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Electrophysiological Effects of Selective Atrial Coronary Artery Occlusion in Humans

Running title: *Álvarez-García et al.; ECG changes in atrial myocardial infarction*

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Abstract

***Background*—**The arrhythmogenesis of ventricular myocardial ischemia has been extensively studied, but models of atrial ischemia in humans are lacking. This study aimed at describing the electrophysiological alterations induced by acute atrial ischemia secondary to atrial coronary branch occlusion during elective coronary angioplasty.

***Methods and Results*—**Clinical data, 12-lead ECG, 12-hours Holter recordings, coronary angiography, and serial plasma levels of high sensitivity troponin T and mid-regional proatrial natriuretic peptide were prospectively analyzed in 109 patients undergoing elective angioplasty of right or circumflex coronary arteries. Atrial coronary branches were identified and after the procedure patients were allocated into two groups: atrial branch occlusion (ABO, n=17) and atrial branch patency (non-ABO, n=92). As compared with the non-ABO, patients with ABO showed: a) higher incidence of periprocedural myocardial infarction (20% vs. 53%, p= 0.01); b) more frequent intra-atrial conduction delay (19% vs. 46%, p=0.03); c) more marked PR segment deviation in the Holter recordings; and d) higher incidence of atrial tachycardia (15% vs. 41%, p=0.02) and atrial fibrillation (0% vs. 12%, p=0.03). After adjustment by a propensity score, ABO was an independent predictor of periprocedural infarction (OR 3.4, CI 1.01-11.6, p<0.05) and atrial arrhythmias (OR 5.1, CI 1.2-20.5, p=0.02).

***Conclusions*—**Selective atrial coronary artery occlusion during elective PTCA is associated with myocardial ischemic damage, atrial arrhythmias, and intra-atrial conduction delay. Our data suggest that atrial ischemic episodes might be considered as a potential cause of atrial fibrillation in patients with chronic coronary artery disease.

Key words: atrial coronary artery occlusion, percutaneous transluminal coronary angioplasty, periprocedural myocardial infarction, PR segment deviation, intra-atrial conduction delay, atrial fibrillation.

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Background

As compared with the well documented arrhythmogenic potential of acute ventricular myocardial ischemia [1], less is known about the electrophysiological alterations induced by selective ischemia at the atrial myocardial level. In clinical practice, atrial myocardial ischemia often coexists with ischemia at the ventricular myocardium in patients with acute coronary artery occlusion and, therefore, the distinctive effects of ischemia at either of the two levels cannot be ascertained. It is accepted that the occurrence of atrial fibrillation (AF) in patients with ST-segment elevation myocardial infarction reflects extensive myocardial ischemia involving the atrial chambers [2]. However, a direct link between atrial myocardial ischemia and AF has been only demonstrated in experimental animal models submitted to selective occlusion of atrial coronary branches [3–6]. These studies revealed that atrial ischemia induced local atrial conduction slowing and favored the electrical induction and maintenance of AF.

Considering the fact that the atrial coronary branches emerge from the right and/or circumflex coronary arteries, percutaneous transluminal coronary angioplasty (PTCA) directed to these arteries may result in accidental occlusion of the atrial branches and, therefore, this event may emerge as a potential clinical model for the study of selective acute atrial ischemia in humans. Although the incidence of atrial side branch occlusion (ABO) was found about 21.5% in a retrospective analysis in our institution [7], the clinical and electrophysiological consequences of this complication have not yet been described.

The aim of this study was to prospectively analyze the electrocardiographic changes and arrhythmogenic potential of selective acute atrial myocardial ischemia in humans and, moreover, the clinical and biochemical consequences of accidental ABO during elective PTCA.

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Methods

Study design

We conducted a prospective cohort study which included consecutively all patients undergoing elective PTCA of the right or circumflex coronary artery in our institution since December 2010 to March 2014. The inclusion criteria were: a) presence of sinus rhythm on the admission electrocardiogram (ECG), b) need to deploy the stent in a coronary segment encompassing the exit of an atrial coronary artery, or in a close proximity (≤5 mm) of the origin of an atrial branch assessed by Quantitative Coronary Assessment (QCA) software (Philips Allura Xper FD 10). The exclusion criteria were: a) patients with acute coronary syndrome, b) previous history of atrial arrhythmias, and c) concurrent occlusion of coronary ventricular side-branch at the end of PTCA. All patients had to fulfill the inclusion and none of the exclusion criteria. The study was approved by the Ethics committee of our institution and all patients gave written consent prior to the coronary intervention.

Study protocol

The patients were admitted to the hospital in a stable clinical condition. In all cases the clinical history, physical examination, 12-lead ECG, blood tests including high sensitivity cardiac troponin T (hs-cTnT) (Elecsys, Roche Diagnostics©), and mid-regional proatrial natriuretic peptide (MR-proANP) (ThermoFisher Scientific©) were collected prior and after PTCA. At the end of the coronary intervention, patients were allocated into two groups according to the post PTCA atrial branch patency. The ABO group included those patients in whom the coronary artery flow in the atrial branch assessed by TIMI score [8] fell from grades 2–3 to grades 0–1 after the procedure. The non-ABO group consisted of those patients in whom the baseline TIMI in the atrial branch was normal and did not change after PTCA. Cardiac rhythm was continuously

monitored during 12 hours in all patients starting in the catheterization laboratory immediately after the PTCA intervention using a Holter DigiTrak Plus Recorder (Philips Medical Systems, Bothell, USA). During this recording period, the patients remained at rest in the recumbent position in the ward. Serial plasma levels of hs-cTnT and MR-proANP were also measured at 2-, 4-, 8- and 12-hours after angioplasty, and the 99th reference percentile used for hs-cTnT was 14 ng/L. A second 12-lead ECG was collected prior to hospital discharge.

Angiographic analysis

Coronary angiography was reviewed by two interventional cardiologists. All frames were calibrated with the tip of the catheter as a reference guide before contrast injection. Two orthogonal projections were used prior and after PTCA. In each coronary artery segment, we measured the luminal diameter and the percentage of stenosis using the QCA software. The coronary arterial blood flow was qualitatively evaluated using the TIMI score [8]. We also evaluated the length of the coronary lesion and the plaque characteristics according to the American College of Cardiology/American Heart Association (ACC/AHA) classification [9]. In each atrial coronary artery, we specifically analyzed the presence of atherosclerotic plaques, the maximal luminal diameter, and the TIMI flow before and after PTCA. To define the spatial relationship between the location of the target atherosclerotic plaques for PTCA and the site of origin of the atrial branch, we followed the Medina's classification [10]. We also registered the type of vascular access, the indication for angioplasty, the characteristics of the implanted stent, and all technical procedures related with PTCA.

ECG and Holter analysis

Variables collected from the conventional ECG include the duration of the P wave, PR interval, and QRS complex. The ECG tracings were digitized and the parameters were measured with

electronic calipers (Cardio-Calipers software, Iconico©) under appropriate image magnification. Intra-atrial conduction delay was defined by the presence of a P wave duration ≥ 120 milliseconds, usually with a bimodal or biphasic shape in leads II, III, or aVF [11]. Furthermore, we analyzed the P wave morphology and PR segment displacement during two epochs (the first and last ten minutes in each 12-hour Holter recording), using signal averaging techniques to attain low noise level. From each epoch an averaged beat was obtained from a 3-minute block using conventional ensemble averaging of the normal sinus beats. Signal-averaging procedure and ECG delineation was performed using the software developed by the Signal Processing Group, Lund University, Sweden [12,13]. This algorithm allows calculation of the deviation of the PR segment with respect to the TP segment (isoelectric line) taking a set of 20 points that are part of the TP-segment and selecting the median potential as reference level.

The ECG and Holter recordings were blindly examined by two investigators. In case of doubt, a third senior investigator reviewed the studies.

Statistical analysis

Categorical variables were described by frequencies and percentages and statistical differences were analyzed using the χ^2 test or Fisher´s exact test when any expected cell frequency was <5. Continuous variables were described by the mean and standard deviation and statistical differences were analyzed using the Student's t test in the case of a normal distribution. To evaluate the effect of ABO to predict the presence of myocardial infarction related with PTCA and atrial arrhythmias in the Holter study, a multivariable logistic regression model was performed adjusting for a propensity score including the covariates statistically significant at the univariable analysis (p value less than 0.20 as a criterion of entry into multivariable analysis). Periprocedural myocardial infarction was defined according to the current criteria of the third

universal definition of myocardial infarction [14]. To assess the predictive ability of our model, we calculated the area under the receiver operating characteristics curve assuming a nonparametric distribution. A p value of less than 0.05 was considered statistically significant. For all calculations we used the software SPSS (IBM, 22 version).

Results

From a total number of 3,306 patients submitted to PTCA between December 2010 and March 2014 in our institution, 109 fulfilled the inclusion criteria and entered in the analysis. The flow-chart study is shown in Figure 1.

Clinical characteristics of the study population

Accidental ABO after elective PTCA occurred in 17 (15.6%) out of 109 patients. Table 1 summarizes the clinical characteristics of the study population. There were no significant clinical differences between the two study groups. Specifically, the prevalence of previous myocardial infarction and the need for PTCA or coronary bypass surgery were comparable among patients with and without atrial branch occlusion. Figure 2 illustrates an example of post PTCA occlusion of an atrial coronary artery occlusion arising from the right coronary artery.

Angiographic and intervention procedural findings

Atrial coronary arteries arose from both right and circumflex coronary arteries in at least 98% of patients. The atrial branches supplying the sinus atrial node and the atrio-ventricular node originated in most instances from the right coronary artery (57% and 88%, respectively). Among the 17 patients with occluded branches, these exited the circumflex coronary artery in 2 cases and the right coronary artery in 15 patients. The average sizes of the atrial branch in the ABO and non-ABO group were 1.25 and 1.41 mm, respectively. There were no significant differences

between both groups in any of previous variables. However, the ABO group presented more frequently atherosclerotic plaques at the ostium of atrial branch than non-ABO group (77 vs. 23%, p<0.01). The presence of a bifurcation lesion and a longer length of the stent were significantly more common in ABO patients than in the group without the loss of atrial artery. Table 2 shows the remaining angiographic and PTCA procedural characteristics of the study population.

Plasma biomarkers

Figure 3A illustrates the time course of plasma concentrations of hs-cTnT in both groups of patients. Patients with ABO depicted significantly higher values in the samples obtained after 8 hours of PTCA, thus reflecting myocardial damage. According to these data, the incidence of periprocedural myocardial infarction was significantly higher in the group with ABO (53% vs. 20%, p= 0.01). After adjustment by the propensity score including all significant variables of the Table 2, the occurrence of ABO was an independent predictor of periprocedural infarction (OR 3.4, 95%CI 1.01-11.6, p<0.05).

The time course of plasma levels of MR-proANP after coronary intervention is shown in the Figure 3B. In both groups the PTCA was followed by a release of the natriopeptide during the first 4 hours after the intervention. Moreover, both curves showed a parallel trend, with higher values in the ABO than in the non-ABO group, although this difference was not statistically significant (MR-proANP peak: 204 pmol/L vs. 164 pmol/L; p= 0.195).

ECG and Holter findings

As summarized in Table 3, analysis of the 12-lead ECG showed that both groups of patients had an increase in the duration of the P wave after PTCA, but the new onset intra-atrial conduction delay was almost three times more frequent in the ABO group (Figure 4A). Of notice, new ST-

segment changes or Q-waves were not observed in any case. The 12-hour Holter recording (Table 4) showed that ABO patients presented atrial arrhythmia and atrial fibrillation episodes more frequently than patients without ABO (Figure 4B). The episodes of atrial arrhythmia consisted of about 3 to 20 ectopic beats with a mean frequency of 125 beats per minute. The episodes of atrial fibrillation in the two ABO patients lasted less than 10 seconds and reverted spontaneously to sinus rhythm. Electrical cardioversion was not required in any patient After adjustment by the propensity score including the same significant variables of Table 2, ABO was also an independent predictor of the presence of atrial arrhythmias (OR 5.1, 95%CI 1.2-20.5, p=0.02). During the Holter recording, 8 patients presented self-limited episodes of monomorphic ventricular tachycardia (3 in the ABO group and 5 in the non-ABO group, p=0.076). However, 3 in the ABO group and 4 in the non-ABO group have already previous history of episodes of non-sustained monomorphic ventricular tachycardia. Signal averaging analysis revealed that patients with ABO had a significant PR deviation that was maximal during the first 10 minutes of the study and declined thereafter progressively (Figure 4C). Moreover, the amplitude of the P wave was smaller in patients with ABO (Figure 4D).

Discussion

Main findings

This is the first study analyzing prospectively the electrophysiological alterations induced by acute atrial infarction in humans. As a clinical model of atrial myocardial ischemia we recruited patients presenting selective occlusion of atrial coronary arterial branches during elective PTCA. Compared to patients with patent atrial vessels, patients with ABO presented a plasma hs-cTnT pattern of periprocedural myocardial infarction associated with higher incidence of interatrial

conduction disturbances, PR segment deviation, and episodes of atrial tachycardia and atrial fibrillation.

Electrophysiological effects of atrial myocardial ischemia

The local electrophysiological derangements induced by atrial myocardial ischemia have not been directly investigated in humans and only electrocardiographic abnormalities bounded to the morphology of the P wave and to the position of the PR segment (P-Ta segment) over the isoelectric line have been reported [15,16]. Direct characterization of the atrial ischemic electrophysiological substrate has been attempted in a restricted number of experimental studies in animals submitted to selective ligature of atrial coronary arterial branches [3–6]. In these experimental models mapping of local electrograms over the atrial surface revealed a significant slowing of local conduction in the ischemic zone creating conditions for increased inducibility and maintenance of atrial fibrillation [3,5]. The local conduction delay will therefore explain the changes in the duration and shape of the P wave in our patients with atrial branch occlusion. The ischemic etiology of interatrial conduction disturbances was indirectly suggested in a previous study in 27 coronary atherosclerotic patients with established interatrial block who presented a higher incidence of right coronary involvement than 42 control patients without conduction delay [17]. Slowing of local conduction and propensity to reentrant arrhythmias are, on the other hand, classical features observed during acute ischemia at the ventricular myocardium [1]. Deviation of the PR segment was formerly described in single case reports of atrial infarction [18] and a systematic analysis of the ECG patterns was later compiled by Liu et al [19]. Understanding of the PR segment deviation is founded on the concept that local atrial action potential repolarization occurs at the time of the inscription of the PR segment in the ECG as denoted when simultaneous recording of atrial monophasic potentials and conventional ECG leads are taken in humans [20].

Consequently, the local ST segment elevation that is induced by atrial injury is in fact indirectly represented in the ECG as a displacement of the PR segment [21]. The location of the atrial ischemic area may influence the pattern of ST segment behavior in the different ECG leads and ultimately, may determine the positive or negative deviation of the PR segment. In the dog heart, selective injury in left atrial segments elicited positive PR deviation in leads I, aVL and negative displacement in leads II,III, and aVF whereas an opposite pattern was observed in dogs with right atrial injury [21].

It is widely accepted that the occurrence of atrial fibrillation in patients with ST-segment elevation myocardial infarction denotes extensive myocardial ischemia involving the atrial chambers [2] but in the acute phase of myocardial infarction an associated hyperadrenergic nerve tone [22] or an increase of atrial filling pressures might also play a role [23]. Thus a relevant contribution of our study is the proof of concept that atrial infarction is *per se* a cause of atrial arrhythmias in men. Considering the fact that atrial infarction is rarely recognized ante mortem, our data would support the assumption that clinically silent episodes of atrial coronary branch occlusion should be considered as a cause of atrial fibrillation in patients with chronic coronary artery disease.

Accidental atrial coronary artery occlusion

This study shows that about 15% of patients undergoing elective PTCA of the right or circumflex coronary arteries are at risk of presenting accidental occlusion of coronary atrial branches. Despite this notorious incidence, the clinical consequences of atrial branch occlusion have not been prospectively investigated and this complication is often disregarded in the PTCA procedural clinical reports. Our results are the first showing that the accidental occlusion of atrial branches should far from be considered an uneventful complication because it causes structural

myocardial damage denoted by the rise of plasma hs-cTn levels and it favors atrial arrhythmogenesis. Moreover, we identified the presence of atherosclerotic plaques at the ostium of atrial branches, the bifurcated lesions, and the need for implanting longer stents as independent predictors of the accidental atrial vessel occlusion. Thus, new technical measures aimed to protect the patency of atrial branches should be implemented in patients undergoing elective PTCA of right of circumflex coronary arteries, as occurred in the field of SBO prevention [24].

Considerations on the model

Due to the relatively small sample size and modest event frequencies, the results of our study should be interpreted cautiously.

The accidental occlusion of an atrial coronary branch offers the opportunity to selectively investigate the pathophysiology of atrial myocardial ischemia provided the absence of concurrent ischemia at the ventricular level. Consequently, we did not include patients presenting simultaneous accidental occlusion of both ventricular and atrial coronary branches.

In our study, the diagnosis of atrial coronary occlusion was based on the coronary angiography performed just at the end of the PTCA procedure and therefore a later spontaneous reperfusion of the atrial vessel cannot be entirely discarded. To rule out this possibility a second follow-up angiography would be required but at present time, this procedure is not justified because the current guidelines for percutaneous coronary interventions do not take into consideration the accidental occlusion of atrial branches during elective PTCA.

Since about half of our patients had suffered previous myocardial infarction, they might have developed collaterals in the ventricular but also possibly in the atrial myocardium. These circumstances could influence the size of atrial infarction resulting from the atrial branch

occlusion [25]. However, the prevalence of previous myocardial infarction and the need for PTCA or coronary bypass surgery were comparable in the two groups of patients, suggesting that the likelihood to develop coronary collaterals would have been similar in patients with and without atrial coronary branch occlusion.

We studied atrial electrophysiological derangements over a 12-hour period in patients undergoing elective PTCA and therefore knowledge of the long-term impact of these findings would require further specific follow-up studies.

Conclusions

As a new study model of atrial ischemic injury, we found that selective atrial coronary artery occlusion during elective PTCA is associated with myocardial ischemic damage, atrial arrhythmias, and interatrial conduction delay. These data support the assumption that atrial ischemic episodes might be a potential cause of atrial fibrillation in patients with chronic coronary artery disease.

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Conflict of Interest Disclosures: None.

References:

1. Cinca J, Janse MJ, Moréna H, Candell J, Valle V, Durrer D. Mechanism and time course of the early electrical changes during acute coronary artery occlusion. An attempt to correlate the early ECG changes in man to the cellular electrophysiology in the pig. *Chest*. 1980;77:499–505.

2. Lazar EJ, Goldberger J, Peled H, Sherman M, Frishman WH. Atrial infarction: diagnosis and management. *Am Heart J*. 1988;116:1058–1063.

3. Sinno H, Derakhchan K, Libersan D, Merhi Y, Leung TK, Nattel S. Atrial ischemia promotes atrial fibrillation in dogs. *Circulation*. 2003;107:1930–1936.

4. Yamazaki M, Morgenstern S, Klos M, Campbell K, Buerkel D, Kalifa J. Left atrial coronary perfusion territories in isolated sheep hearts: implications for atrial fibrillation maintenance. *Heart Rhythm*. 2010;7:1501–1508.

5. Nishida K, Qi XY, Wakili R, Comtois P, Chartier D, Harada M, Iwasaki Y, Romeo P, Maguy A, Dobrev D, Michael G, Talajic M, Nattel S. Mechanisms of atrial tachyarrhythmias associated with coronary artery occlusion in a chronic canine model. *Circulation*. 2011;123:137–146.

6. Alasady M, Shipp NJ, Brooks AG, Lim HS, Lau DH, Barlow D, Kuklik P, Worthley MI, Roberts-Thomson KC, Saint DA, Abhayaratna W, Sanders P. Myocardial infarction and atrial fibrillation: importance of atrial ischemia. *Circ Arrhythm Electrophysiol*. 2013;6:738–745.

7. Álvarez-García J, Vives-Borrás M, Ferrero A, Aizpurua DA, Peñaranda AS, Cinca J. Atrial coronary artery occlusion during elective percutaneous coronary angioplasty. *Cardiovasc Revasc Med*. 2013;14:270–274.

8. The Thrombolysis in Myocardial Infarction (TIMI) trial. Phase I findings. TIMI Study Group. *N Engl J Med*. 1985;312:932–936.

9. Ryan TJ, Faxon DP, Gunnar RM, Kennedy JW, King SB, Loop FD, Peterson KL, Reeves TJ, Williams DO, Winters WL. Guidelines for percutaneous transluminal coronary angioplasty. A report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Translu. *Circulation*. 1988;78:486–502.

10. Medina A, Suárez de Lezo J, Pan M. A new classification of coronary bifurcation lesions. *Rev española Cardiol*. 2006;59:183.

11. Bayés de Luna A, Platonov P, Cosio FG, Cygankiewicz I, Pastore C, Baranowski R, Bayés-Genis A, Guindo J, Viñolas X, Garcia-Niebla J, Barbosa R, Stern S, Spodick D. Interatrial blocks. A separate entity from left atrial enlargement: a consensus report. *J Electrocardiol*. 2012;45:445–451.

12. Pahlm O, Sörnmo L. Data processing of exercise ECG's. *IEEE Trans Biomed Eng*. 1987;34:158–165.

13. Pettersson J, Pahlm O, Carro E, Edenbrandt L, Ringborn M, Sörnmo L, Warren SG, Wagner GS. Changes in high-frequency QRS components are more sensitive than ST-segment deviation for detecting acute coronary artery occlusion. *J Am Coll Cardiol*. 2000;36:1827–1834.

14. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Katus HA, Apple FS, Lindahl B, Morrow DA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow JJ, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky

BF, Steg PG, Wijns W, Bassand J-P, Menasche P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker R V, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon J-L, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S, Baumgartner H, Ceconi C, Dean V, Deaton C, Fagard R, Funck-Brentano C, Hasdai D, Hoes A, Kirchhof P, Knuuti J, Kolh P, McDonagh T, Moulin C, Popescu BA, Reiner Z, Sechtem U, Sirnes PA, Torbicki A, Vahanian A, Windecker S, Morais J, Aguiar C, Almahmeed W, Arnar DO, Barili F, Bloch KD, Bolger AF, Botker HE, Bozkurt B, Bugiardini R, Cannon C, de Lemos J, Eberli FR, Escobar E, Hlatky M, James S, Kern KB, Moliterno DJ, Mueller C, Neskovic AN, Pieske BM, Schulman SP, Storey RF, Taubert KA, Vranckx P, Wagner DR. Third universal definition of myocardial infarction. *J Am Coll Cardiol*. 2012;60:1581–1598.

15. Cushing EH, Feil HS, Stanton EJ, Wartman WB. Infarction of the cardiac auricles (atria): clinical, pathological, and eperimental studies. *Br Heart J*. 1942;4:17–34.

16. Hellerstein HK. Atrial infarction with diagnostic electrocardiographic findings. *Am Heart J*. 1948;36:422–430.

17. Ariyarajah V, Fernandes J, Apiyasawat S, Spodick DH. Angiographic localization of potential culprit coronary arteries in patients with interatrial block following a positive exercise tolerance test. *Am J Cardiol*. 2007;99:58–61.

18. Langendorf R. Elektrokardiogramm bei Vorhof-Infarkt. *Acta Med Scand*. 1939;100:136–149.

19. Liu CK, Greenspan G, Piccirillo RT. Atrial infarction of the heart. *Circulation*. 1961;23:331–338.

20. Olsson SB. Atrial repolarization in man Effect of beta-receptor blockade. *Br Heart J*. 1974;36:806–810.

21. Kamae M. Electrocardiographic studies on experimental atrial injury in dogs. *Jpn Circ J*. 1965;29:1053–1062.

22. DeSanctis RW, Block P, Hutter AM. Tachyarrhythmias in myocardial infarction. *Circulation*. 1972;45:681–702.

23. Kobayashi Y, Katoh T, Takano T, Hayakawa H. Paroxysmal atrial fibrillation and flutter associated with acute myocardial infarction: hemodynamic evaluation in relation to the development of arrhythmias and prognosis. *Jpn Circ J*. 1992;56:1–11.

24. Depta JP, Patel Y, Patel JS, Novak E, Yeung M, Zajarias A, Kurz HI, Lasala JM, Bach RG, Singh J. Long-term clinical outcomes with the use of a modified provisional jailed-balloon stenting technique for the treatment of nonleft main coronary bifurcation lesions. *Catheter Cardiovasc Interv*. 2013;82:E637–646.

25. James TN. Complex causes of fatal myocardial infarction. *Circulation*. 1997;96:1696–1700.

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Clinical Perspective

We handled the accidental occlusion of atrial coronary arteries during elective percutaneous coronary intervention as a prospective clinical model for the study of the electrophysiological effects of acute atrial myocardial infarction. Patients with selective atrial branch occlusion depicted a troponin rise pattern of infarction associated with higher incidence of interatrial conduction delay, PR segment deviation, atrial tachycardia and atrial fibrillation on 12-h Holter recording than patients free of this complication. Atherosclerosis of atrial coronary arteries was more frequent in patients of the atrial branch occlusion group. Our study afforded a proof of concept that acute atrial ischemia *per se* promotes atrial arrhythmias in humans and supported the assumption that clinically silent occlusion of atrial branches might be a cause of atrial fibrillation in patients with chronic coronary heart disease. Moreover, technical measures to protect the patency of atrial coronary arteries should be implemented in patients submitted to percutaneous interventionism over the right or circumflex coronary arteries.

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Table 1. Clinical characteristics of the study population.

	Patients with ABO (n=17)	Patients without ABO (n=92)	p value
Age, years, $\bar{x}$ (SD)	63.6 (11.8)	66.0 (10.3)	0.39
Male, n (%)	13 (77)	72 (78)	1.00
Smokers, n (%)	4 (24)	20 (22)	0.40
Hypertension, n (%)	12 (71)	72 (78)	0.53
Dyslipemia, n (%)	16 (94)	70 (76)	0.12
Diabetes mellitus, n (%)	8 (47)	36 (39)	0.54
Previous MI, n (%)	8 (47)	37 (40)	0.56
Previous PTCA, n (%)	8 (47)	45 (49)	0.89
Previous CABG, n (%)	2 (12)	9 (10)	0.68
LVEF, %, $\bar{x}$ (SD)	58 (12)	58 (10)	0.98
eGFR<60mL/min/1.73m^2,n(%)	2 (12)	10 (11)	1.00
COPD or asthma, n (%)	3 (18)	6 (7)	0.15

*List of abbreviations: ABO: atrial coronary branch occlusion; SD: standard deviation; MI: myocardial infarction; PTCA: percutaneous transluminal coronary angioplasty; CABG: coronary artery bypass grafting; LVEF: left ventricular ejection fraction; eGFR: estimated glomerular filtration rate; COPD: chronic obstructive pulmonary disease.

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Table 2. Coronary angiographic and procedural characteristics.

	Patients with ABO (n=17)	Patients without ABO (n=92)	p value
AB diameter, mm, $\bar{x}$ (SD)	1.25 (0.44)	1.41 (0.45)	0.19
AB ostial atherosclerotic plaque, n (%)	13 (77)	21 (23)	<0.001
ACC/AHA C type, n (%)	7 (41)	27 (29)	0.33
Diameter coronary stenosis, %, $\bar{x}$ (SD)	89 (10)	87 (10)	0.53
Length of coronary lesion, mm, $\bar{x}$ (SD)	30 (12)	29 (18)	0.83
Bifurcation lesion, n (%)	14 (82)	37 (40)	0.001
Predilatation, n (%)	17 (100)	87 (95)	1.00
Max pressure during dilatation, atm, $\bar{x}$ (SD)	17 (2)	17 (3)	0.37
Cutting balloon, n (%)	6 (35)	28 (30)	0.69
Rotational atherectomy, n (%)	1 (6)	7 (8)	1.00
Number of stents implanted, $\bar{x}$ (SD)	1.8 (1.2)	1.4 (0.7)	0.21
Characteristics of index stent			
Length, mm, $\bar{x}$ (SD)	28 (9)	23 (8)	0.021
Diameter, mm, $\bar{x}$ (SD)	3.2 (0.6)	3.0 (0.5)	0.26
DES, n (%)	13 (77)	76 (83)	0.71
Platform, n (%) *Stainless steel* *Cobalt-chrome* *Platinum-chrome* *Absorbable*	 3 (18) 8 (50) 2 (13) 3 (19)	 29 (32) 42 (51) 8 (10) 7 (8)	0.52
Strut diameter, µm, $\bar{x}$ (SD)	85 (5)	84 (16)	0.80
Max pressure during implantation, atm, $\bar{x}$ (SD)	16 (3)	15 (3)	0.16
Postdilatation, n (%)	12 (71)	59 (64)	0.61
Max pressure during dilatation, atm, $\bar{x}$ (SD)	19 (2)	19 (3)	0.76

*List of abbreviations: ABO: atrial coronary branch occlusion; AB: atrial branch; SD: standard deviation; ACC/AHA: American College of Cardiology/American Heart Association; atm: atmosphere; DES: drug eluting stent; µm: micrometers.

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Table 3. ECG findings in the study population.

	Patients with ABO (n=17)			Patients without ABO (n=92)		
	Baseline	**Post-PTCA**	**p value**	**Baseline**	**Post-PTCA**	**p value**
HR, bpm, $\bar{x}$ (SD)	68 (12)	67 (11)	0.79	63 (11)	60 (11)	0.004
P wave duration, ms, $\bar{x}$ (SD)	118 (13)	128 (14)	0.017	119 (15)	122 (15)	0.001
Incident intra-atrial conduction delay, n (%)	6 (46)			12 (19)		0.031
PR interval, ms, $\bar{x}$ (SD)	164 (31)	167 (27)	0.67	172 (25)	178 (30)	0.005
QRS duration, ms, $\bar{x}$ (SD)	90 (15)	92 (17)	0.33	96 (20)	97 (20)	0.28
QTc interval, ms, $\bar{x}$ (SD)	405 (31)	416 (37)	0.18	416 (27)	419 (30)	0.40

*List of abbreviations: ABO: atrial coronary branch occlusion; PTCA: percutaneous transluminal coronary angioplasty; HR: heart rate; bpm: beats per minute; SD: standard deviation; ms: milliseconds.

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Table 4. Electrophysiological findings in the study population.

	Patients with ABO (n=17)	Patients without ABO (n=92)	
12-hours Holter study			
Averaged HR, bpm, $\bar{x}$ (SD)	66 (9)	63 (9)	0.16
ASDNN, $\bar{x}$ (SD)	48.4 (24.6)	47.5 (22.0)	0.87
Advanced AV block, n (%)	2 (12)	1 (1)	0.11
Premature atrial beats, $\bar{x}$ (SD)	99 (216)	48 (98)	0.35
Atrial arrhythmia, n (%)	7 (41)	13 (15)	0.020
Atrial fibrillation, n (%)	2 (12)	0 (0)	0.025
Ventricular tachycardia, n (%)	3 (18)	5 (6)	0.076
Averaged Holter signal analysis			
PR_f-PR_i, μV, $\bar{x}$ (SD)	12 (27)	-0.3 (14)	0.004
P_i wave voltage, μV, $\bar{x}$ (SD)	75 (35)	106 (46)	0.007

*List of abbreviations: ABO: atrial coronary branch occlusion; HR: heart rate; bpm: beats per minute; SD: standard deviation; ASDNN: averaged standard deviation N-N; AV: auricular-ventricular; μV: microvolts.

Figure Legends:

Figure 1. Flow-chart of the study. *List of abbreviations: PTCA: percutaneous transluminal coronary angioplasty.

Figure 2. Atrial coronary branch occlusion during elective percutaneous transluminal coronary angioplasty. Panel A: the arrow indicates an atrial branch (AB) emerging from the proximal segment of right coronary artery (RCA). Panel B: loss of AB (\\) after the stent implantation.

Figure 3. Time course of mean plasma levels of high-sensitivity troponin and mid-regional proatrial natriuretic peptide in the study population. Panel A: The ABO group showed greater values of plasma levels of high sensitivity Troponin T at 8-, 12-, and 24-hours than the non-ABO

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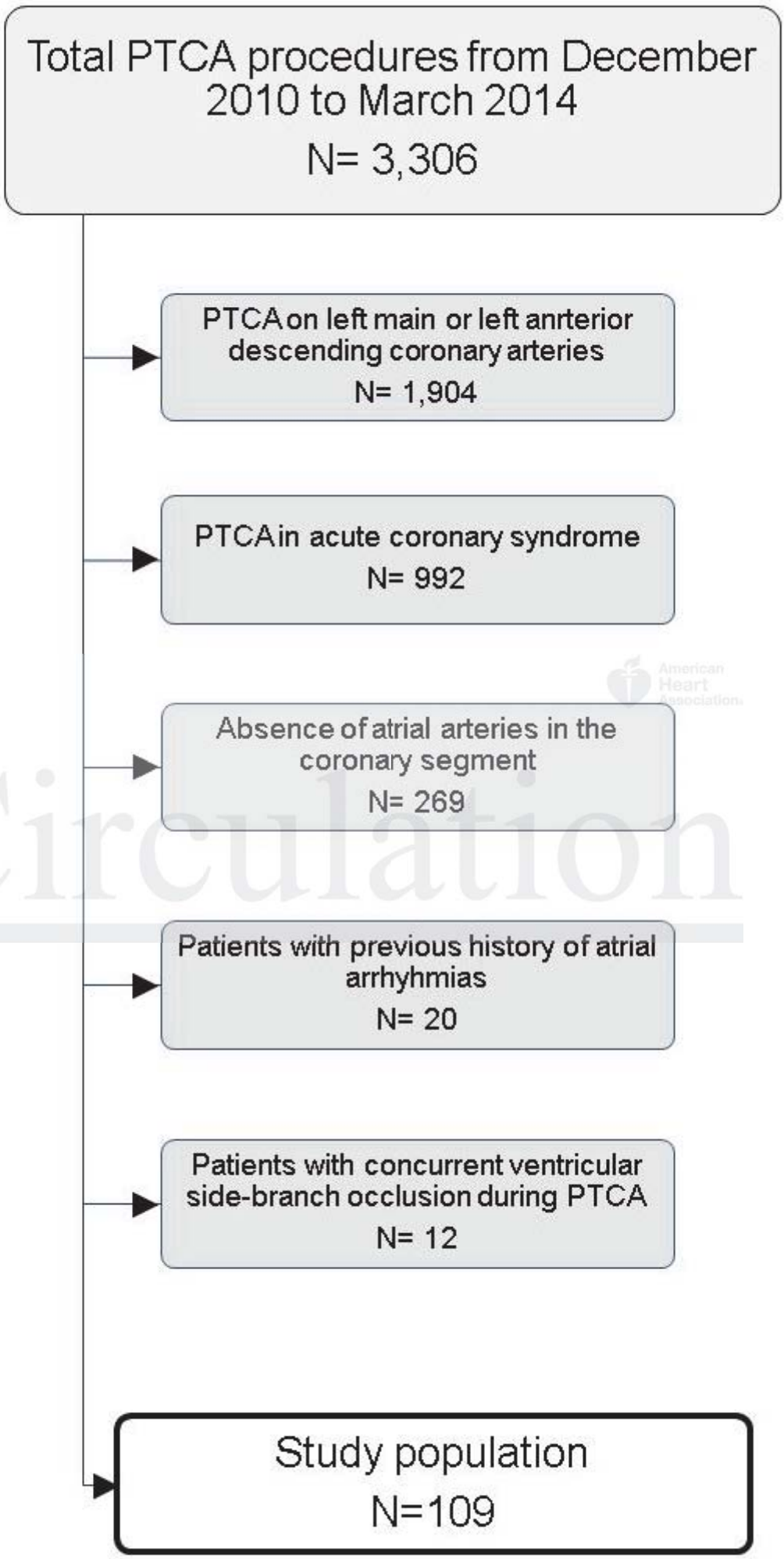
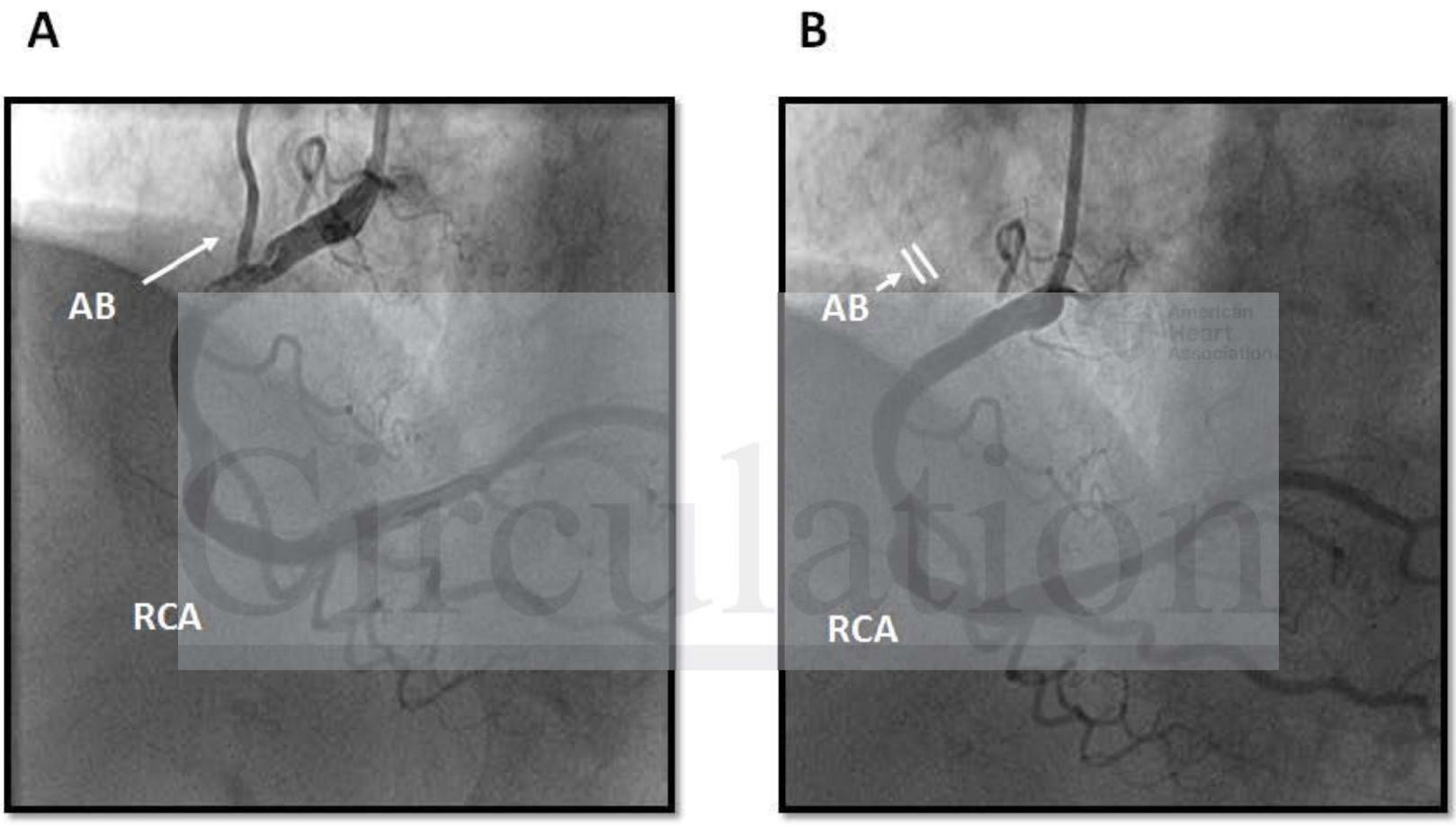
patients. Panel B: Both groups of patients showed parallel plasma level values of mid-regional proAtrial Natriuretic Peptide but with higher values in the ABO group at each time point. *Whiskers represent the standard error of the mean.

Figure 4. Averaged signal analysis of the PR segment displacement in the 12 hours Holter recording in two representative cases. Panel A illustrates an example of intra-atrial conduction delay in a patient of the ABO group. Panel B shows an atrial fibrillation episode recorded in the Holter study of the same patient of ABO group. Panel C1 shows evolving PR segment deviation in a patient of the ABO group. Panel C2 shows the lack of evolving PR segment deviation in a patient of the non-ABO group. Panel D illustrates an example of change of P wave shape in a patient of the ABO group.





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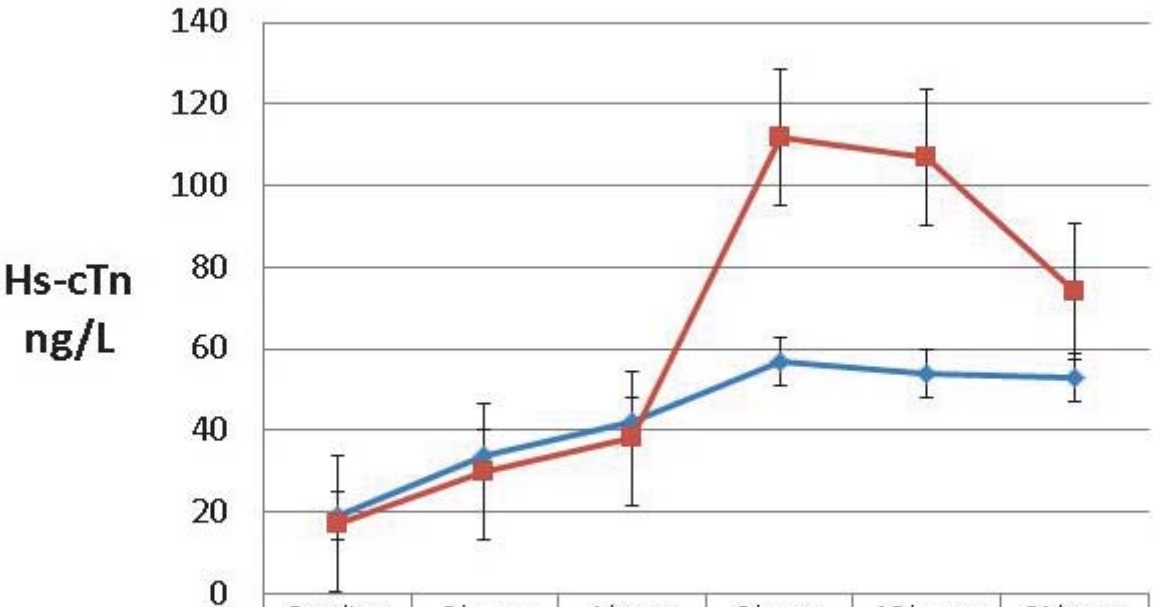
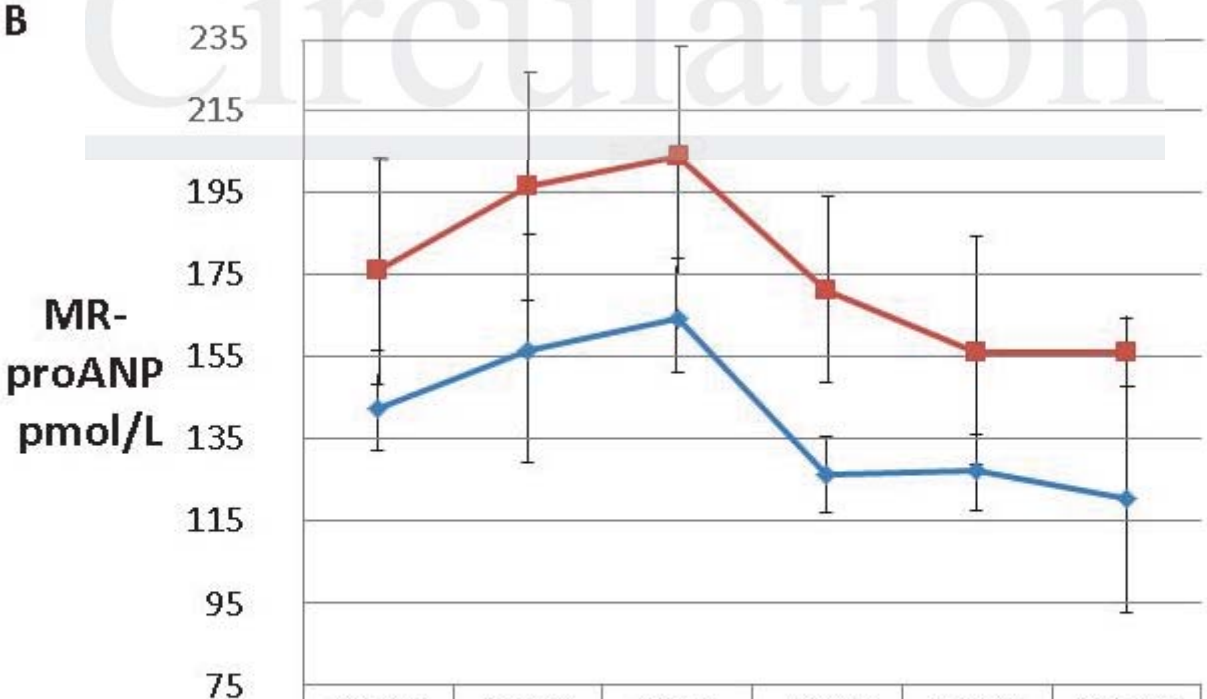
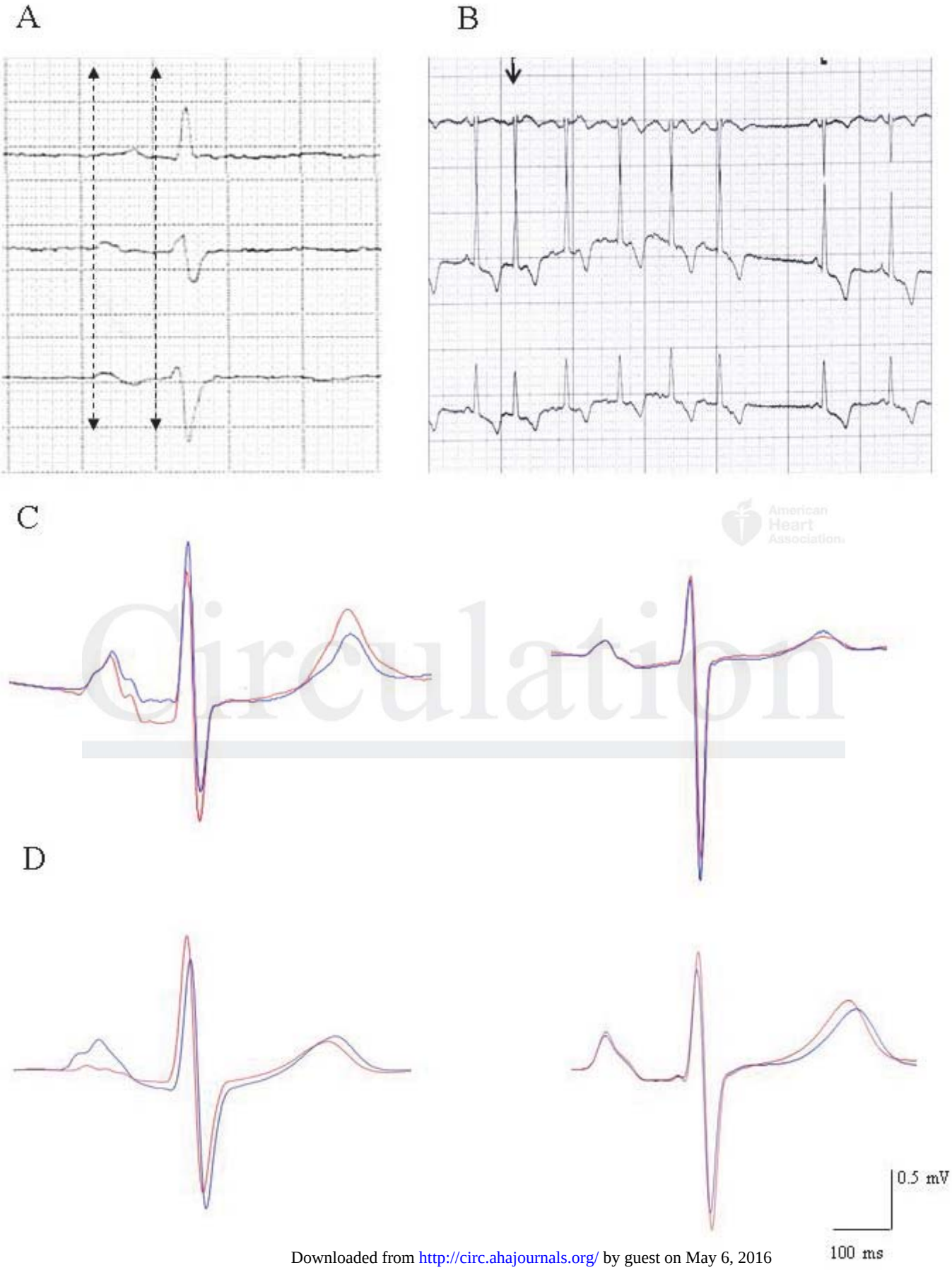


	Baseline	2 hours	4 hours	8 hours	12 hours	24 hours
Non-ABO group	19	34	42	57	54	53
ABO group	17	30	38	112	107	74

B



	Baseline	2 hours	4 hours	8 hours	12 hours	24 hours
Non-ABO group	142	157	164	126	127	120
ABO group	176	196	204	171	156	156



Electrophysiological Effects of Selective Atrial Coronary Artery Occlusion in Humans

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