

REVIEW ARTICLE

Impedance Cardiography in the Evaluation of Patients with Arterial Hypertension

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Abstract

Arterial hypertension is responsible for high morbidity and mortality. Despite increasing awareness of the consequences of uncontrolled hypertension and the publication of several recommendations and guidelines, blood pressure control rates are suboptimal, and approximately half of the patients do not reach the targets. Defined as an increase in blood pressure, hypertension is characterized by hemodynamic abnormalities in cardiac output, systemic vascular resistance, or arterial compliance. Therefore, the approach to arterial hypertension can be improved by the knowledge of the hemodynamics underlying the blood pressure increase. Impedance Cardiography has emerged as a new strategy to customize therapy and monitor patients aiming to improve blood pressure control according to the hemodynamic profile, rather than a blind intensive care approach. This is a review of impedance cardiography evidence, its benefits, actual and future applications in the approach and management of arterial hypertension.

Introduction

Hypertension is a condition characterized by elevated blood pressure (BP). A comprehensive definition, published by the American Society of Hypertension in 2005, describes hypertension as “a progressive cardiovascular syndrome (CV) arising from complex and interrelated etiologies”. Early markers of this syndrome are often present before blood-pressure (BP) elevation

Keywords

Hypertension / physiopathology; Blood Pressure; Cardiography, Impedance; Hemodynamics.

occurs; thus, hypertension cannot be solely classified by discreet blood-pressure thresholds. Disease progression is strongly associated with cardiac and vascular functional and structural abnormalities that damage the heart, kidneys, brain, vasculature and other organs, leading to early morbidity and mortality.¹

It is estimated that hypertension affects approximately 1 billion individuals and causes more than 7 million deaths annually worldwide (13% of overall mortality). In Portugal, the prevalence of hypertension in the adult population aged 18 to 90 years is 42.2% (44.4% in men and 40.2% in women).² According to the World Health Organization (WHO), BP greater than 115 mmHg (systolic BP) is responsible for 62% of cerebrovascular diseases and 49% of ischemic cardiac pathologies, with little variation between the genders. These BP values are considered by the WHO as the main risk factor for mortality worldwide.^{3,4}

Although BP control is a growing concern, with a consequent increase in the number of treated and controlled patients, there is still a large percentage of treated patients who do not reach their therapeutic targets. In Portugal, only 55.6% of treated hypertensive patients have controlled BP.^{2,5,6}

To optimize BP control, new therapeutic strategies have been developed, namely the Plasma Renin Activity (PRA)-guided therapy, Impedance Cardiography (ICG)-guided therapy, and in some patients, renal denervation.⁷⁻⁹ The choice of antihypertensive therapy based on hemodynamic systems is not new, but it has progressively become more accessible through the noninvasive hemodynamic parameters of the ICG. This is based on the knowledge that elevated BP results from changes in its hemodynamic components (cardiac output – CO, peripheral vascular resistance and / or blood volume). ICG is a non-invasive, operator-

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independent and low-cost hemodynamic monitoring tool that allows defining the patients' hemodynamic profiles, leading to a more adequate selection of the antihypertensive therapy.¹⁰

Impedance cardiography

Biological tissues are complex anisotropic conductors with reactive and resistive components. The bioimpedance value depends on the type of tissue analyzed and can be altered by translocation of organs or tissues, by changes in shape or structure, by the volume or location of intracellular fluids, or by the frequency of the current used. The ICG consists in the evaluation of the electrical properties of the biological tissues of the chest.¹¹ The bioimpedance measures the way the tissues conduct the alternating electric current and varies according to the amount of body fluids. Thus, the chest impedance increases or decreases, depending on the changes in intrathoracic fluid with each heartbeat.^{12,13}

The most common technique uses four electrodes, two of which are the current electrodes and the two that detect voltage changes. Since the current amplitude is constant, the detected voltage is proportional to the tissue impedance.¹⁴ Figure 1 represents the four-pole impedance measurement scheme. The effective evaluation of the chest impedance during a cardiac cycle is hindered by several factors, such as chest size and shape, obesity,

body weight, position and posture, thoracic circulation and respiratory rate. For this reason, although this method was published in 1940 by Nyboer et al.,¹⁵ it took several years and many studies to reach a system that would correct them.^{14,16-19} Current technology, with data processing and modeling techniques, has demonstrated that ICG has a high correlation, reproducibility and precision when compared to invasive hemodynamic monitoring techniques and echocardiography – which was considered more time-consuming, operator-dependent and technically demanding. Therefore, the ICG allows safe, non-invasive and low-cost hemodynamic and cardiac cycle monitoring.²⁰⁻²⁵

The ICG detects, analyzes, and records hemodynamic changes by measuring electrical resistance changes in the thorax, graphically translating them as impedance and electrocardiography waves (Figure 2). It allows the calculation of several hemodynamic parameters such as systolic volume (SV), cardiac output (CO), systemic vascular resistance (SVR), velocity and acceleration indexes, thoracic fluid content (TFC), pre-ejection period, left ventricular ejection time, systolic time ratio, left cardiac work, heart rate and mean BP.²⁶ The assessed parameters and respective formulas are shown in table 1.

The first derivative of the waveform (ΔZ) describes fluid velocity and is a smooth wave, which corresponds to the systole, called S wave. The initial slope of the S

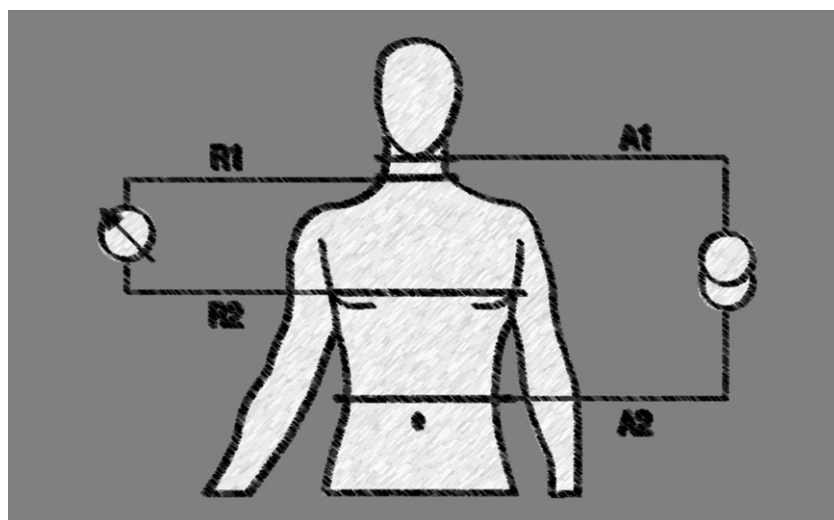
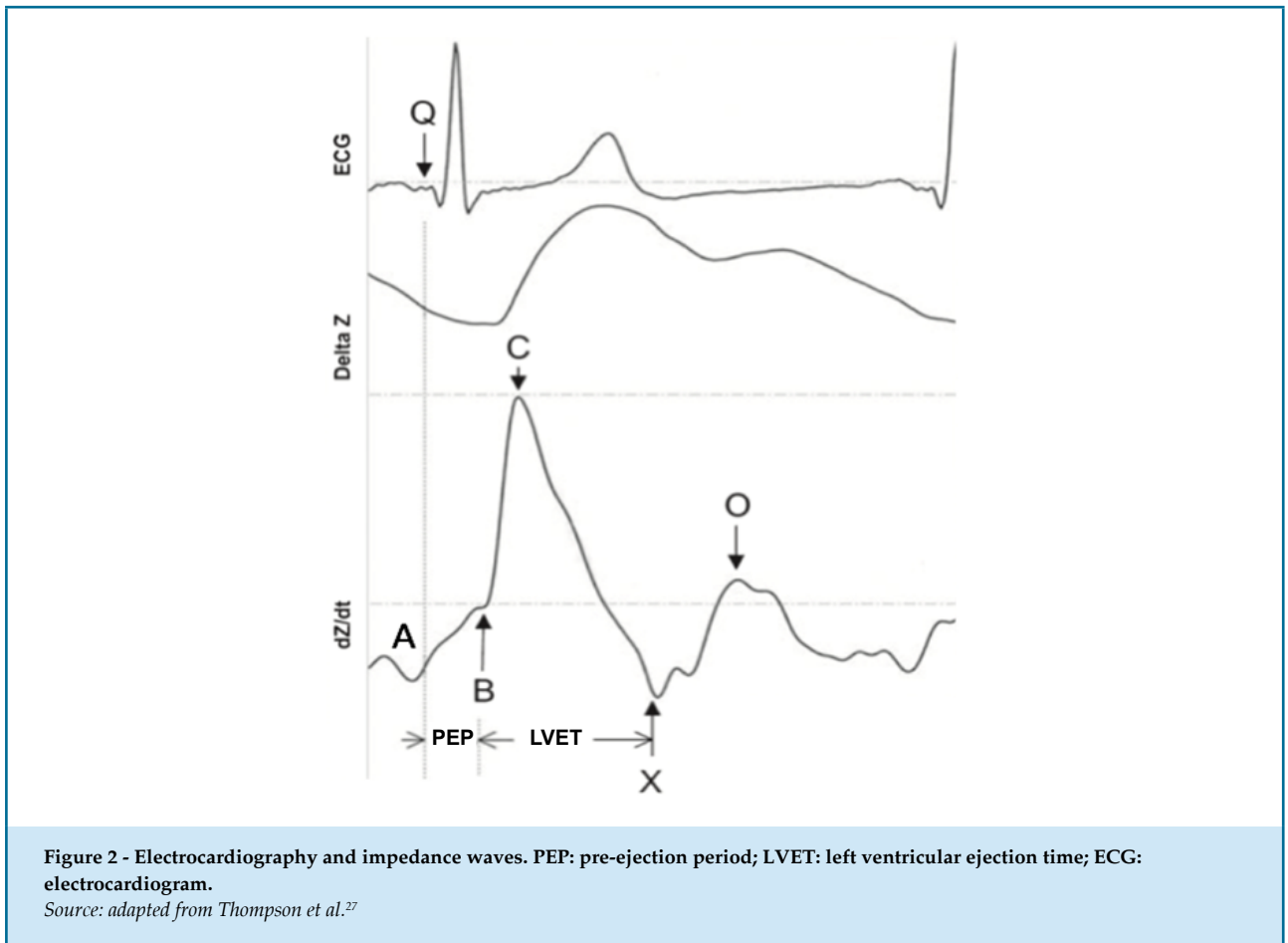


Figure 1 - Schematic illustration of impedance cardiography application, four-pole technique. A1 and A2 correspond to the current-applying electrodes; R1 and R2 to the current-receptor electrodes.

Source: adapted from Cybulski et al.¹⁴



wave correlates with cardiac contractility, and its height and width, with systolic volume. Several indices, such as pre-ejection period, left ventricular ejection time, velocity index, acceleration index, left cardiac work index, and so on, can be obtained through the waveform, allowing non-invasive monitoring of CO and contractility, for instance. The second derivative of the waveform (dZ/dt), describes fluid acceleration and represents a more detailed wave, containing four reference points (A, B, C, and X) associated with both atrial and ventricular systole, and the point o, which is related to the onset of diastole.

Point A coincides with the electrocardiogram (ECG) p-wave and marks the beginning of the end of diastolic filling. The A wave only exists in the presence of an atrial contraction, being small and round, with its end clearly separated from the beginning of the S wave. The basal impedance corresponds to point B. Point C defines the maximum acceleration of blood output from the ventricles. The slope corresponding to the rise from point B to point C is associated with cardiac contractility:

the steeper the upward curve, the greater the cardiac contractility. After reaching point C, there is a rapid deceleration to point X, which represents the inversion point of the intrathoracic fluid and corresponds to the closure of the aortic valve. After point X, the wave returns to the baseline and starts to form an early diastolic wave, associated with the opening of the mitral valve, the O wave. The moment of greatest opening of the mitral valve is represented by the peak of the S wave – point O. This interval between points X and O corresponds to the time of isovolumetric relaxation.²⁸

This technology can be used, for instance, to evaluate postural cardiac rehabilitation, pacemaker optimization, sleep studies, hemodynamic monitoring in pregnant women and outpatients, and therapy and/or monitoring of hypertensive patients.^{13,29-39}

ICG is a technique that has evolved in recent years and has become an attractive and cost-effective method of improving patients' clinical approach.

Table 1 - Parameters evaluated by impedance cardiography

Parameters	Definition	Normal values	Formula
HR	Number of beats per minute	58-96 bpm	RR interval measurement on the ECG and extrapolation to bpm
MAP	Mean pressure exerted by the blood on the arterial walls	84-100 mmHg	Manual = ((SBP-DBP) x KP) + DBP Automatic (oscillometric method) = MAP is measured directly through SBP and DBP
CO	Amount of blood pumped by the left ventricle per minute	4.5-8.5 L/min	CO = EjV x HR
CI	Standard CO for BSA	2.5-4.7 L/min/m ²	CI = CO/BSA
SV	Amount of blood pumped by the left ventricle per heartbeat	60-130 mL/heartbeat	SV = VEPT x LVET x VI (Z MARC® Algorithm)
SI	Standard stroke volume for BSA	35-65 mL/heartbeat/m ²	SI = SV/BSA
SVR	Resistance of circulating blood to the arterial system	742-1,378 dynes sec/cm ⁵	SVR = 80 x ((MAP - CVP)/CO)
SVRI	Standard SVR for BSA	1,337-2,483 dynes.sec.m ² /cm ⁵	SVRI = 80 x ((MAP - CVP)/ CI)
AI	Initial acceleration of blood in the aorta that occurs within the first 10-20 milliseconds after opening of the aortic valve	Male: 70-150/100 sec ² Female: 90-170/100 sec ²	AI = (d2Z/ dt2Max)/ TFC
VI in the aorta	Peak velocity of blood flow in the aorta	33-65/1,000 sec	VI = (dZ/ dtMax)/ TFC
TFC	Electrical conductivity of the thoracic cavity (determined by intravascular, interalveolar and interstitial fluid)	Male: 30-50/kohm Female: 21-37/kohm	TFC = 1/ TFI
LCW	Indicator of the amount of work exerted by the left ventricle in each minute to pump blood into the systemic circulation	5.4-10 kg.m	LCW = (MAP - PAOP) x CO
LCW index	Standard LCW for BSA	3.0-5.5 kg m/m ²	LCW index = (MAP - PAOP) x CI
PEP	The time interval from the beginning of electrical stimulation of the ventricles to the opening of the aortic valve (electrical systole)	Depends on HR, contractility and resistance to diastolic filling	Time interval between the beginning of the Q wave on the ECG and the B point on the dZ/dt wave (aortic valve opening)
LVET	Time interval from the opening to the closing of the aortic valve (mechanical systole)	Depends on HR, contractility and resistance to diastolic filling	Time interval between point B and point X of dZ/dt wave
STR	Ratio between the time of electrical and mechanical systole	0.3-0.5	STR = PEP / LVET

HR: heart rate; ECG: electrocardiogram; MAP: mean arterial pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; KP: variable that depends on the pulse pressure ratio (usually varies between 0.25-0.33); CO: cardiac output; EjV: ejection volume; CI: cardiac index; BSA: body surface area; SV: stroke volume; VEPT: volume of electrically participating tissue (conductive volume for thorax size, affected by weight, height and gender); LVET: left ventricular ejection time; VI: Velocity index; SI: Stroke index; SVR: systemic vascular resistance; CVP: central venous pressure (pressure in the thoracic vena cava upon reaching the right atrium - the standard value of 7 mmHg is considered); SVRI: systemic vascular resistance index; AI: acceleration index; d2Z/ dt2Max: maximum of the second derivative of ΔZ; TFI: thoracic fluid index (baseline thoracic impedance, Z0); TFC: total fluid content; LCW: left cardiac work; PAOP: Pulmonary artery occluded pressure (the standard value is 10 mmHg); PEP: pre-ejection period; STR: systolic time ratio.

Arterial hypertension and impedance cardiography

Classically defined as an increase in BP, this parameter alone is an incomplete indicator of the cardiovascular system status, particularly in patients with resistance to drug therapy or hypervolemic ones.⁷ The mean BP consists of the product of two hemodynamic parameters (CO and SVR), and arterial hypertension is the result of a disorder in one or both hemodynamic variables.⁴⁰ These findings, associated with the fact that the results obtained with empirical therapy based on current guidelines are suboptimal, have led some specialists to propose new approach pathways for the hypertensive patient, particularly a therapeutic approach guided by the patient's hemodynamic profile.⁴¹⁻⁴⁵ Historically, the use of BP as an indicator of cardiovascular status in hypertensive patients comes from the fact that hemodynamic parameters are assessed using invasive techniques.⁴⁶ More recently, echocardiography has been used to accurately estimate CO, but when compared with ICG, the latter was considered more time-consuming and technically demanding.¹⁹ Thus, ICG emerges as a non-invasive, simple, accurate and inexpensive method to evaluate patients hemodynamically, characterizing the profile and guiding the therapeutic optimization in hypertensive patients.^{44,45,47}

The use of ICG can improve our knowledge about arterial hypertension, especially regarding its hemodynamic characteristics and consequences. Hypertensive cardiopathy is a continuum, involving structural changes (myocardial fibrosis) and left ventricular geometry (hypertrophy and concentric

remodeling), which progressively develop into systolic and/or diastolic function disorder.⁴⁸ Close to its end, the IMPEDDANS study (ClinicalTrials.gov; Identifier: NCT03209141) intends to verify the ability to screen for left ventricular diastolic dysfunction in its asymptomatic phase in hypertensive patients, which may allow an early diagnosis, as well as the study of the disease evolution and therapeutics. The growing interest in hemodynamic changes in arterial hypertension and orthostatic and emotional stress responses, led researchers to use ICG to study autonomic dysfunction in hypertension. The technological evolution of the ICG, with the development of monitors for the assessment of outpatients, is a new area of research in arterial hypertension. With this technique, one can assess cardiac performance for 24 to 48 hours, as well as the hemodynamic changes that occur during Daily Life Activities, and the hemodynamic responses to changes in body position and blood pressure control, for instance.⁴⁹⁻⁵³

Antihypertensive therapy guided by impedance cardiography

Hypertension management includes lifestyle measures such as sodium restriction and weight loss, and, in most cases, the use of one or more antihypertensive drugs. Considering this approach to arterial hypertension as a hemodynamic pathology, drugs are proposed according to the pathophysiological mechanism responsible for BP increase (Figure 3).

Drugs are selected according to elevated hemodynamic parameters. Therefore, it is first

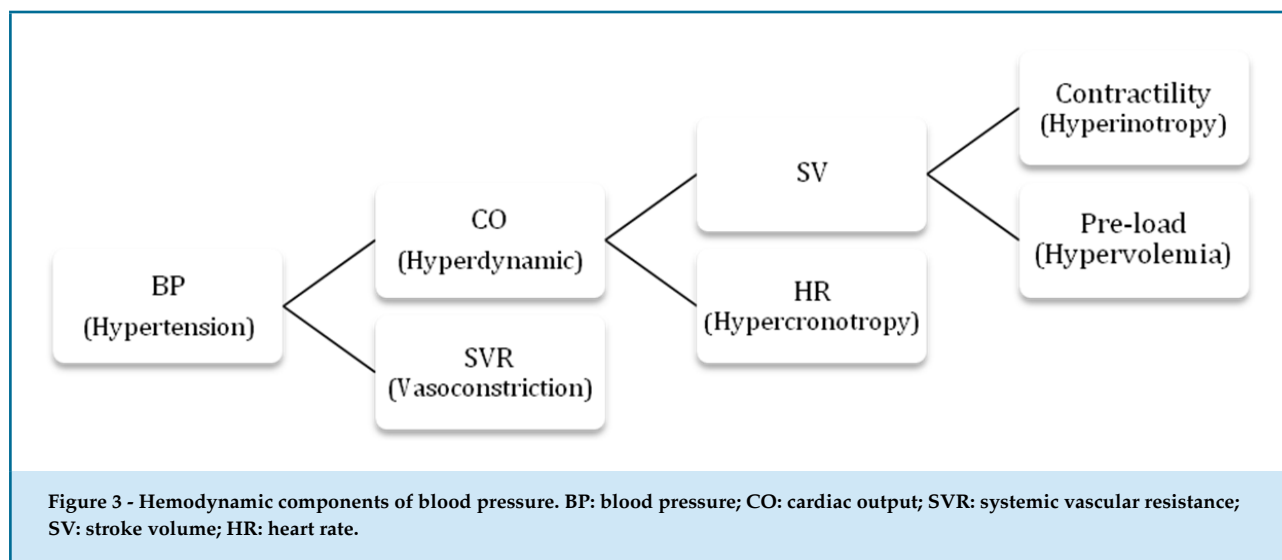


Figure 3 - Hemodynamic components of blood pressure. BP: blood pressure; CO: cardiac output; SVR: systemic vascular resistance; SV: stroke volume; HR: heart rate.

necessary to evaluate the hemodynamic variables to be able to target the therapy at a high cardiac or SVR index. Likewise, if any of these parameters is decreased, the drug responsible for the effect should be identified, its dose reduced, or the drug withdrawn (Figure 4).^{10,25,44,45} Several studies have highlighted the apparent superiority – although never assessed in long-term studies – of the personalized therapeutic approach to the hemodynamic profile, both regarding its efficacy and cost-effectiveness (Table 2).

Conclusion

Hemodynamic-guided therapy can be valuable in the evaluation and management of hypertensive patients. Impedance cardiography is a cost-effective assessment that allows the diagnosis, therapeutic optimization, and follow-up of hypertensive patients, helping them to achieve therapeutic targets, even in those with resistant hypertension. This therapeutic approach, which focuses on the cause of blood pressure increase

and its pathophysiological mechanism, allows better blood pressure control and a potential reduction in cardiovascular events, mortality and costs associated with arterial hypertension.

Future studies in the ICG area should broaden our understanding of the pathophysiology and hemodynamic changes of arterial hypertension and demonstrate that early diagnosis and treatment of hemodynamic characteristics have a positive impact on patient outcomes, reducing morbidity and mortality associated with high blood pressure.

Author contributions

Conception and design of the research: Leão RN, Silva PM. Acquisition of data: Leão RN, Silva PM. Analysis and interpretation of the data: Leão RN, Silva PM. Writing of the manuscript: Leão RN, Silva PM. Critical revision of the manuscript for intellectual content: Leão RN, Silva PM. Supervision / as the major investigator: Leão RN.

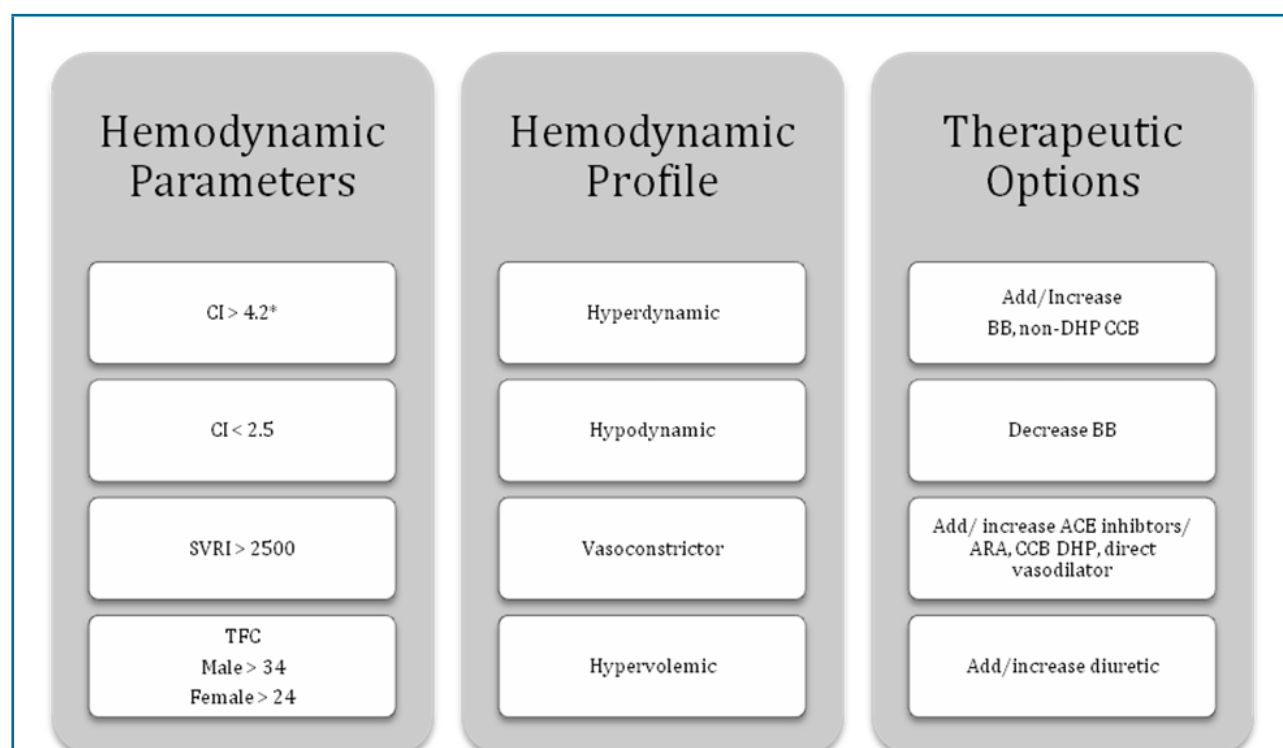


Figure 4 - Algorithm for choice of antihypertensive therapy guided by impedance cardiography. If the values do not correspond to the exposed criteria, the patient has a balanced profile. *If neither the cardiac index (CI) nor the systemic vascular resistance index (SVRI) are high, the therapy should be selected according to the highest parameter, within the normal range. TFC: total fluid content; BB: beta-blocker; DHP: dihydropyridine; CCB: calcium channel blocker; ACE inhibitors: angiotensin-converting enzyme inhibitor; ARA: angiotensin II receptor antagonist.

Table 2 - Main clinical trials on hemodynamically-guided antihypertensive therapy

Author	n	Study design	Results
Smith et al. ⁴⁴	164	Multicenter, randomized	After 3 months, a higher reduction in blood pressure was observed in the treatment group guided by ICG, 55% vs. 27%; OR 2.32 (1.27-5.35), p = 0.007
Taler et al. ⁴⁵	104	Single-center, randomized	After 3 months, 56% of the individuals in the ICG-based approach to hypertension achieved blood pressure < 140/90 mmHg vs. 18 (33%); OR 2.55 (1.15-5.64); p = 0.02
Sramek et al. ⁵⁴	322	Single-center prospective, non-randomized	After 3 weeks of ICG-based therapy, 63% of patients became normotensive; success rate of 58-68%
Sharman et al. ⁵⁵	21	Single-center, prospective, non-randomized	After 7 months, 57% of patients with resistant hypertension had BP control (blood pressure <140/90 mmHg); p < 0.001
Krzesinski et al. ⁵⁶	82	Single-center, randomized	After 3 months, more patients in the ICG-guided group achieved BP control in both ABPM (23.5 vs. 43.9%, p = 0.117) and OBPM (23.5 vs. 36.6%, p = 0.22)
Krzesinski et al. ⁵⁷	128	Single-center, randomized	After 3 months, all blood pressure values were lower in the ICG-guided treatment group, with statistical significance in OBPM and nocturnal blood pressure (p < 0.05)
Krzesinski et al. ⁵⁸	272	Single-center, randomized	After 3 months, final BP values were significantly lower in the ICG-guided treatment group for OBPM (p = 0.01), especially in patients with higher blood pressure (p = 0.003)
Krzesinski et al. ⁵⁹	144	Single-center, randomized	After 12 months, the final blood pressure values were lower in the ICG-guided treatment group, with a BP reduction of at least 20 mmHg in the office measurements of diastolic pressure (27.3% vs. 12.1%; = 0.034), 24-hour mean systolic blood pressure (49.1% vs. 27.3%, p = 0.013) and improvement in left ventricular diastolic dysfunction (delta E/A 0.34 vs. 0.12; = 0.017).

ICG: impedance cardiography; OR: odds ratio; ABPM, ambulatory blood pressure monitoring; OBPM, office blood pressure measurement.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This article is part of the thesis of Doctoral submitted by Rodrigo Nazário Leão, from Universidade Nova de Lisboa.

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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