

# Refractory Hypotension in Hypertensive Patients Treated with ARAII Undergoing General Anesthesia in Elective Surgery

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## Abstract

**Introduction:** In the surgical environment, the number of patients with arterial hypertension has increased significantly. Adequate advice to patients regarding the management of their preoperative antihypertensive medication is intended to reduce complications throughout the perioperative period, both due to its suspension and maintenance. However, despite the indications for antihypertensive management in many hospitals, the incidence of refractory hypotension during surgery is a frequent complication.

**Objective:** To describe the incidence of refractory hypotension in hypertensive patients treated with ARA II undergoing general anesthesia in elective surgery at a public hospital in the State of Durango, Mexico.

**Material and Methods:** Observational, descriptive, longitudinal, retrospective study. The sample size was calculated with a 95% confidence level and an expected frequency of 30%. The files in compliance with the selection criteria were randomized through the SPSS statistical program to be incorporated for analysis.

**Discussion and Conclusions:** Seventy-six records of individuals undergoing surgery under general anesthesia with ARAII-based treatment for hypertension were analyzed. The incidence of refractory hypotension was 3%. The incidence of trans-surgical hypotension was 69%. The most frequently identified risk factor was failure to discontinue antihypertensive treatment before surgery. Antihypertensive medication should be continued until the day of surgery, apart from renin-angiotensin blocking agents, which should not be administered on the day of surgery and can be resumed after surgery.

**Keywords:** Refractory hypotension • Transsurgical hypotension • ARAII • Antihypertensive management

## Introduction

Annually, 1.6 million deaths due to cardiovascular diseases occur in the Americas region, of which about half a million are people under 70 years of age, which is considered a premature and avoidable death. Hypertension affects between 20% and 40% of the adult population and means that about 250 million people suffer from hypertension [1, 2].

One out of every four Mexicans suffers from hypertension; in men the prevalence is 24.9% and in women 26.1%. Prevalence estimated at 30% according to the 140/90 mm Hg criterion, which is equivalent to about 22.8 million corresponding to the diagnosis of hypertension, but with the new

criteria of the American Heart Association the population with hypertension will be at least double [3].

With the increase in life expectancy of the population, associated with the improvement of surgical techniques, it is more frequent to see older patients undergoing surgeries of increased complexity. In addition, an increase in the prevalence of pathologies not related to the cause of surgery has been observed in these patients, as well as the use of pharmacological therapy for the comorbidities control [4].

## Material and Methods

This study was analyzed and approved by the research ethics committee of the Hospital General 450 of the city of Durango. All procedures were carried out following the Good Clinical Practice Guidelines and the provisions of current national regulations, in relation to the type of study in question: descriptive, observational, cross-sectional and retrospective. The sample size was calculated using the formula for prevalence studies in a finite population, with a 95% confidence level and an expected frequency of the study phenomenon of 30%, which resulted in a sample of 76 individuals to be considered [5, 6]. The records of men and women of any age, with a diagnosis of hypertension, under treatment with ARAII, who underwent elective surgery under general anesthesia, ASA I, II and III, were included. After approval, the records of patients undergoing elective surgery under general anesthesia in the period January 2022 to December 2022 were requested, and all those corresponding to hypertensive patients under treatment with ARAII were selected. Cases of patients who developed refractory hypotension were identified to calculate their prevalence within the study population. Each case was assigned an ID which was entered into the SPSS program in order to be randomized, finally obtaining 76 files.

## Results

A total of 180 patients with arterial hypertension treated with ARAII, who underwent surgery and general anesthesia, were registered. The 76 patients corresponding to the sample size calculation were registered and of these, 69% developed trans-surgical hypotension and 3% presented refractory hypotension with the need for amine administration (Figure 1). A median age of 62.5 years (54-69; q25-q75) with a BMI ranging from 27 kg/m<sup>2</sup> to 32 kg/m<sup>2</sup> (median 29.5) was identified. Regarding gender, it was identified that most of the individuals with transsurgical hypotension were male (57.4%) and the remaining 42.6 corresponded to female (Table 1). The risk factors were classified into three categories:

1. Those associated with the individual,
2. With the anesthetic and
3. With the management of the antihypertensive treatment.

The frequency of each one was 11.1%, 94.4% and 92%, respectively (Figure 2). Regarding the specific characteristics of the patients who developed refractory hypotension, we observed that they were both male; the age of the individuals was 67 and 90 years, with a BMI of 38 kg/m<sup>2</sup> and 19 kg/m<sup>2</sup> respectively. Risk factors were associated with the individual, the anesthetic and the antihypertensive management in both cases, one of them had congestive heart failure. The antihypertensive treatment used in the first case was candesartan and in the second case telmisartan; in neither of the cases was the drug suspended, or the administration schedule modified (Table 2). Among the risk factors associated with the individual, the most frequent was congestive heart failure (3.7%), followed by valvular heart disease (1.9%); no patients with renal failure or a previous record of acute myocardial infarction were identified (Figure 3). In patients who presented with trans-surgical hypotension, a median fasting time of 10 hours (8-12;

q25-q75) was identified (Suppl No1). Regarding the anesthetic used, all patients received fentanyl, propofol and sevoflurane, 57.4% also received cistracurium and 35.2% received vecuronium (Figure 4). The most frequently used medication for the management of hypertension was losartan (53.8%), in second place, telmisartan (42.3%) and in third place candesartan (3.8%) (Suppl No2). A total of 77.8% of the patients were classified as ASAIII risk and only 13% corresponded to ASAII (13%). Finally, regarding the suspension of antihypertensive treatment before surgery, it was identified that in 66.3% of the cases the medication had not been suspended and was administered as usual, only in 11.5% of the cases the treatment was suspended, and the scheme was modified in 22.2% (Figure 5).

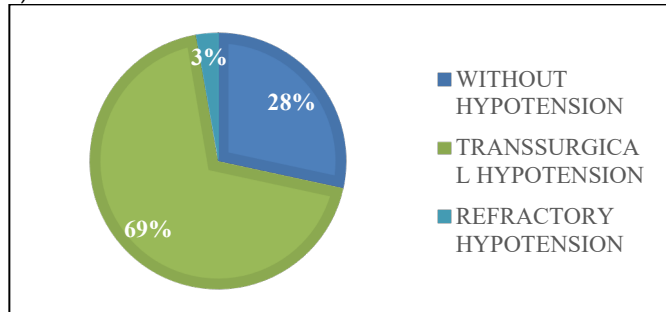


Figure 1. Incidence of trans-surgical and refractory hypotension

Table 1. General characteristics of the study population

N=54		
AGE (years)*	62.5	(54-69)
BMI (kg/m <sup>2</sup> ) **	29 ± 5	
Sex	n	%
Female	23	42.6
Male	31	57.4

\*Data are presented as mean and standard deviation. \*\* Data are presented as median (q25-q75).

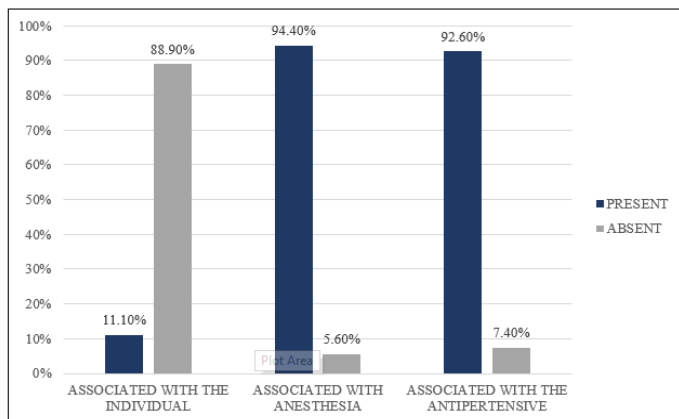


Figure 2. Risk factors present in the population that developed transsurgical hypotension

Table 2. Characteristics of individuals who developed refractory hypotension

N=2	Age	Sex	BMI	
PATIENT1	67	M	38	
PATIENT2	90	M	19	
	FRAI	FRAA	FRAAH	ICC
PATIENT1	SI	SI	SI	SI
PATIENT2	SI	SI	SI	No
	Antihypertensive		PQ Suspension	
PATIENT1	Candesartan		No	
PATIENT2	Telmisartan		No	

BMI: body mass index; ARRF: risk factors associated with the individual; ARRF: risk factors associated with the anesthetic; ARRFH: risk factors associated with the antihypertensive drug; CHF: congestive heart failure.

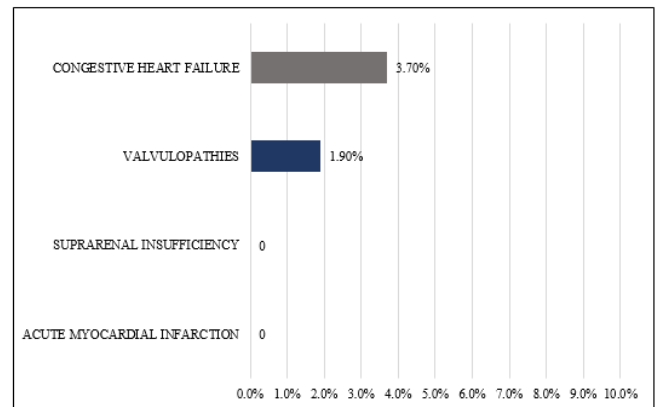


Figure 3. Factors associated with the individual that increase the risk developing transsurgical hypotension

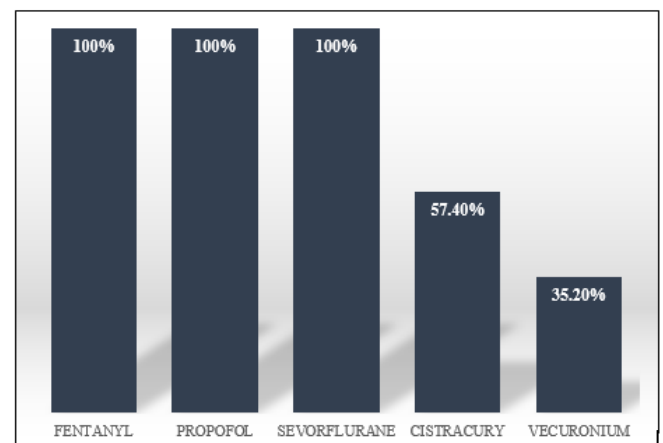


Figure 4. Frequency of anesthetics used in patients who presented transsurgical hypotension

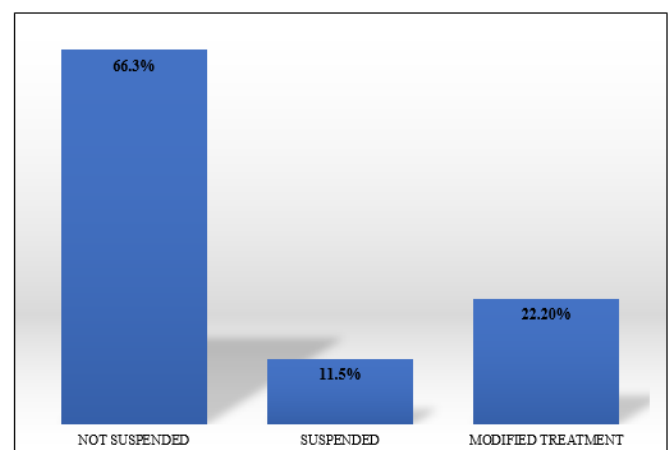


Figure 5. Suspension of antihypertensive medication in patients before surgery

## Discussion

Elevated blood pressure causes damage to vital organs such as the heart, brain and kidneys, and can lead to coronary heart disease, stroke, as well as heart and kidney failure. Antihypertensive drugs have been shown to improve long-term survival in people with hypertension [7]. However, it is not clear whether hypertension during the perioperative period increases the risk of cardiovascular complications, nor is there conclusive information on whether treatment of hypertension before surgery reduces perioperative risk [8].

In our study, we observed that the incidence of refractory hypotension was 3%. According to research conducted by Gonzalez-Chon et al, more than

100 million noncardiac surgeries are performed annually worldwide, with most of these procedures being elective with a complication rate ranging from 0.5% to 1%. These complications include perioperative death, nonfatal infarctions, acute kidney injury, and cerebral vascular events. Hypotension during surgery is a frequent complication and is considered an independent risk factor for cerebrovascular events, myocardial infarction and both short- and long-term mortality [9]. In our study, a 69% incidence of trans-surgical hypotension was also observed. The VASQIP cohort found that a systolic pressure below 70 mmHg for more than five minutes increased the risk of 30-day mortality, with an OR of 2.898 (95% CI: 1.719-4.886). In addition, maintaining mean arterial pressure between 40 mmHg-49 mmHg was associated with increased 30-day mortality with an OR of 2.433 (95% CI: 1.285-4.608), and if mean arterial pressure was below 40 mmHg for more than five minutes, the OR for 30-day mortality was 20.826 (95% CI: 8.884-48.822) [10].

Transoperative hypotension can cause organ damage due to ischemia-reperfusion, with the kidney and heart being the organs most susceptible to decreased systolic blood pressure. Hypotension-related acute kidney injury (prerenal type) affects 7% of hospitalized patients and 7.5% of patients undergoing non-cardiac surgery. As for the two cases of refractory hypotension recorded in the study, one of them had a congestive heart failure antecedent, which significantly increases the risk of complications and long-term sequelae [11].

All the patients included in our study were receiving antihypertensive treatment with ARAII, although only 2 cases (3%) developed refractory hypotension, 69% of the cases developed trans-surgical hypotension and in more than half of the patients antihypertensive treatment was not interrupted or modified.

Steven Bravant et al. conducted a study in which they analyzed the prevalence and severity of hypotension after induction of general anesthesia in 12 patients who had received angiotensin ii receptor subtype 1 antagonist (ARAII) until the morning of surgery. Compared with patients who had received other hypotensive drugs, such as Beta-adrenergic Blockers (BB) and/or calcium channel blockers and angiotensin-converting enzyme inhibitors, Bravant observed that hypotensive episodes occurred more frequently after anesthetic induction in patients who had received ARAII. In addition, the team described that patients treated with ARAII had a lower response to the vasopressors ephedrine and phenylephrine [12].

Hypertensive patients who need to undergo surgery may face difficult situations for the anesthesiologist, not only related to medical management, but also to making decisions about the most appropriate time to perform surgery. This situation is especially true for those patients with uncontrolled arterial hypertension or in an advanced stage of the disease. In this group of patients, objective parameters are required to identify which patient can undergo surgery with the lowest possible risk associated with their cardiovascular pathology, specifically regarding the risk factors for developing hypotension during surgery, the most frequent one identified in our study was the failure to suppress or modify antihypertensive treatment before surgery [13].

The goal of antihypertensive management should be to maintain mean arterial pressure within 20% of baseline values whenever possible. Several therapeutic options are available for use perioperatively, and when oral intake cannot be resumed postoperatively, intravenous or patch options are available. The ideal antihypertensive agent should provide immediate onset of action, act selectively on the arterial circulation, and be easy to dose accurately. Antihypertensive medication should be continued until the day of surgery, except for renin-angiotensin blocking agents, which should not

be administered on the day of surgery and can be resumed after surgery [14].

## Conclusion

The results of this work help us to expose that, even with all the information we have at hand related to the preoperative management of patients with comorbidities, the frequency of iatrogenic hypotension continues to be a reality. The incidence of refractory hypotension was 3%, however, trans-surgical hypotension was 69%. The main risk factor identified was failure to discontinue antihypertensive treatment.

Given the evidence of the risk posed by the presence of hypotension during surgery, it is recommended that a campaign be developed within the host hospital, with emphasis on the management of hypertensive patients before their admission to surgery, especially those treated with ARAII, where a higher risk of trans-surgical hypotension has been demonstrated compared to other antihypertensive medications.

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