic outcomes. (Anesth Analg 2014;118:938–44)

Conflicting studies in the literature over the past 2 decades have debated the risks and benefits of continuing chronic angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II subtype I receptor antagonists (ARBs) during the perioperative period. Continued uninterrupted use was recommended to reduce myocardial ischemia and provide renal protection in high-risk patients.[1,2] Several investigations of perioperative complications and mortality, primarily in inpatients with advanced vascular disease undergoing vascular surgery or coronary artery bypass grafting (CABG), reported significant hypotension after induction of general anesthesia in patients who had continued taking ACEIs or ARBs on the morning of their procedures.[2–10] These patients were also found to be refractory to standard treatment for hypotension intraoperatively.[4,11] More recent studies on similar inpatients undergoing such surgeries confirmed these findings and raised concern about the safety of continuing these classes of renin-angiotensin-system medications before surgery.[12,13] These findings led to the view that withholding ACEIs and ARBs preoperatively would reduce hemodynamic instability after induction of general anesthesia.

A randomized prospective study of 40 inpatients with normal left ventricular function showed that, while patients who discontinued ACEIs did not have more hypotension after induction than those who continued ACEIs, they did experience an increase in arterial blood pressure (BP) postoperatively that necessitated the administration of vasodilators.[14]

From the *Department of Anesthesiology, and †School of Public Health, SUNY Downstate Medical Center, Brooklyn, New York.

Vasudha Goel, MD, is currently affiliated with Medical Advanced Pain Specialists, Minneapolis, Minnesota.

Accepted for publication November 15, 2013.

Funding: None.

The authors declare no conflicts of interest.

Reprints will not be available from the authors.

Address correspondence to Rebecca S. Twersky, MD, MPH, Department of Anesthesiology, Box 6, SUNY Downstate Medical Center, Brooklyn, NY 11203. Address e-mail to rebecca.twersky@downstate.edu.

DOI: 10.1213/ANE.0000000000000076

Studies are lacking on the consequences of discontinuing ACEIs and ARBs in the perioperative period in ambulatory surgery patients.[15] A retrospective study of 267 outpatients and same-day admission patients analyzed the timing of preoperative administration of ACEIs/ARBs on intraoperative BPs.[6] The authors reported a small increase in incidence of moderate hypotension only within the first 30 minutes after induction of general anesthesia in the group that continued taking the medications within the 10-hour period, leading up to anesthetic induction compared with the group that discontinued the medications. There were no differences intraoperatively between the 2 groups in the incidence of severe hypotension or the number of patients requiring vasopressor treatment. The study did not address the risk of preoperative hypertension (HTN) in patients who discontinued ACEI/ARB medications before induction.

Would discontinuation of these medications in ambulatory surgery patients cause clinically significant preoperative HTN resulting in cancellation or postponement of elective surgery? Would discontinuation predispose such patients to poorly controlled perioperative HTN? There is no consensus among physicians that ACEIs or ARBs should be discontinued preoperatively in ambulatory surgery patients. Furthermore, it is unclear as to whether the reported inpatient findings regarding postinduction hypotension are applicable, because outpatients generally present with less severe disease and undergo surgical procedures with less potential risk. We designed a randomized, controlled trial (RCT) to evaluate the impact of discontinuing ACEIs or ARBs on preoperative hemodynamics in ambulatory and same-day admission patients to provide evidence for the choice that best supports safe practice. We hypothesized that discontinuing ACEIs or ARBs in ambulatory and same-day admission patients in the preoperative period would not result in poorly controlled BP during the immediate preoperative period. During the study, we added BP measurements in the postanesthesia care unit (PACU), based on the possibility that rebound HTN in the immediate postoperative period might be associated with discontinuation of the medications.

METHODS

The following prospective, single-blinded RCT was approved by the SUNY Downstate IRB. Patients were recruited between July 2006 and January 2011 during their presurgical and preanesthesia visit when written informed consent was obtained. Because of logistical constraints, not every eligible patient was approached for enrollment. Patients were seen by anesthesiologists or physician assistants during their preanesthesia appointment, at which time their medications were identified. Eligible patients included adult patients 18 years or older, ASA physical status II to III receiving ACEI or ARB therapy primarily for HTN for >6 weeks as prescribed and adjusted by the primary care physician, who were scheduled for any ambulatory or same-day admission surgery. Patients taking diuretics, β-blockers, or calcium channel blockers scheduled for all types of surgery and anesthesia were eligible. Exclusion criteria included patients who took ACEIs or ARBs only in the evening (to reduce variability from time of last medication to surgery), concomittant use of ACEIs and ARBs, patients with severe, uncontrolled HTN defined as ≥180 systolic or ≥110 mm·Hg during presurgical testing, patients classified as unstable ASA physical status III or greater, pregnant patients and patients with a body mass index >45 kg/m^2. With the use of computer-generated numbers, patients were randomized into 2 groups: The discontinuation group was instructed to take the ACEI or ARB on the day before surgery but to discontinue on the day of surgery; the continuation group was instructed to take the ACEI or ARB on the day of surgery at least 2 hours preoperatively, along with other prescribed medications as indicated. Patients were instructed to continue all other antihypertensive medications on the day of surgery except for diuretics. Research personnel contacted study participants on the day before their procedure to confirm preoperative instructions as per the study protocol and to remind patients to document the times that BP medications were taken. On the day of surgery, patients were interviewed in the preoperative holding area by a member of the research team to determine that criteria for enrollment had been met and to ascertain the time and dose of the last ACEI or ARB medication and other medications. Demographic variables including age, sex, race, surgical procedure, ASA physical status, and comorbid conditions (coronary artery disease, diabetes mellitus, and renal insufficiency) were recorded. Noninvasive preoperative BPs were obtained by blinded nursing personnel while patients were comfortably seated or on a stretcher in the ambulatory or same-day admission preoperative holding area. An appropriately sized cuff was applied to either upper extremity and measurement obtained by using the Welsh Allyn Non-Invasive Blood Pressure Machine Model #42NTB (Skanealeles Falls, NY). Research personnel repeated any abnormally high or low BP measurement on the same or contralateral upper extremity. Staff anesthesiologists assigned to individual cases and not involved in the study were informed of any such measurement, and management decisions were left to their discretion.

Management in the PACU was per usual standard of care and left to the discretion of the assigned personnel not involved in the study. Before discharge from the PACU, each patient's record was reviewed to obtain the maximum and minimum recorded BPs and any interventions that were required postoperatively to treat hemodynamic instability.

The primary outcome measure was the presence of HTN while the patient was in the preoperative holding area before the surgical procedure as defined by the JNC 7 classifications:[16] Stage 1 HTN: systolic blood pressure (SBP) ≥140 mm·Hg or diastolic blood pressure (DBP) ≥90 mm·Hg; Stage 2 HTN: SBP ≥160 or DBP ≥100 mm·Hg. Secondary outcome measures were preoperative cancellations or postoperative admissions due to unstable BP (defined as Stage 1 or 2 HTN; hypotension defined as SBP <90 mm Hg for at least 5 continuous minutes or a >30% reduction in mean arterial BP compared with baseline reading in the holding area), incidence of HTN during the immediate postanesthesia recovery period and any other adverse effects (increased length of stay in the PACU [>2 hours postoperatively], unanticipated hospitalizations, myocardial infarction, stroke, death). Patients who were enrolled but cancelled before the day of surgery were excluded from further analysis, and the reasons for cancellation were documented.

Patients who were enrolled during the preadmission visit but did not follow randomization (i.e., "crossover" from original group assignment by continuing or discontinuing ACEIs or ARBs when instructed otherwise) were included as "intent-to-treat" enrollees.

Sample Size Analysis

The principal measurement was preoperative BP. Since we hypothesized no meaningful difference between treatment arms, we characterized this as a noninferiority study. Based on the study by Wax et al.[17] that retrospectively analyzed >200,000 electronic anesthesia and hospital records of adult patients undergoing nonemergent inpatient and outpatient surgery, and, independent of any medical diagnoses, reported an incidence of preinduction HTN (defined as >140/90 mm·Hg) to be 10%, we projected the HTN prevalence in our discontinuation group to be 10%. We considered that a clinically meaningful difference between the groups would be a 5 percentage point greater prevalence of HTN in the discontinuation group. At the 0.05 significance level, 80% power is associated with $N = 446$ in each group. Allowing for a 20% dropout rate led to a projection of 557 patients in each group. Had we been less conservative and considered a 10 percentage point difference to be clinically significant, then allowing for a 20% dropout rate, we would have required only 140 patients per group.

Data Analysis

Differences in preoperative patient demographics, drug therapy, and study outcomes between the discontinuation and continuation groups were evaluated by using Fisher Exact test or the Wilcoxon rank sum test. Continuous data were expressed as median (range) and categorical data as percentages. For the primary outcome of preoperative HTN 95% 1-sided confidence intervals (CI) for prevalence was calculated around the observed differences by using Method 10 of Newcombe.[18] We chose a 1-sided CI because we were concerned whether discontinuation could cause an increase in the prevalence of HTN, not a decrease the prevalence of HTN. To determine whether the pattern of BP changed over time for an individual patient, a 3 × 3 concordance table was constructed for baseline presurgical screening period versus day of surgery HTN stages (none, Stage 1 and Stage 2) separately for each group.

Post Hoc Analysis

To address the issue of possible interaction between treatment and ethnicity on the primary outcome, a multinomial logistic regression model was constructed, with HTN (normal, Stage I, and Stage II) as the dependent variable; independent variables were treatment (continue, discontinue), ethnicity (African American, non-African American), and their interaction. Data were analyzed by using SAS (SAS Institute, Cary, NC) Release 9.2 software.

RESULTS

Six hundred forty-four patients were initially enrolled and randomized: of these, 62 had surgery cancelled, 11 withdrew, 33 had crucial data missing, 8 were found to be duplicate enrollees, and 24 met exclusion criteria. Randomization of the remaining 526 resulted in assignment of 262 to the discontinuation group and 264 to the continuation group. The 51 crossover patients were equally distributed between the treatment arms and were included in this intent-to-treat analysis. Demographics were similar between the treatment arms (Table 1). Differences were neither found between the 2 treatment groups in the frequency of use of monotherapy and multidrug therapy, $P = 0.211$ (Appendix 1) nor in the distribution of drugs with a half life ≤6 hours or >6 hours, $P = 0.223$ (Appendix 2). More patients in the continuation group had chronic renal insufficiency, 10 vs 1 < P =0.011; however, the numbers were too small to plausibly affect the outcome variables.

A more detailed scrutiny of the demographic data indicated that baseline BPs during the presurgical screening period were similar between treatment arms (not shown) according to the JNC 7 classification: overall, 44.4% of those enrolled were normotensive, 38.1% had Stage 1 HTN, and 17.5% had Stage 2 HTN. No patients with severe HTN were recruited. Median time from last medication administration to surgery was 1405 minutes in the discontinuation group and 160 minutes in the continuation group ($P < 0.001$).

On the day of surgery in the preoperative holding area, no significant differences were found between the 2 groups in the primary outcome variable. The distribution of SBP, DBP, or mean arterial BPs, and the percentage of total patients in each group with Stage 1 or 2 HTN were similar (Table 2). The upper bound of a 95% CI for the difference in prevalence of Stage 1 and 2 HTN between study arms indicates

Table 1. Demographics, Antihypertensive Therapies, and Comorbidities for the Discontinuation (DG) and the Continuation (CG) Groups

	DG (n = 262)	CG (n = 264)	P
Age in years: median (range)	61.0 (38–91)	62.0 (27–90)	0.239
Female: n (%)	172 (66%)	175 (66%)	1.000
African Americans: n (%)	143 (55%)	163 (62%)	0.171
ASA III: n (%)	100 (38%)	104 (39%)	0.789
Patients using ACEIs: n (%)	129 (49%)	142 (54%)	0.337
Patients using ARBs: n (%)	133 (51%)	122 (46%)	0.337
*Patients using β-blockers: n (%)	82/253 (32%)	86/257(33%)	0.851
[a]Patients using CCBs: n (%)	60/258 (23%)	76/256 (30%)	0.110
[a]Patients with diabetes: n (%)	89/258 (35%)	90/263 (34%)	1.000
[a]Patients with coronary artery disease: n (%)	32/258 (12%)	33/263 (13%)	1.000
[a]Patients with chronic renal insufficiency: n (%)	1/258 (0%)	10/263 (4%)	0.011

ACEIs = angiotensin-converting enzyme inhibitors; ARBs = angiotensin II subtype I receptor antagonists; CCBs = calcium channel blockers.
[a]Specific denominators are given for variables with missing data.

Table 2. Preoperative Arterial Blood Pressure Results on the Day of Surgery Before Surgical Procedure for the ACEIs/ARBs Discontinuation (DG) and the Continuation (CG) Groups

	DG (*N* = 262)	CG (*N* = 264)	*P*
Systolic blood pressure: median (range)	132 (95–199)	133 (88–207)	0.933
Diastolic blood pressure: median (range)	78 (36–103)	76 (43–109)	0.174
Mean arterial blood pressure: median (range)	96 (68–133)	95 (65–128)	0.452
Stage 1 HTN (>140/90 but not ≥160/100): *n* (%)	72 (27.5%)[a]	77 (29.2%)	0.775*
Stage 2 HTN (>160/100): *n* (%)	26 (9.9%)[b]	22 (8.3%)	0.775*

ACEIs = angiotensin-converting enzyme inhibitors; ARBs = angiotensin II subtype I receptor antagonists.

[a]The upper bound of a 95% confidence interval for the difference in prevalence of Stage 1 HTN = hypertension between treatment groups is 4.8 percentage points.

[b]The upper bound of a 95% confidence interval for the difference in prevalence of Stage 2 HTN between treatment groups is 5.8 percentage points.

**P* value applies to a 3 × 2 Fisher exact test table.

that discontinuation of study medication is unlikely to be associated with an increase in Stage 1 HTN of >4.8 percentage points and in Stage 2 HTN of no >5.8 percentage points.

Analysis of the primary outcome by treatment and ethnicity showed that among African American patients prevalence of Stage 1 HTN was 31% (44/143) for discontinue vs 34% (55/163) for continue; corresponding Stage 2 figures were 12% (17/143) vs 6% (9/163). For non-African Americans, Stage 1 prevalence was 24% (28/119) for discontinue vs 22% (22/101) for continue; corresponding Stage 2 figures were 8% (9/119) for discontinue vs 13% (13/101) for continue. A test of treatment by ethnicity interaction yielded $P = 0.075$. With the interaction term removed, ethnicity-adjusted odds ratios (continue versus discontinue) for Stage 1 vs normal and Stage 2 vs normal were 1.03 and 0.84, respectively; these values are very close to the unadjusted odds ratios (1.06 [95% CI, 0.72–1.57] and 0.84 [95% CI, 0.46–1.54], respectively).

The pattern of measurable BP over time was similar between groups (Appendix 3).

Maximum postoperative BP was available for 136 discontinuation subjects and 150 continuation group subjects. Stage 1 HTN was present in 64/150 (42%) patients in the discontinuation group vs 56/136 (41%) in the continuation group; Stage 2 HTN was found in 34/150 (23%) patients in the discontinuation group and in 30/135 (22%) patients in the continuation group ($P = 0.934$). There were too few patients in either group who received treatment in the PACU for HTN to be considered for analysis. No cases were cancelled preoperatively or admitted to hospital postoperatively, due to uncontrolled perioperative HTN. There were no deaths or any hospital admissions related to adverse events (myocardial infarction or stroke).

DISCUSSION

We investigated the consequences, if any, of instructing patients scheduled for elective surgery on an ambulatory or same-day surgery basis to discontinue their ACEIs or ARBs preoperatively. These instructions were based primarily on earlier inpatient literature, suggesting that patients continuing to take ACEIs and ARBs before surgery were more likely to experience hypotension after induction of general anesthesia.[2–10] More recent literature continues to recommend discontinuation of these medications preoperatively because of reported increased risk of death, use of inotrophic support, postoperative renal dysfunction, and atrial fibrillation in patients undergoing CABG or major vascular procedures.[12,13] In addition, the presence of ACEIs might inhibit the effectiveness of other endogenous or exogenous vasoconstrictors needed to treat postinduction hypotension.[19] However, few investigators looked for or evaluated unintended effects of discontinuing the medication. Pigott et al.[14] studied 40 patients undergoing cardiac surgery and found that, although patients in the group that suspended ACEI therapy experienced less of a reduction in BP after anesthetic induction, they did experience a marked increase in BP postoperatively that necessitated the administration of vasodilators.

This has created a clinical dilemma: is the benefit, after anesthetic induction, of discontinuing treatment offset by the risk of HTN preoperatively or postoperatively? After nearly 2 decades of discussion of the pros and cons of perioperative ACEI and ARB therapy, there is no evidence-based consensus. The uncertainty stems in part from the absence of RCTs designed to examine potential deleterious consequences.

The current study, which is the largest, prospective RCT related to continuation of ACEI/ARB therapy before surgery, conducted on ambulatory and same-day surgery patients, demonstrated that discontinuing ACEIs and ARBs does not put patients at risk for preoperative HTN, increased cancellations, admissions, or significant HTN in the PACU. In addition, patients who continued treatment did not have a more stable preoperative BP than those who discontinued treatment and were no less likely to be hypertensive postoperatively than those who discontinued their medications. The question of whether the effect of drug discontinuation varies by ethnic group cannot be answered with great confidence from these data, because the test of interaction yielded a *P* value of marginal statistical significance. We can, however, state with some confidence that reported results for the primary outcome are not meaningfully biased by a confounding effect of ethnicity. Further study is needed in African Americans who have already been identified in the medical literature as having more difficult to treat HTN.[20–22]

A meta-analysis (3 RCTs and 2 observational studies) totaling 434 patients undergoing nonemergency surgery[15] suggested that patients receiving immediate preoperative ACEI or ARB medication were more likely (relative risk [RR] 1.5, 95% CI, 1.15–1.96) to develop hypotension requiring a vasopressor at or shortly after induction. The 3 RCTs[3,7,14] were limited to CABG and vascular surgery and were small with 20 to 30 patients in each arm. One of the observational studies was conducted in a broader population of patients (including outpatients and same-day surgery patients) but was retrospective, nonrandomized, and did not report on preoperative HTN.[6] Insufficient data in this meta-analysis limited further conclusion about the consequences of potential hemodynamic changes on adverse outcomes. Unfortunately, it is trials like these that have formed the basis for publications, recommending the withholding of ACEIs on the day of surgery.[20]

Because the primary outcome measurement in our study was preoperative BP, patients were not excluded based on the types of surgery or anesthesia and included monitored anesthesia care, regional and general anesthesia. As there are other intraoperative factors that affect BP under various surgical and anesthesia conditions, we did not evaluate the intraoperative hemodynamics. As the study continued, we considered whether discontinuation might be associated with rebound HTN in the immediate postoperative period and therefore added as a secondary outcome, measurement of postoperative BP in the PACU. We did not find the incidence of PACU Stage 1 and Stage 2 HTN to differ between the 2 groups. The lack of rebound HTN in the ACEI/ARB-treated groups might be related to a persistent tissue effect of ACEIs/ARBs,[7,21] although we did not measure this. Chronic ACEI/ARB treatment exerts long-lasting beneficial effects on the structural and or functional vascular myocardial alterations that accompany chronic hypertensive disease.[7,21] The point might be made that many of our patients were taking multiple additional antihypertensive medications and that this might explain the absence of significant preoperative or postoperative HTN changes in the discontinuation group, or any differences between the 2 groups in the various measurements. However, the relevant information is that there were no differences between the 2 groups in the additional antihypertensive medications taken (Appendix 1, 2).

In the absence of large RCTs, propensity scoring has been used to analyze large patient databases and focus on the consequences of continuing the ACEI/ARB medications.[22,23] Most recently, Turan et al.[23] reported the results of propensity matching of 9028 ACEI users who did not take their medication on the day of surgery and controls (patients not taking ACEIs or ARBs) and reported similar intraoperative hemodynamic characteristics at various time points for both groups, similar interventions with vasopressors, and use of crystalloid infusions. They did not extend their measurements into the postoperative period.

We recommend that because of the unresolved nature of the continuing debate medication recommendations be tailored to specific patient populations based on their comorbidities, intended surgery, and concurrent therapies, rather than a 1-size-fits-all approach. Some have suggested the withholding of ACEIs and ARBs for patients who are receiving multiple antihypertensive medications, while, as a safe practice, continuing ACEIs and ARBs on the day of surgery where the only mode of HTN control is renin-angiotensin-system blockade.[24] We agree that this is reasonable for many patient scenarios.

Our study involves ambulatory and same-day admission patients undergoing a large variety of relatively low-risk surgical procedures and anesthetics and allows for the study results to be applied more generally to a diverse urban population. The limitations of our study, however, are that our primary and secondary end points are confined to a brief perioperative period. We cannot address whether withholding medications had any significant long-term outcome.

Showing the lack of an effect is always more challenging than demonstrating an effect, especially for infrequent events. In our study, preoperative Stage 2 HTN occurred in 10% of patients who discontinued and 8% of patients who continued ACEI/ARB medications, and therefore, a sample size closer to the original power analysis will be needed to definitively affirm our hypothesis. Although we acknowledge that the study is underpowered with respect to initial projections, the prevalence of preoperative HTN found in both arms of this study was considerably higher than projected based on Wax et al.[17] (37% when combining Stage 1 and Stage 2 prevalence as seen in Table 2); also, the CI around observed differences in HTN between discontinuation and continuation groups is so small that it is unlikely to be associated with a clinically meaningful difference between populations. As seen in Table 2, HTN prevalence was almost identical between treatment arms, and a difference of up to 4.8 percentage points for Stage 1 HTN and up to 5.8 percentage points for Stage 2 is not clinically significant. It is unlikely that discontinuation would increase Stage 1 HTN or Stage 2 HTN in any clinically significant way. We have supported our hypothesis that in our population of patients, the prevalence of Stage 1 or Stage 2 HTN would be no different between patients who discontinued versus continued their medications. Finally, the relevance of these findings may be limited without the concurrent study of postinduction hypotension and postoperative outcomes. We are currently conducting a large prospective RCT to evaluate postinduction BPs and perioperative hemodynamic control in ambulatory and same-day patients undergoing general anesthesia, with the intent of providing additional data for development of evidence-based guidelines for the continuation or discontinuation of ACEI/ARB medications perioperatively.

CONCLUSIONS

Discontinuing ACEIs and ARBs in patients on the day of surgery did not substantively result in a greater incidence of pre- or postoperative HTN compared with patients who continued these medications, as monotherapy or multidrug therapy on the day of surgery. Our results provide

Appendix 1. Treatment Arm by Medications

Frequency *n*,%	(Meds)	(Continue ACEI or ARB) Disc	Cont	Total
	ACEI + (Unk)	6	8	14
		2.29	3.03	
	ACEI + β-blocker	37	25	62
		14.12	9.47	
	ACEI + CCB + β-blocker	9	19	28
		3.44	7.20	
	ACEI + CCB	20	29	49
		7.63	10.98	
	ACEI alone	57	61	118
		21.76	23.11	
	ARB+(Unk)	7	3	10
		2.64	1.14	
	ARB + β-blocker	25	33	58
		9.54	12.50	
	ARB + CCB + β-blocker	10	9	19
		3.82	3.41	
	ARB + CCB	19	18	37
		7.25	6.82	
	ARB alone	72	59	131
		27.48	22.35	
	Total	262	264	526

Pearson chi-square test $P = 0.211$.

ACEIs = angiotensin-converting enzyme inhibitors; ARBs = angiotensin II subtype I receptor antagonists.

Appendix 2. Distribution of Drugs by Treatment Group and Half Lives

	≤ 6-h half life	> 6h half life	Total
Discontinue (*n*,%)	118, 45.04	144, 54.96	262
Continue (*n*,%)	133, 50.38	131, 49.62	264
Total	251	275	526

Fisher exact test $P = 0.223$.

Appendix 3. Baseline Presurgical Screening HTN by Day of Surgery HTN for Concordance Discontinuation Group

	Day of surgery HTN			
Baseline HTN	**None**	**Stage 1**	**Stage 2**	**Total**
None	91	16	5	112
Stage 1	59	35	9	103
Stage 2	14	20	12	46
Total	164	71	26	261

Baseline Presurgical Screening HTN by Day of Surgery HTN for Concordance Continuation Group

	Day of surgery HTN			
Baseline HTN	**None**	**Stage 1**	**Stage 2**	**Total**
None	99	18	4	121
Stage 1	49	40	8	97
Stage 2	17	19	10	46
Total	165	77	22	264

Generalized exact Fisher text of null hypothesis that the pattern of off-diagonal entries (i.e., people who HTN status changed over time) is the same across treatment arms; $P = 0.940$.

an evidentiary basis for the safety of discontinuing ACEIs and ARBs on the day of surgery without increasing adverse hemodynamic outcomes. Analysis of the intraoperative and postoperative effects of these interventions is ongoing with the intent of providing evidence-based guidelines for safe management of patients taking ACEIs and ARBs scheduled for ambulatory and same-day surgery.

DISCLOSURES

Name: Rebecca S. Twersky, MD, MPH.
Contribution: This author designed and conducted the study, analyzed the data, and prepared the manuscript.
Attestation: Rebecca S. Twersky, MD, MPH, approved the final manuscript. Dr. Rebecca S. Twersky attests to the integrity of the original data and the analysis reported in this manuscript. Dr. Rebecca S. Twersky is the archival author.
Name: Vasudha Goel, MD.
Contribution: This author helped conduct the study and collect and analyze the data.
Attestation: Vasudha Goel, MD, approved the final manuscript and attests to the integrity of the original data and the analysis reported in this manuscript.
Name: Preeti Narayan, MD.
Contribution: This author helped with data collection and conduct of the study.
Attestation: Preeti Narayan, MD, approved the final manuscript and attests to the integrity of the original data and the analysis reported in this manuscript.
Name: Jeremy Weedon, PhD, MA, BS.
Contribution: This author contributed to study design, power analysis, and conducted the statistical data analysis.
Attestation: Dr. Jeremy Weedon attests to the integrity of the original data and the analysis reported in this manuscript.
This manuscript was handled by: Peter S. A. Glass, MB, ChB.

ACKNOWLEDGMENTS

We gratefully acknowledge the numerous staff, residents, and medical students who participated in the study: Drs. Julia Griffin, Roy Braid, Jacqueline Njiapa, Leon Perel, David Rahmani, Donna Bracken, Monika Jadhav, Dmitry Roizen, Navdeep Nayyar and thank Dr. John Hartung, Dr. Julie Rushbrook, and Dr. Chineze Igboechi for their editorial assistance with the manuscript.

REFERENCES

1. Colson P, Ryckwaert F, Coriat P. Renin angiotensin system antagonists and anesthesia. Anesth Analg 1999;89:1143–55
2. Prys-Roberts C. Withdrawal of antihypertensive drugs before anesthesia. Anesth Analg 2002;94:767–8
3. Bertrand M, Godet G, Meersschaert K, Brun L, Salcedo E, Coriat P. Should the angiotensin II antagonists be discontinued before surgery? Anesth Analg 2001;92:26–30
4. Brabant SM, Bertrand M, Eyraud D, Darmon PL, Coriat P. The hemodynamic effects of anesthetic induction in vascular surgical patients chronically treated with angiotensin II receptor antagonists. Anesth Analg 1999;89:1388–92
5. Colson P, Saussine M, Séguin JR, Cuchet D, Chaptal PA, Roquefeuil B. Hemodynamic effects of anesthesia in patients chronically treated with angiotensin-converting enzyme inhibitors. Anesth Analg 1992;74:805–8
6. Comfere T, Sprung J, Kumar MM, Draper M, Wilson DP, Williams BA, Danielson DR, Liedl L, Warner DO. Angiotensin system inhibitors in a general surgical population. Anesth Analg 2005;100:636–44
7. Coriat P, Richer C, Douraki T, Gomez C, Hendricks K, Giudicelli JF, Viars P. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. Anesthesiology 1994;81:299–307
8. Reich DL, Hossain S, Krol M, Baez B, Patel P, Bernstein A, Bodian CA. Predictors of hypotension after induction of general anesthesia. Anesth Analg 2005;101:622–
9. Schirmer U, Schürmann W. [Preoperative administration of angiotensin-converting enzyme inhibitors]. Anesthesist 2007;56:557–61
10. Tuman KJ, McCarthy RJ, O'Connor CJ, Holm WE, Ivankovich AD. Angiotensin-converting enzyme inhibitors increase vasoconstrictor requirements after cardiopulmonary bypass. Anesth Analg 1995;80:473–9
11. Brabant SM, Eyraud D, Bertrand M, Coriat P. Refractory hypotension after induction of anesthesia in a patient chronically treated with angiotensin receptor antagonists. Anesth Analg 1999;89:887–8
12. Miceli A, Capoun R, Fino C, Narayan P, Bryan AJ, Angelini GD, Caputo M. Effects of angiotensin-converting enzyme inhibitor therapy on clinical outcome in patients undergoing coronary artery bypass grafting. J Am Coll Cardiol 2009;54:1778–84
13. Railton CJ, Wolpin J, Lam-McCulloch J, Belo SE. Renin-angiotensin blockade is associated with increased mortality after vascular surgery. Can J Anaesth 2010;57:736–44
14. Pigott DW, Nagle C, Allman K, Westaby S, Evans RD. Effect of omitting regular ACE inhibitor medication before cardiac surgery on haemodynamic variables and vasoactive drug requirements. Br J Anaesth 1999;83:715–20
15. Rosenman DJ, McDonald FS, Ebbert JO, Erwin PJ, LaBella M, Montori VM. Clinical consequences of withholding versus administering renin-angiotensin-aldosterone system antagonists in the preoperative period. J Hosp Med 2008;3:319–25
16. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The

Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003;289:2560–72
17. Wax DB, Porter SB, Lin HM, Hossain S, Reich DL. Association of preanesthesia hypertension with adverse outcomes. J Cardiothorac Vasc Anesth 2010;24:927–30
18. Newcombe RG. Interval estimation for the difference between independent proportions: comparison of eleven methods. Stat Med 1998;17:873–90
19. Licker M, Schweizer A, Höhn L, Farinelli C, Morel DR. Cardiovascular responses to anesthetic induction in patients chronically treated with angiotensin-converting enzyme inhibitors. Can J Anesth 2000;47:433–40
20. Wolf A, McGoldrick KE. Cardiovascular pharmacotherapeutic considerations in patients undergoing anesthesia. Cardiol Rev 2011;19:12–6
21. Richer C, Mulder P, Fornes P, Richard V, Camilleri JP, Giudicelli JF. Hemodynamic and morphological effects of quinapril during genetic hypertension development. J Cardiovasc Pharmacol 1991;18:631–42
22. Kheterpal S, Khodaparast O, Shanks A, O'Reilly M, Tremper KK. Chronic angiotensin-converting enzyme inhibitor or angiotensin receptor blocker therapy combined with diuretic therapy is associated with increased episodes of hypotension in noncardiac surgery. J Cardiothorac Vasc Anesth 2008;22:180–6
23. Turan A, You J, Shiba A, Kurz A, Saager L, Sessler DI. Angiotensin converting enzyme inhibitors are not associated with respiratory complications or mortality after noncardiac surgery. Anesth Analg 2012;114:552–60
24. Smith I, Jackson I. Beta-blockers, calcium channel blockers, angiotensin converting enzyme inhibitors and angiotensin receptor blockers: should they be stopped or not before ambulatory anaesthesia? Curr Opin Anaesthesiol 2010;23:687–90