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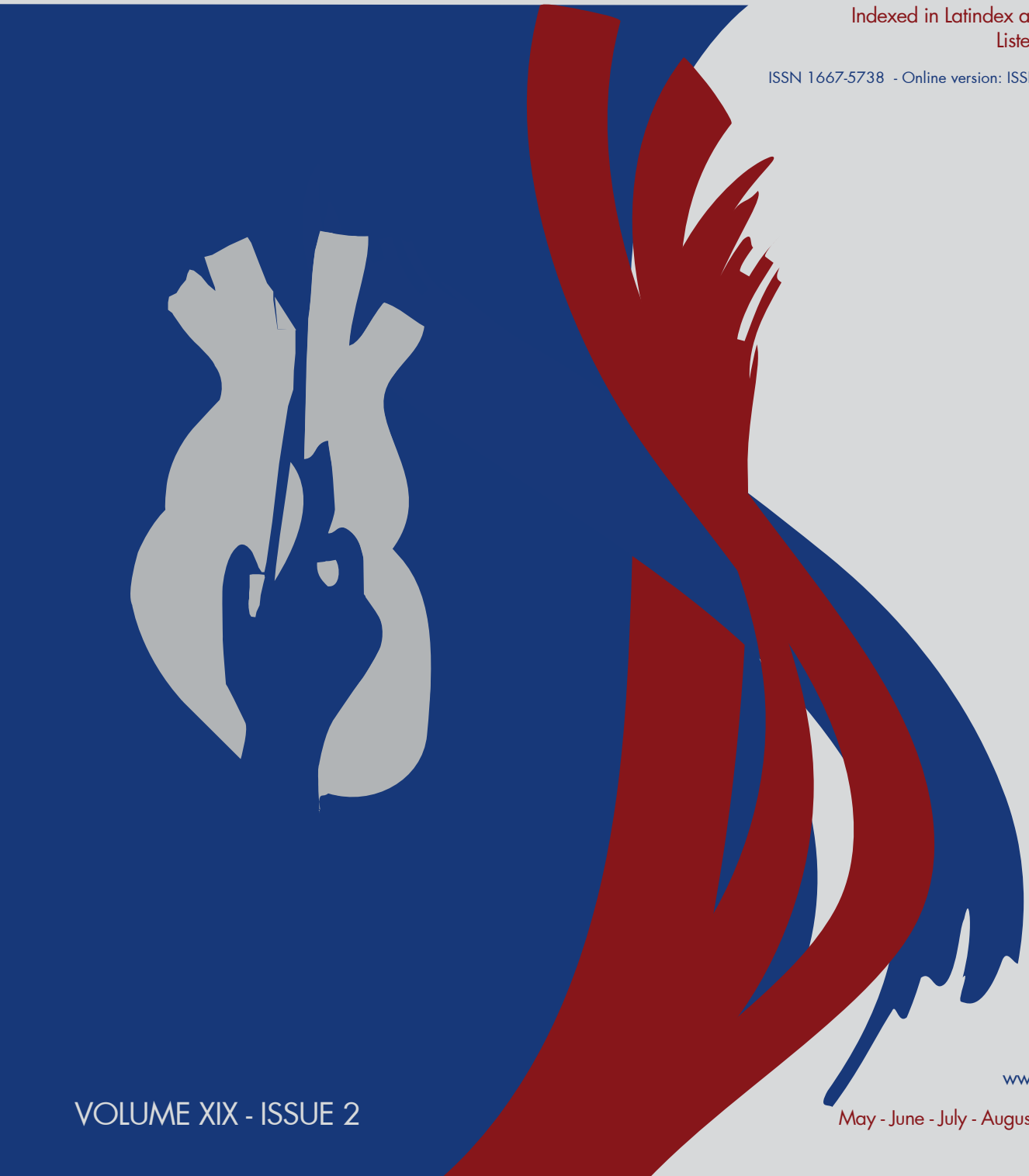

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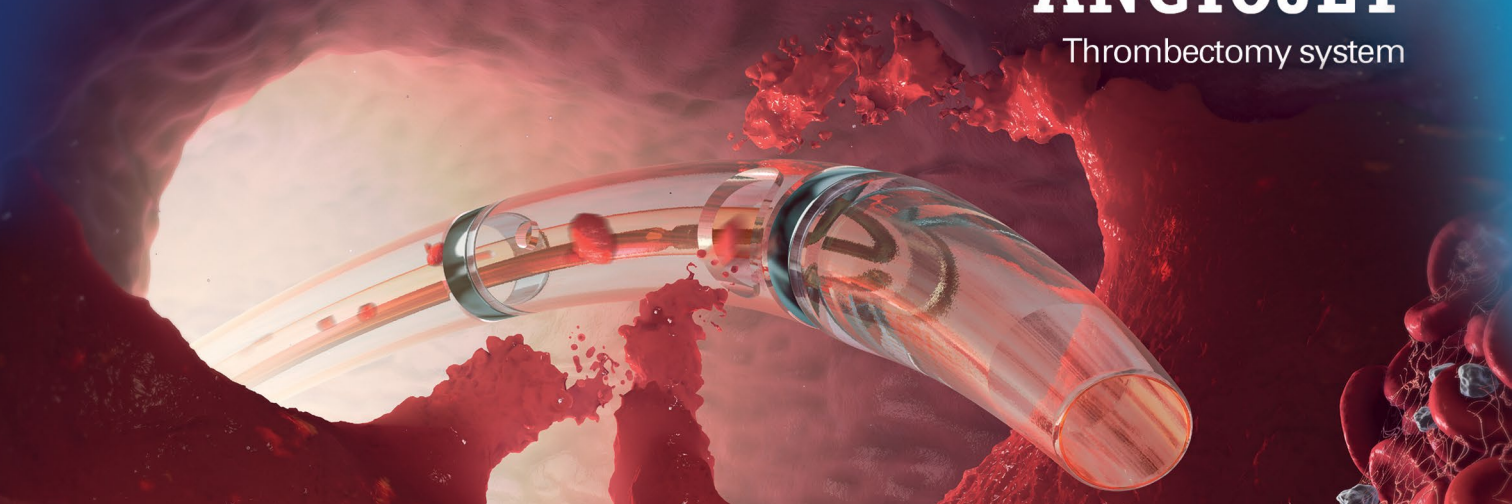

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SUMMARY

ORIGINAL ARTICLE

RISK INDEX TO PREDICT IMMEDIATE MORTALITY IN MYOCARDIAL REVASCULARIZATION SURGERY

ABSTRACT

Introduction: The current trend is to improve the quality of life of patients treated by coronary surgery and reduce complications and resources. **Objectives:** To construct and validate a risk index to predict immediate mortality in myocardial revascularization surgery. **Method:** Development research was carried out in the Cardiovascular Surgery service of the Cardiology Center of Hospital "Hermanos Ameijeiras", from March 2012 to 2017, the sample included 340 patients. The investigation work was divided into two phases, the first one for the construction of the instrument and the second for its validation. **Results:** The logistic regression model had a good calibration given by the Hosmer and Lemeshow analysis (p = 0.914). The final score resulted from multiplying the value of each variable by its weight. The area under the ROC curve for the probability of dying was 0.902 (95% CI: 0.852-0.952). By dividing the calculated probability into three zones, it was observed that the majority of patients with immediate mortality were grouped into high risk. The area under the ROC curve for the quantitative index was 0.869 (95% CI: 0.825–0.913), showing good discrimination. The intraclass correlation coefficient for the probability-based index was 0.966 (95% CI: 0.955-0.975) and for the quantitative index it was 0.935 (95% CI: 0.913-0.952). Conclusions: The index for the prediction of immediate mortality in myocardial revascularization surgery demonstrates validity and reliability that make it a feasible and useful instrument to be applied.

Keywords: *Predictive mortality index, myocardial revascularization surgery, coronary surgery, mortality, risk scale, risk score.*

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INTRODUCTION

Coronary artery disease (CAD) is the first cause of death for cardiovascular diseases worldwide[1]. In the Middle East, Latin America and the Far East, the prevalence of risk factors increases at the same rate of coronary events[2]. In 2019, 16,397 individuals died in Cuba as a result of ischemic cardiopathy[3]. Myocardial revascularization surgery (MRS) is the most common treatment option for ischemic cardiopathy, being the most frequent cardiothoracic intervention[4,5,6]. The Hospital Clínico Quirúrgico Hermanos Ameijeiras has over 50 years of experience in MRS, with over 150 interventions a year[3]. Coronary surgery implies risks, which requires planning to improve quality of life. Creating algorithms to support decision-making seeks the purpose of identifying the populations that can benefit the most[7]. Cardiologists and cardiovascular surgeons can thus predict potential adverse events and mortality related to the surgery. In the past, this risk was estimated in an intuitive and inaccurate way. At present, there are different risk indexes, including: EuroSCORE, SYNTAX, Mayo Clinic Risk Score, Parsonnet, STS and ACEF[8,9,10,11]. The most broadly used indexes are EuroSCORE II and STS, the usefulness of both has been proven in cohorts of patients treated with MRS[12].

Said risk models were not developed in Latin American populations and their application in different populations may lead to less efficiency due to regional differences, with a negative effect in decision-making and in the results of surgical procedures. In 1999 a risk model was developed in Argentina for intrahospital mortality in cardiac surgery, the Argentinean System for Cardiac Operative Risk Evaluation (ArgenSCORE), recalibrated in 2007 and later in 2009. Its application in populations with similar geographic and demographic characteristics as those for which it was developed has shown better performance than the EuroSCORE[13].

All models developed to predict mortality in cardiac surgery have limitations resulting from the specific definitions, the methodology applied, the feasibility of the calculation, the impossibility to reflect all relevant variables in morbidity and mortality or an insufficient external validation. These have been elaborated with specific populations and in different periods of time, with variables selected in contexts that differ from Cuba. Each territory and hospital should determine what scale or index is more appropriate for each specific "reality", which has led to conducting this study with the purpose of elaborating a risk index for the prediction of immediate mortality in myocardial revascularization surgery and validating it.

METHODS

This work has been considered as development research as it consists in the elaboration and validation of a measurement instrument by the Cardiovascular Surgery Department of Hospital Clínico Quirúrgico Hermanos Ameijeiras. Patient data was collected from March 2012 to March 2017; based on such data a score was elaborated from 2019 to January 2021.

Scope: all patients with a diagnosis of ischemic cardiopathy that required surgery and were treated in this hospital, taking into consideration the indications established by the protocol and clinical practice guidelines[14].

Exclusion criteria: patients that could not be followed-up, were not willing to collaborate with the study or required combined surgery.

Sample: 340 patients treated with MRS from March 2012 to March 2017.

The study was conducted in two phases: the first consisted in the elaboration of the instrument, during which two indexes were created, and the second phase consisted in the validation of said indexes.

Phase I: Elaboration of both quantitative indexes

Selection of variables: up-to-date literature was reviewed, including articles in books and specialized journals, Internet and PubMed, Scielo and Hinari data bases. Based on this review an instrument was elaborated with proposed variables that were submitted to the consideration of experts who were to contribute new variables for the proposed index.

A search was conducted in Hinari, Medline and Lilacs in July 2020 to identify authors with experience in cardiovascular surgery, more specifically in MRS, and investigations on prognosis, elaboration, application or validation or risk scores to predict mortality in this group. Contacts were made with expert cardiologists and surgeons of the Cardiology and Cardiovascular Surgery Institute in Havana, the Hospital Clínico Quirúrgico Hermanos Ameijeiras and other cardiology centers in other provinces, all with over 10 years of experience as specialists and researchers. As a result, 45 professionals were identified, including cardiovascular surgeons and cardiologists who, based on published studies and investigations could be rated as experts. Finally, 20 experts accepted to participate in the investigation. There was no discrepancy in the individual criterium of specialists, for which reason it was necessary to reach a consensus through a group discussion.

Upon analyzing the surveys sent to experts, the variables to be considered for the elaboration of the proposed index were the following: age over 70,

sex, hypertension, diabetes Mellitus, recent acute myocardial infarction, angina functional class IV, chronic obstructive pulmonary disease (COPD), extracardiac arteriopathy, low and moderate glomerular filtration rate (GF), left ventricular ejection fraction (LVEF) lower than 50%, incomplete revascularization, body mass index (BMI), complications during the immediate postoperative period, perioperative AMI, urgency surgery and prolonged surgical time.

Variables to predict immediate mortality for cardiac causes: death of cardiovascular etiology or related to surgery occurred after MRS up to 30 days following surgery.

Data collection

At first the data obtained were: informed consent, general data, preoperative, intraoperative and postoperative variables and immediate mortality. Follow-up was implemented 30 days after the MRS, immediate mortality was documented by means of an interview with the attending physicians, a review of the clinical record and death certificates. This information was collected in an individual file elaborated by the authors and these data were used to create an Excel spreadsheet with items that were later used for the elaboration of the index and statistical processing in SPSS version 20.

The sample was randomly divided into two equal groups (estimation and validation), with approximately 50% of patients in each group, in such a way that the sample comprised 179 patients for the elaboration of the index and another with 161 patients for validation.

Elaboration of the index based on the probability of dying immediately: the multivariate logistic regression function with dichotomic response was used to calculate the probability of immediate mortality after myocardial revascularization surgery.

Determination of the final score: in the investigation sample and using the formula obtained, the probability of each patient dying immediately was calculated *(See Results)*.

Index and probability-of-dying zones: with the idea of the index having a more practical value, three zones were established for values limited by empirical percentiles 33.3 and 66.6 in order to divide the possible range of values into three equal zones. In this way three zones would be established, the first, from the lowest value to percentile 33.3 a zone with a very low risk of dying (<0,01), an intermediate zone between percentile 33.3 and 66.6, that would imply the intermediate risk of dying and could be called a doubtful zone or "grey area", or medium intermediate (0.01-0.04), and above percentile 66.6 high risk (>0.04), would be the zone with the highest risk of dying. By way of validation (conceptual) of these divisions, the percentage of immediate deaths was calculated for each zone and an evaluation was made to determine whether there were differences between these percentages. It was expected to find the highest frequency of deaths in the high score zone and the lowest frequency in the low score zone.

Construction of the quantitative index: the same variables used for the construction of the probability-based index were used for the construction of this index, perhaps more practical, to be used by attending physicians in the regular practice given the ease of calculation.

Scale for each variable: these variables, with the exception of BMI, were classified into dichotomic categories, a value of 1 was assigned if it was present and 0 if it was absent. Then, odds ratio (OR) results, estimated by means of the logistic regression function and rounded to whole numbers and in some cases to a decimal number, and the weights for each variable, were estimated on the basis of the importance assigned to each one.

Determination of the final score: it was found to be the summation of all values reached by each variable after having multiplied by the corresponding weight based on the importance assigned *(See Results)*.

Scales and zones for the quantitative index: the same as with the probability value, the score was calculated for each patient, and this empirical distribution was divided into three parts (terciles) by means of percentiles 33.6 and 66.7 to classify into three risk groups for each patient, low (37), medium (37-45) and high (>45).

Phase II: Validation of both indexes

Since a truth criterion is applied (immediate mortality), the validation of indexes was elaborated with the values of both indexes, two ROC curves to assess discrimination (capacity to discriminate between immediate deaths or non-deaths). Calibration (the measure by which the estimated probability reflects the true death risk) of the logistic regression model was determined applying the Hosmer and Lemeshow statistical test. Contingency tables were built for the different risk stratifications according to the values of the two scores (risk zones) and the presence of immediate mortality variable (yes or no) and using the Bartholomew χ^2 test the existence of a correlation between these two variables was determined.

Reliability: since the variables were evaluated by specialists, the most useful reliability measure is the one that measures inter-observer variability.

The reliability coefficient was obtained (intraclass correlation coefficient) based on the repeated measures ANOVA, which is useful to assess the concordance among observers for quantitative variables. This coefficient was obtained for the proposed index. The score was calculated independently by two specialists.

Ethical considerations: the results of the study will be used for scientific purposes without disclosing data that would affect the patient´s privacy. The Helsinki declaration for research involving human subjects was observed[15].

RESULTS

Phase I: Construction of both quantitative indexes

Index based on the probability of immediate death calculated by the logistic regression model

The estimated logistic regression model had a good calibration (the predicted probability of dying matched the observations) given by the results of the Hosmer and Lemeshow statistical analysis (p= 0.914).

The probability of dying immediately calculated for each patient for said function was an indicator to predict said event and therefore is be given a value from 0 to 1. (Estimated logistic regression equation).

Estimated logistic regression equation

P (y=immediate mortality) 1/1+ exp-(4.230+2.021× age+0.682× gender-0.077× HTA+1.065× DM-0.751× recent IMA-0.395× functional class IV with angina+0.939× EPOC+0.317× extracardiac arteriopathy-1.6592× low to moderate GF +1.057× LVEF >50 %-0.639× type of myocardial revascularization+2.147× postoperative complications +2.264×perioperative AMI+0.017× BMI-1.221× prolonged surgical time+1.115× emergency surgery.

Quantitative index

It was created with the same variables described in the previous index, weighted by their respective odds ratios (OR), estimated by the logistic regression function and rounded to whole numbers and in

TABLE 1. Variables according to their coefficient of variation, categories and weight

VARIABLES	CATEGORIES	VALUE	WEIGHT (W_i)
Age >70 years	Yes	1	8
	No	0	
Sex	Male	0	2
	Female	1	
Hypertension	Yes	1	1
	No	0	
DM	Yes	1	3
	No	0	
Recent AMI	Yes	1	1
	No	0	
Functional class IV angina	Yes	1	1
	No	0	
COPD	Yes	1	3
	No	0	
Peripheral arteriopathy	Yes	1	1
	No	0	
Low to moderate GFR	Yes	1	0.2
	No	0	
LVEF <50	Yes	1	3
	No	0	
Incomplete revascularization	Yes	1	1
	No	0	
BMI	Quantitative		1
Complications in the immediate postop	Yes	1	9
	No	0	
Perioperative AMI	Yes	1	10
	No	0	
Emergency surgery	Yes	1	3
	No	0	
Prolonged surgical time	Yes	1	0.3
	No	0	

AMI: acute myocardial infarction, LVEF: left ventricle ejection fraction, FC: functional class, GF: glomerular filtration, DM: diabetes mellitus, HTA: hypertension, BMI: body mass index, ST: surgical time.

some cases to a decimal number. The final score was the result of multiplying the value of each variable by the number corresponding to its weight, as shown in *Table 1*.

Phase II: Validation of both indexes

Index based on the probability of immediate death calculated by the logistic regression model

The area under the ROC curve for the probability of dying immediately after myocardial revascularization was 0.889 (95 % CI: 0.835-0.944), *(Graphic 1)*.

Division into three zones according to the immediate death probability, calculated by the logistic regression model

When dividing the probability, calculated by the logistic regression model in three zones according to percentiles 33.6 and 66.7, it was observed that most immediate mortality patients were in the high-risk group, represented by 89.3%, and none had been classified as low risk. These differences were significant (89.3 % vs 28.2 %) p<0.001 *(Table 2)*.

The area under the ROC curve for the quantitative index was 0.856 (95 % CI: 0.801-0.911) which shows good discrimination between patients that die immediately and those who do not *(Graphic 2)*.

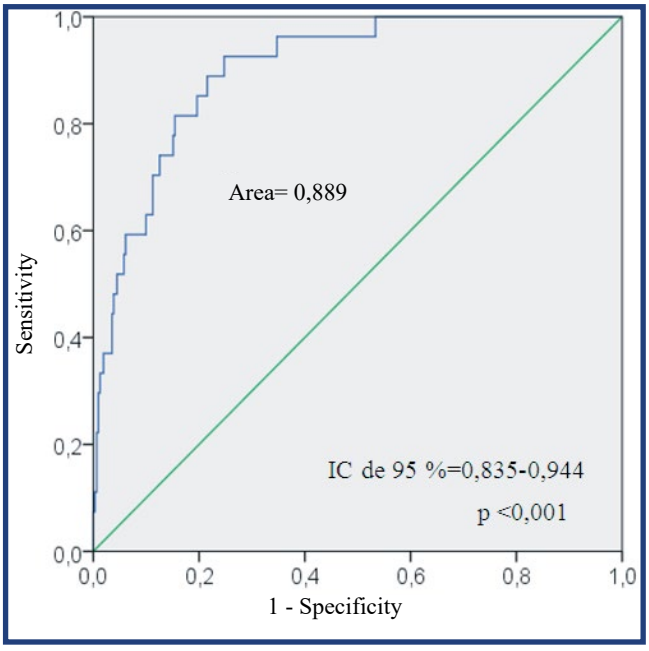
When dividing the quantitative index score into three zones based on percentiles 33.6 and 66.7, it was observed that most of the patients that died immediately had been classified as high-risk, represented by 82.1% and none had been classified as low risk. These differences were highly significant, 82.1% vs 25.3 %), *(Table 3)*.

Reliability

As can be observed in *Table 4*, the intraclass correlation coefficient for the index based on probability was 0.966 (95% CI: 0.955-0.975) and for the quantitative index it was 0.935 (95% CI: 0.913-0.952).

DISCUSSION

The impact of cardiovascular risk factors vary according to age[16]. This is compatible with the results of this investigation, in which the weight of the different variables is presented in individuals older than 70 years old. Rocha *et al.*[17] described higher mortality and complication rates in patients older than 70 years old treated by MRS.



GRAPHIC 1. Area under the ROC curve according to the probability of immediate death index calculated by the logistic regression model

TABLE 2. Distribution of patients by category of index risk for the probability of immediate death calculated by the logistic regression model

RISK	IMMEDIATE MORTALITY				TOTAL	
	Yes		No			
	Number	%	Number	%	Number	%
Low (<0.01)	0	0.0	110	35.3	110	32.4
Medium (0.01-0.04)	3	10.7	114	36.5	117	34.4
High (>0.04)	25	89.3	88	28.2	113	33.2
Total	28	100	312	100	340	100

Bartholomew Chi-Square test p<0.001.

GRAPHIC 2. Area under the ROC curve according to the quantitative index for immediate mortality

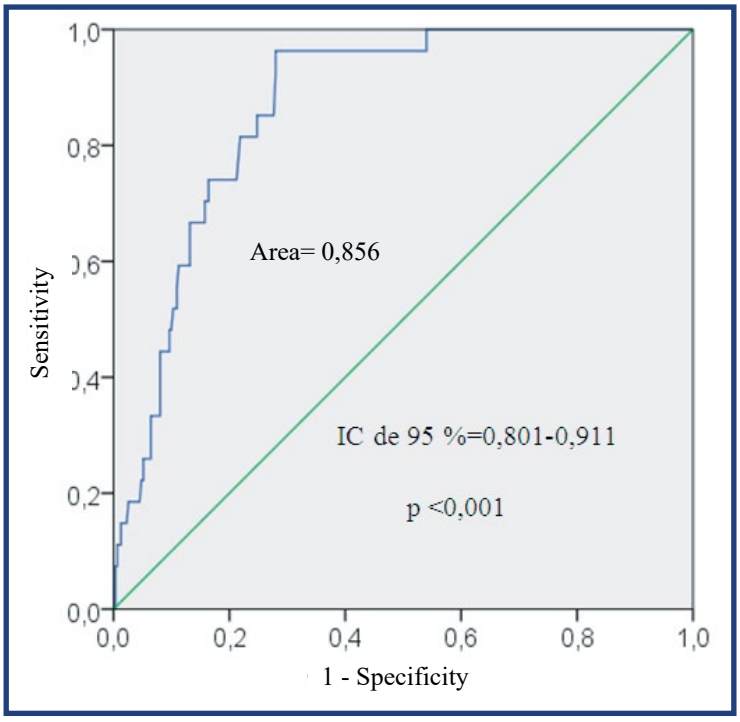


TABLE 3. Distribution of patients by risk category of the quantitative index for immediate mortality

RISK	IMMEDIATE MORTALITY				TOTAL	
	Yes		No			
	Number	%	Number	%	Number	%
Low (<37)	0	0.0	103	33.0	103	30.3
Medium (37-45)	5	17.9	130	41.7	135	39.7
High (>45)	23	82.1	79	25.3	102	30.0
Total	28	100	312	100	340	100

Source: clinical record, Bartholomew Chi-Square test : p<0.001.

TABLE 4. Intraclass correlation coefficient for the two scores or indexes

INTRACLASS CORRELATION COEFFICIENT	POINT ESTIMATION	IC DE 95 %	P
Index (probability)	0.966	0.955-0.975	<0.001
Quantitative index	0.935	0.913-0.952	<0.001

Prolonged ECC time may contribute to hemolysis, blood loss and need for transfusion[17]. Perioperative myocardial infarction (pAMI) after an isolated MRS is associated with poor prognosis[18]. Rao *et al.*[19], identified in the MRS postoperative period, LVEF <20%, female sex, diabetes, age > 70 years, recent AMI and multivessel disease as independent predictors of mortality, similar findings as this study. Postoperative infection and renal lesion were associated to higher mortality in the Brazil study[20]. The results were equivalent to those of this investigation, where complications presented a high weigh. Dessotte *et al.*[21] found that mortality in MRS was closely related to age, sex and comorbidities, similar variables as that of the score created in the investigation. In turn, Lopez *et al.*[22] in the Hermanos Ameijeiras study, concluded that the variables that kept an independent relation with immediate mortality were: longer surgery time, low glomerular filtration and complications, where the possibility of dying increased by approximately 16 times. These results match with the variables that had the greatest weight to predict mortality in this study and greater importance in the created score.

Validity

The ROC curve is used to assess the prognostic (or diagnostic) capacity of a quantitative indicator[23]. For the scale proposed in its two variants (reduced and extended), the criterium of truth is death. The validity of the index may be considered highly acceptable

given the results of the ROC curve elaborated with the application of immediate mortality as a criterium of truth, since areas between 0.7 and 0.8 are considered acceptable for indexes of this type. In the case of the two indexes created in this research, the areas under the curve were significant p<0,001and are very good. One area with good capacity to discriminate between living and dead individuals must be 0.80 or higher, it is to be noted that the lower limits of the 95% CI of the two areas are very distant from 0.5, that is the value of said curve for non-discrimination[22,24,25,26]. Thus, the discrimination capacity of both indexes to predict immediate mortality in this study was very high. The ArgenSCORE presents good discrimination power for mortality and capacity to assign risk by showing an excellent relation between observed and predicted mortality[13]. Similar characteristics as for the indexes created in this study that are only applicable to patients treated by MRS. Studies[14,27] indicate that the EuroSCORE II has shown good general capacity to differentiate between dead and live patients with an area under the curve greater than 0.792 (95% CI, 0.773-0.811). In the indexes created as part of this investigation for MRS, the area under the curve is much greater, which indicates that its discriminatory and predictive capacity is higher.

Reliability

When there are scales that give rise to continuous variables (or that may be considered as such), the appropriate index to measure concordance among observers is the intraclass correlation coefficient (ICC). This coefficient indicates which part of the total variance of the index observations obtained is due to the sample; when it is high (close to 1 or 100%), it is assumed that the variation among observers is low, since there are only two sources of variation: among subjects and among observers[28,29]. The values obtained for the intraclass correlation coefficient, both in the estimation sample as in the validation, may be considered highly satisfactory in terms of the concordance between the two specialists, as values above 0.75 have been rated as excellent by authors like Casado *et al.*[30], Fleiss *et al.*[31] and Rosner[32]. Other experts on the topic have published that values above ICCI are considered adequate[33]. In this way, according to this criterium, the value obtained in this study is highly acceptable.

CONCLUSIONS

An instrument is built with two variants: an index based on the probability of dying immediately and another, quantitative and practical and applicable in the context of coronary surgery. Both indexes are valid and reliable for the prediction of immediate mortality after myocardial revascularization surgery, which means that they are feasible and useful when applied.

Conflicts of interest
The authors have no disclosures to declare.

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SCIENTIFIC LETTER

COMPLEX ARTERIOVENOUS FISTULA OF THE ILIAC SECTOR. RENAL EXPLANT COMPLICATION

ABSTRACT

Presentation of a clinical case with endovascular resolution of an arteriovenous fistula of the left external iliac artery and left external iliac vein with an occluder plug. A 34-year-old male patient with a history of obstructive nephropathy and chronic renal insufficiency. Surgical history: left kidney transplant, kidney explant, presented pain, edema and functional impotence of the left lower limb, a thrill was palpated in the left inguinal region. Endovascular treatment with an occluder plug is indicated at the level of the fistula, which was well tolerated by the patient, with rapid recovery and a significant decrease in symptoms.

Keywords: *Renal explant, arteriovenous fistula, high-flow iliac sector, endovascular treatment.*

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INTRODUCTION

Iatrogenic vascular lesions of the iliac sector are associated with high morbidity and mortality in the postoperative period after conventional surgery. They are more commonly associated to neurosurgical interventions of the spine (discectomies) specially of disks L4-L5 or L5-S1[1,2]. Iatrogenic vascular lesions subsequent to renal explants are extremely rare in the literature.

CLINICAL CASE

A 34-year-old male patient consults for pain, edema and light functional impotence of the lower left limb. In the physical exam the patient shows signs of chronic venous insufficiency with pigmentation and eczema.

Medical history: Obstructive nephropathy with chronic renal insufficiency and tri-weekly hemodialysis.

Surgical history: Left renal transplant (2002), renal explant (2008).

Following explant (2008) the above described symptomatology starts, in addition to the heaves and thrill identified during the physical examination in the left inguinal region. Complementary studies start with an arterial echo Doppler which evidences a turbulent flow compatible with high flow arteriovenous fistula at the level of the external iliac vein.

An angiography is performed (Figures 1 and 2) in which evidences of high flow arteriovenous fistula dependent on the distal third of the left external iliac artery with significant growth of the venous sector. Furthermore, a natural bypass is observed dependent on the left hypogastric artery to the common femoral chamber (Diagram 1).

After planning, it is decided to perform embolization of the affected arterial sector.

FIGURE 1. Angiographic image showing high-flow arteriovenous fistula dependent on the distal third of the left external iliac artery.

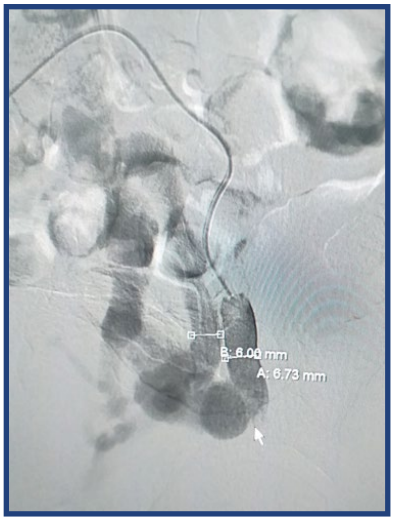

FIGURE 2. The same study reveals a significant development of the venous system and a natural bypass dependent on the left hypogastric artery to the common femoral chamber.

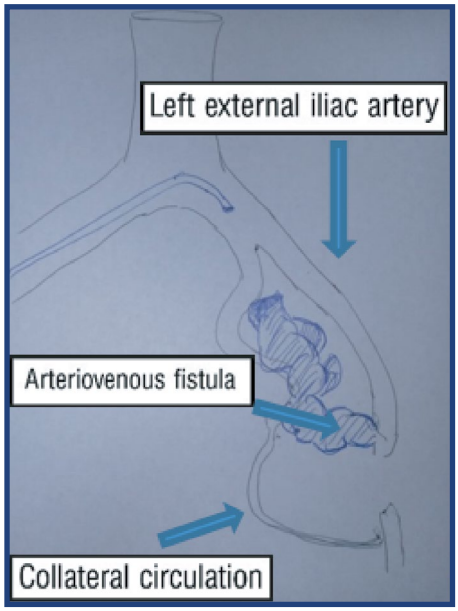

DIAGRAM 1. Schematic interpretation of the identified pathology where occlusion of the iliac artery is observed as well as the arteriovenous fistula and the bypass of the hypograstric artery to the common femoral chamber.

Under spinal anesthesia, we proceed to lateral placement of a 6 Fr introducer, selective cannulation with Simmons 1 catheter due to intense tortuosity and with hydrophilic wire a 9 Fr sheath is placed at the bottom of the sac of the left external iliac artery (assuming that it had been ligated in the explant surgery). An occluder, 12mm diameter MemoPart device (Figure 3) is placed. Closure is performed by conventional surgery using the introducer diameter.

Control angiography evidences the occluder plug optimally inserted, the thrombosed external iliac artery and the obliteration of the venous communication (Figures 4 and 5, and Diagram 2). There are not clinical symptoms of chronic ischemia nor venous insufficiency.

CONCLUSIONS

Iatrogenic lesions of the iliac vessels could go unnoticed in the intraoperative or immediate postoperative periods. Modern imaging techniques allow for an accurate diagnosis of the lesion and planning of a suitable treatment, although these lesions are unusual[3].

Conflicts of interest
The authors have no disclosures to declare.

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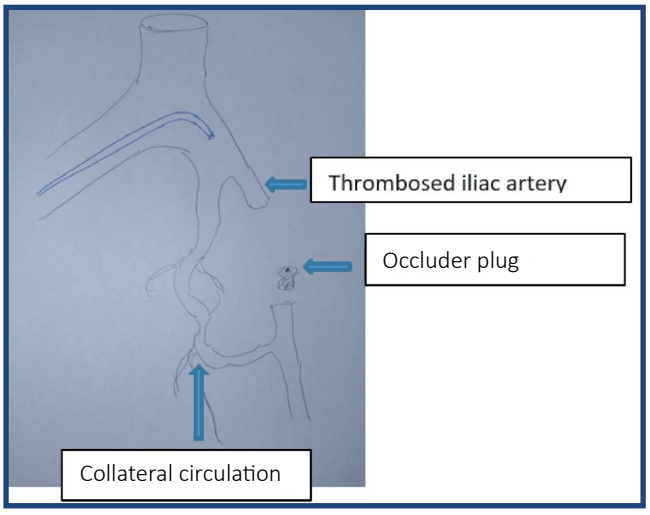
FIGURE 3. Placement of the occluder device.

DIAGRAM 2. Interpretation of the images in Figures 4 and 5.



FIGURES 4 AND 5. Angiographic verification of the appropriate placement of the occluder and closure of the arteriovenous fistula.

SCIENTIFIC LETTER

EXERCISE-INDUCED ILIAC ARTERY FIBROSIS

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ABSTRACT

Exercise-induced iliac endofibrosis (IE), initially known as cyclist iliac endofibrosis, is a low prevalence disease that presents characteristic symptoms of ischemia in patients without classical risk factors. We present a 45-year-old triathlete female patient. She consulted for intermittent claudication at 100 m in the lower right limb for about one year. She presented to the consultation with right external iliac artery thrombosis. Endarterectomy and plastic with vein patch were performed with favorable evolution. Iliac endofibrosis is a rare disease but it is one of the diagnoses to consider when dealing with young athlete patients with symptoms of lower limb ischemia.

Keywords: *Iliac endofibrosis, acute ischemia, exercise-induced endofibrosis, ciclyst endofibrosis*

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INTRODUCTION

Cases of young patients with no cardiovascular risk factors and clinical symptoms of arterial ischemia, be it acute or chronic, are rather unusual and frequently lead to a delayed, difficult and inappropriate diagnosis. In particular this is due to the fact that symptoms do not usually appear at rest or are not very severe, and all pulses may be palpable. These patients tend to be evaluated by different specialists and undergo multiple studies and physical therapy. Some of the pathologies to be ruled out (without limitation) are popliteal trapping, chronic compartment syndrome, adventitial cystic disease and other less frequent presentations such as peroneal, pedal or tibial trapping.

In spite of this, the diagnosis becomes a firm suspicion when taking note that the patient is a high-endurance athlete with many years of practice and many kilometers of cycling or long-distance running.

CLINICAL CASE

A female, 45-year old patient who complains of intermittent claudication at 100 meters in the right lower limb but regularly exercises in the bicycle without difficulty. The patient reports to have experienced an episode of pain in that limb during a road cycling session that was relieved in time and with analgesics. The physical examination revealed absence of pulses on the right side and all pulses present with good amplitude in the left lower limb. The right ABI was 0.3 at rest and the left ABI 1.

The Doppler ultrasound scan revealead thrombosis of the right iliac artery all along its extension, except for the first 3 cm of the proximal segment, where parietal thickening could be seen with significant stenosis and the common femoral was patent after the inferior epigastric and iliac circumflex arteries. The angioCT confirmed the diagnosis of iliac endofibrosis of the external iliac, complicated with local thrombosis (C0F5E0) of the Chevallier[1] classification and no signs of distal embolism could be observed (Figure 1). Not significant contralateral stenosis was also observed (probably inicipent endofibrosis).

It was decided to perform external iliac endarterectomy all along its extension and patch plastic thrombectomy of the homolateral saphenous vein through a transaponeurotic retroperitoneal approach (Figures 2 and 3). The pathological anatomy of the endarterectomy revealed fibrosis and chronic inflammation of the intima with thrombosis in organization. After 2 days of hospitalization the patient was discharged. She recovered all pulses after surgery, and the ABI in this limb at rest was 0.0. All flows measured by Doppler ultrasound were triphasic with preserved velocity.

During the first three months she could take walks without any inconvenience and as from the fourth month she reinitiated sports practice without claudication (she was recommended not to go back to cycling).

DISCUSSION

The first cases of cyclist iliac endofibrosis (exercise-induced) were described in the ´80s, which means that this pathology has been recently identified (probably associated to the cycling boom during

FIGURE 1. Stenosis and thrombosis of the external iliac artery

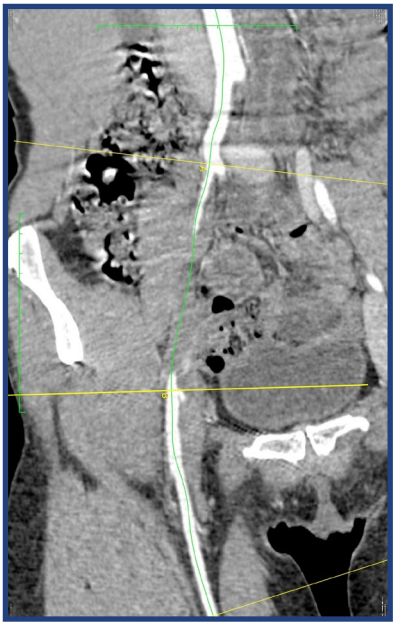


FIGURE 2. Intraoperatory image of iliac endofibrosis and distal thrombosis

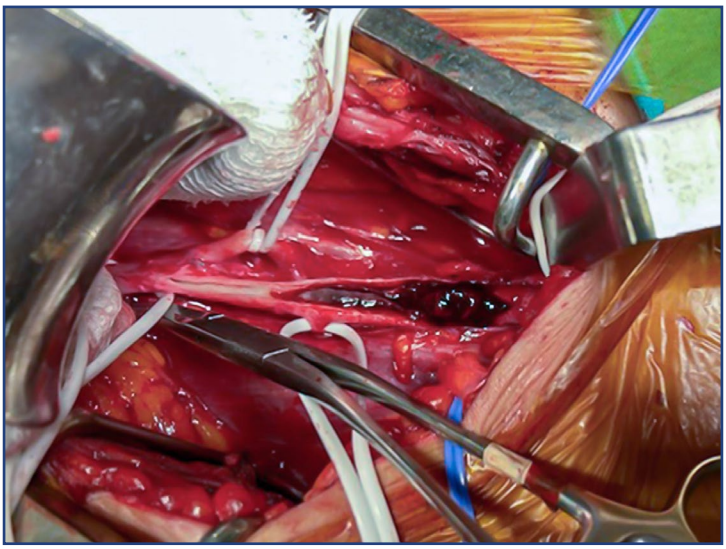
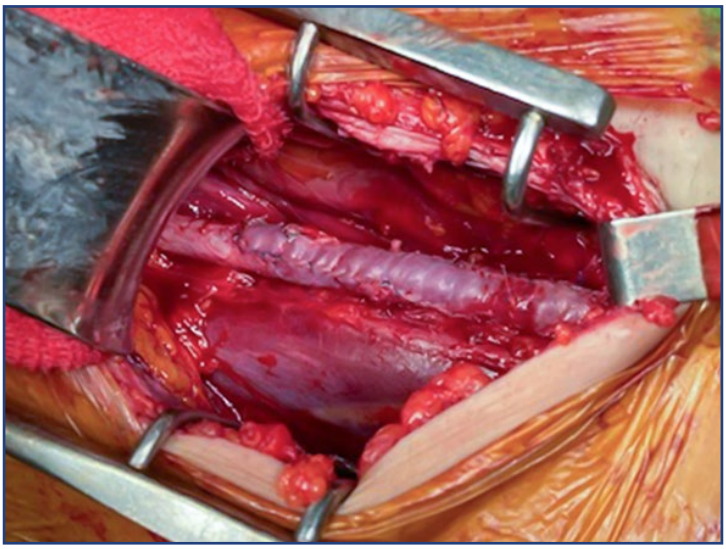


FIGURE 3. Saphenous vein patch



the ´70s and ´80s, and it is not surprising that it was first described in France, a country well-known for the practice of road cycling and in a cycling rehabilitation center)[1-3]. Although it is known as endofibrosis of the external iliac artery (94.9%), it should be considered that fibrosis may also present itself at the level of the common iliac artery (14.4%), the common femoral artery (0.5%) and the profound femoral artery (7.2%), in the latter particularly as stenosis in the form of ostial diaphragm[1]. This pathology has been described mainly in high-endurance long-term cyclists, but it has also been found in runners, triathletes, rowers, body builders and others. In the vast majority these are young patients with many years of high-endurance sports practice. Symptoms may be seen as from the first 5 years of initiation of sports and at 50.000 km run; however, those that require surgical treatment usually are 14 years and older and have run over 130,000 km[1].

This presentation is clearly a cause of non-atherosclerotic stenosis, but its pathophysiology and etiopathogenesis is still unknown. Subintimal thickening takes place with collagen, elastin and smooth muscle cells depositions; and in cases that get complicated dissection and/or localized thrombosis can be seen[4].

Its etiology is rather uncertain. It has been proposed that the shearing stress produced by hyperflow may stimulate fibrosis, which would lead to endothelial malfunction[5]. The cyclist´s position may produce kinking, with the consequent increase in flow velocity and parietal stress, apart from lengthening the external iliac artery, which would in turn increase the degree of kinking. It is not very clear whether the same factors may act in fixed or mobile segments of the arteries[1]. Psoas hypertrophy upon fixation of the external iliac artery by the feeding collaterals of the psoas has been mentioned as an anatomic reason that

might play a role[6]. Localized vasospasm has been identified in some cases, also of an unknown origin (perhaps due to the endothelium-induced arterial dilation)[7]. Vasospasm may be visualized by means of image studies (Doppler ultrasound, CT or MRI) pre and post exercise[7-10].

Suspected initial diagnosis is based on the history of high-endurance sports practice, but other differential diagnosis of non-atherosclerotic arterial disease must be ruled out in individuals without the classical risk factors. Patients frequently present all palpable pulses, thus the importance of performing the ABI at rest and post-exercise (until onset of symptoms). A drop greater than 0.3 is considered the cut-off value. Then, it is possible to continue the evaluation with image diagnostic methods. The Chevalier group usually performs diagnostic angiography and it is important to stress that this must include a lateral projection of the iliac-femoral axis in flexion to identify kinks, stenosis and extrinsic compressions. Based on the angiography, they propose a classification of the pathology assessing the status of the primitive, external, common femoral and profound arteries. They stress that the degree of stenosis is not determinant, since, as has been previously described, the problem has dynamic characteristics (vasospasm, kinking, extrinsic compression, lengthening of the external iliac artery) and they have also seen that the vast majority of treated patients present less than 50% stenosis[1].

As for the treatment, once the diagnosis is confirmed, cycling or the predisposing activity must be discontinued. This is one of the vascular diseases for which surgical treatment continues to be definitive and the first choice. Chevalier et al., since their initial description, suggested endofibrosectomy of the affected area, shortening of the external iliac, reimplantation and plastic with vein patch[1-3]. The same authors perform intraoperatory angioscopy to confirm the diagnosis, and even prefer this option over intravascular ultrasound. Peak et al. suggest the use of bovine pericardium patch so as to preserve the saphenous vein and avoid possible aneurismatic dilation in future[11]. In complicated cases with dissection or extensive thrombosis, iliofemoral bypass may be performed as a first attempt (with vein, Dacron prosthesis or ePTFE). After surgery, most authors agree that the patient must continue antiaggregation treatment with aspirin only (75-100 mg/day). Doppler ultrasound is performed after surgery to ensure patency and confirm that there are no major issues.

Mid-term results (50 m) in most groups is over 90% primary patency and 100% assisted/secondary patency. There are not many references regarding long-term results.

There are a few described cases of endovascular treatment using balloon and drug-coated balloon with unfavorable results that show early symptoms relapse[12,13].

It is suggested to reinitiate sports activity at 3 months, and of course not returning to cycling, although professional cyclists who have resumed have not required reintervention[1].

The consensus of the international group for the study and identification of endofibrosis (INSITE) was published in 2016, suggesting surgery as the treatment of choice (endofibrosectomy whenever possible and eventually bypass in case of extensive occlusions), diagnosis with ABI (to be complemented with image studies) and resuming sports activity at 6-8 weeks[14].

CONCLUSION

Exercise-induced iliac endofibrosis (IE), is a low prevalence vascular disease. It must be initially suspected in patients with typical symptoms of arterial claudication with a background of intense physical activity (particularly cycling) without typical cardiovascular risk factors. Surgical treatment has low morbidity since these are mostly healthy patients and the surgical intervention is not technically demanding. Mid-term results are also promising and provide absolute resolution of the symptoms in more than 90% of patients.

Conflicts of interest

The authors have no disclosures to declare.

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SCIENTIFIC LETTER

RIGHT THORACIC OUTLET SYNDROME DUE TO CERVICAL RIB AND SUBCLAVIAN ARTERY ANEURYSM REPAIR

ABSTRACT

The term Thoracic Outlet Syndrome (TOS) was coined to describe a group of patients with compression of the subclavian vessels, artery or vein and the brachial plexus in the area of the thoracic outlet. TOS is responsible for 5 to 10% of painful symptoms in the upper limb.

A case of a 70-year-old female patient is described, who is admitted due to pain in the right upper limb of about 2 months of evolution, associated with paresthesia, coldness and weakness. Angiography shows aneurysm of the right subclavian artery and cervical rib present and fused to the first thoracic rib. In the surgical intervention, a supernumerary cervical rib resection and aneurysm repair with a PTFE prosthesis were performed.

Keywords: *Cervical rib, aneurysm, subclavian artery*

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INTRODUCTION

The Thoracic Operculum Syndrome (TOS) is responsible for 5 to 10% of painful symptoms in the upper limb. TOS affects 8% of the general population with a frequency of 3-80 cases per 1000 individuals and unknown incidence, involving patients with compression of the subclavian vessels (arteries or veins) and the brachial plexus in the thoracic outlet space[1,4].

This syndrome is more common in women than in men (a 3-4:1 ratio) and occurs more frequently in young adults in the 25 to 40 age range.

Neurogenic symptoms are the most usual, accounting for about 90-95% of all cases, followed by venous in 5-10% and arterial symptoms in approximately <1%.

The cervical rib is the most common cause, with an incidence of 0.2 to 1% of the population, 50 to 80% being bilateral and only 10 to 20% producing symptoms with a 2:1 ratio in women versus men.

There are 3 major etiological groups: bone anomalies, soft tissue anomalies and postural anomalies. Bony anomalies comprise cervical ribs, transverse mega process of C7, anomalies of the first rib, nonunion of the clavicle, hypertrophic callous of the clavicle or tumors; anomalies of soft tissues include cervical muscular hypertrophy (anterior scalene muscle, medium scalene, pectoralis minor and subclavian), fibrous bands (costocoracoid ligaments, costoclavicular membrane) or congenital muscular anomalies.

The TOS may have three different presentations. The first is neurogenic TOS (NTOS), which involves the neurological symptomatology of the syndrome, the second is the venous TOS (VTOS), which produces pure venous symptoms like thrombosis of the subclavian vein, and finally the arterial TOS (ATOS), an extremely rare form, that manifests itself with purely arterial symptomatology, secondary to arterial thrombosis or arterial aneurisms of the subclavian artery.

As for complementary studies: chest and cervical X-rays are used to rule out or confirm bone anomalies. Computarized axial tomography (CT) provides better anatomic information, particularly when bony etiology is suspected. Magnetic resonance (MRI) permits an adequate evaluation of soft tissues, most particularly of the brachial plexus. Arteriography has very limited value in these cases and must only be used when a patient presents symptoms and signs of ischemia and arterial insufficiency[1,2,5].

CLINICAL CASE

We present the case of a female 70-year old patient admitted for pain in the upper right limb with an intensity score of 9/10, 2 months of evolution, associated with paresthesia, cold and weakness. The patient had no history of allergies or diseases and had been smoking 5 cigarettes a day for the last 20 years, was medicated with acenocumarol 1 mg/day and had been subjected to a thrombectomy of the upper right limb one month earlier.

An abnormal physical examination revealed: asymmetric thorax with right supraclavicular pulsatile mass measuring 3x4 cm. Positive Adson test. Positive Wright test. Axillary, humeral, radial and cubital pulse present and weak. Slow capillary filling and distal coldness of the right upper limb.

Angiotomography: aneurism of the right subclavian artery measuring 20 mm, with mural thrombus in the interior and cervical rib present fused to the first thoracic rib (Figure 1).

FIGURE 1. 1. Aneurism of the subclavian artery in an axial section of the CT. **2.** Aneurism of the subclavian artery in a coronal section of the CT. **3.** 3D reconstruction of bony anomaly. **4.** Subclavian vascular bundle with bony anomaly.

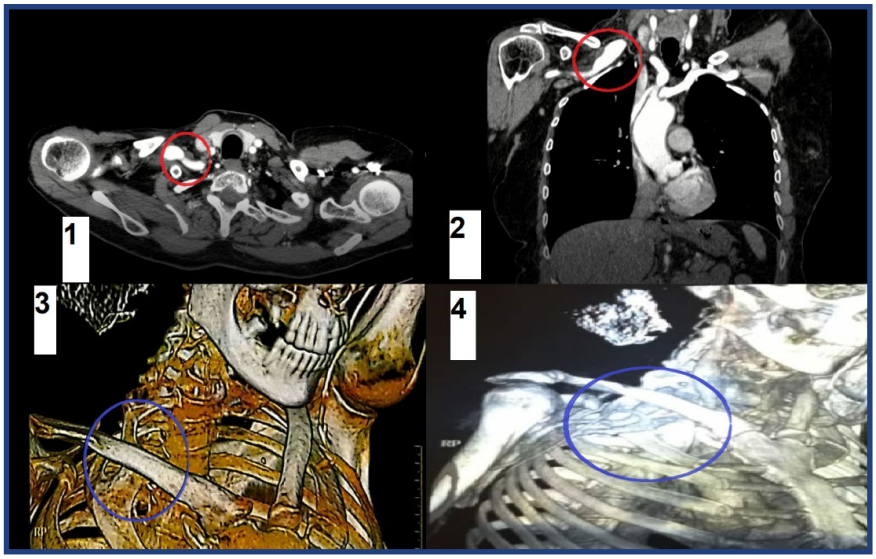
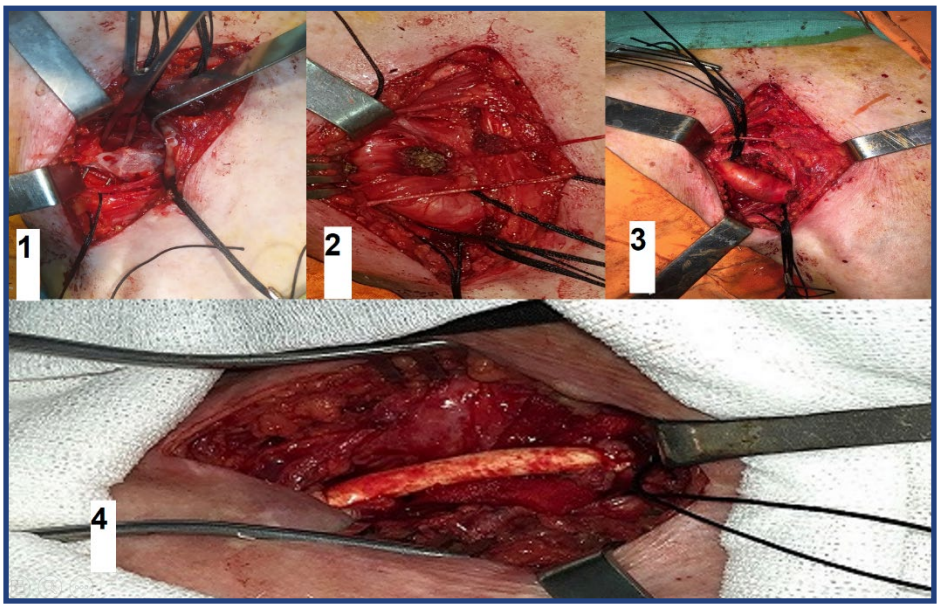


FIGURE 2. 1. Cervical rib fused to the first rib. **2.** Scalene muscle section. **3.** Subclavian aneurism. **4.** Subclavian-axillary bypass with PTFE prosthesis.



Based on the patient´s prior signs and symptomatology, the surgical history and image studies, the condition was interpreted as TOS of vascular etiology. Surgical management was proposed for resolution of the condition prior optimization of the coagulation test and cardiovascular evaluation.

A supraclavicular approach was performed with repair of vascular and nervous structures, section of the scalene muscle, resection of the supernumerary cervical rib and repair of the posstenotic aneurism with PTFE prosthesis *(Figure 2)*.

On day 3 post-op the patient was discharged from hospital with preserved peripheral pulse, good mobility and nervous integrity of the upper limb with the required dose of antiaggregation medication. Follow-up continues in the outpatient thoracic and peripheral vascular surgery service.

CONCLUSION

The treatment of TOS requires multidisciplinary management, focused on three main objectives: reduction of neurovascular compression, pain management, symptoms control and ultimately improving quality of life[3].

Several factors are taken into consideration to proceed with surgical treatment, including no response to conservative management for at least 3 months, motor-sensory involvement, vascular claudication, recognized anatomical anomaly and impairment of daily life activities.

Supraclavicular route is preferred as it permits to perform the resection of the first rib, apart from providing good access to vascular landmarks[6].

It should be noted that the symptomatology presented by this patient is the least frequently found.

Conflicts of interest
The authors have no disclosures to declare.

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SELECTED ARTICLES

We hereby present comments on a selection of articles recently published in internationally acclaimed medical journals. We believe these papers deserve special attention due to the quality and importance of the conclusions reached by the studies. Our objective is to keep an open look on new aspects of scientific research or review articles that may, in turn, update aspects of our own medical specialty.

Also, the Editorial Committee will consider suggestions on recent articles that the readers think deserve to be commented in this section (revista@caccv.org.ar).

IMPORTANCE OF A PREOPERATIVE EXERCISE PROGRAM IN ARTERIOVENOUS FISTULAS FOR DIALYSIS ACCESS

ARAGONCILLO SAUCO I ET.AL. EFFECT OF PREOPERATIVE EXERCISE ON VASCULAR CALIBER AND MATURATION OF ARTERIOVENOUS FISTULA: THE PHYSICALFAV TRIAL, A RANDOMIZED CONTROLLED STUDY

J Nephrol. 2021 Jun;34(3):763-771. DOI: 10.1007/s40620-020-00907-w

It is known that autologous radiocephalic arteriovenous fistula (AVF) is the best vascular option for dialysis access; however, the rate of primary failure ranges from 20% to 50%. Although it is estimated that preoperative isometric exercises are beneficial to improve these results, evidence is scarce. Researchers from the University Hospital Gregorio Marañon and other centers in Spain designed an open, multicenter and prospective trial to evaluate the effects of this type of exercises in the maturation of AVFs in patients with renal disease requiring dialysis. Exclusion criteria were patients with absence of arteries or veins apt for AFV, diagnosis of coagulopathy, existence of prior AVF in the selected arm or other conditions that turn impossible the practice exercise during the 8 weeks prior to surgery. Patients assigned to the isometric exercise group were indicated a routine combining contractions with elastic bands and manual contractions, in which each isometric contraction was to be maintained for 5 to 7 seconds. The intensity of exercises was adjusted according to the maximum strength of each patient measured by dynamometry. Doppler studies were conducted at the beginning during the week prior to surgery (8 weeks as from admission) and an extra study was conducted at 4 weeks of initiation of exercises with patients in the active group. After performing AVF, maturation was assessed by Doppler at weeks 6 and 12. These studies were performed by nephrologists specialized in AVF ultrasound and comprised 6 measurements of the cephalic vein, as well as three measurements of the radial artery in the same anatomic sites before and after the exercises. Follow-up was completed 3 months after the AVF. The main endpoint of the study was the impact of isometric exercise in primary failures of the fistula compared with the control group.

Other studied parameters were venous and arterial caliber, peak systolic velocity and maximum strength. The final analysis included 53 patients in the isometric exercise group and 61 controls. After 8 weeks of exercise, significant differences were found in arterial caliber, systolic arterial velocity, venous caliber and maximum strength. The greatest increase in venous caliber and maximum strength were related to age < 60 years, non-diabetic patients and male sex, whereas the highest increase in the arterial diameter and the highest systolic peak were found in females. After 8 weeks, the indication of radiocephalic AVF was more common in the exercise group than in the control group (77,4% vs. 53,3%), noting that in 8 patients priorly scheduled for fistula in the elbow fold, after completing the exercise program it was decided to change for radiocephalic fistula. Although primary failures in the exercise group were less than in the control group, this difference was not statistically significant.

Authors understand that this lack of significance may be due to the low rate of failures in both groups and an insufficient sample. However, they noted an improvement in the venous caliber and the possibility of performing more distal fistulas after exercise. Further studies are required to draw final conclusions and establish an adequate exercise protocol.

BILATERAL VS. UNILATERAL MAMMARY CORONARY BYPASS: ANALYSIS OF AGE-RELATED EVOLUTION

GAUDINO M ET.AL., ASSOCIATION OF AGE WITH 10-YEAR OUTCOMES AFTER CORONARY SURGERY IN THE ARTERIAL REVASCULARIZATION TRIAL

Gaudino M et.al., Association of Age With 10-Year Outcomes After Coronary Surgery in the Arterial Revascularization Trial.

The impact of age in the evolution of patients with bilateral mammary coronary bypass (bilateral internal thoracic arteries, BITA), vs. single mammary coronary bypass (single internal thoracic arteries, SITA) has not yet been established, as stated by Gaudino et.al in U.S., United Kingdom and Canada research centers. Researchers analyzed the results of ART (Arterial Revascularization Trial), the only controlled, randomized trial that has compared the evolution of BITA vs. SITA in a large number of participants with follow-up data from of over 97% of patients at 10 years. The analysis found no significant differences in mortality for any cause, stroke or myocardial infarction. However, given the large number of crossover and cointerventions (particularly the use of the radial artery in the control group), a post-hoc analysis was conducted to assess the differences in the number of arterial grafts, finding higher overall survival and event-free survival rates in the group with multiple grafts. Observational evidence suggests that the long-term benefits of bypass with the BITA strategy shall only be evident in younger patients. The overall analysis showed no significant differences. However, in conducting the analysis of 50 to 70 year-old patients, those in the BITA group had a significantly lower incidence of major adverse events. These results suggest that younger patients would obtain greater benefit from the bilateral mammary bypass, although the authors maintain that since this is a post-hoc analysis, further randomized studies are required to confirm this hypothesis.

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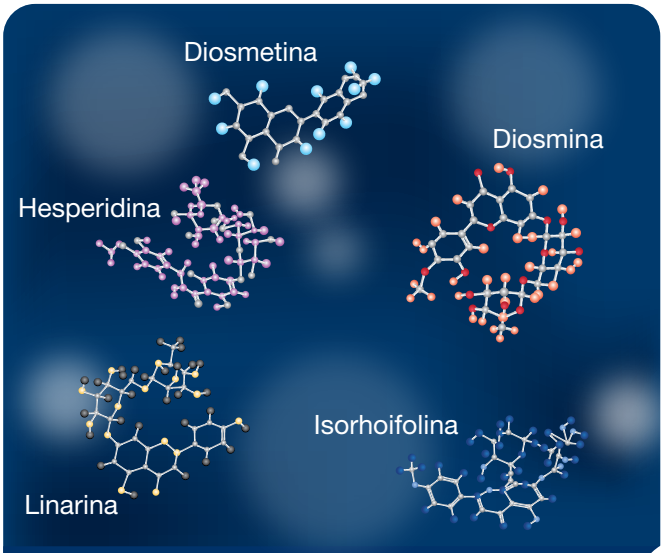

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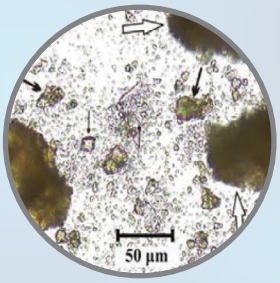

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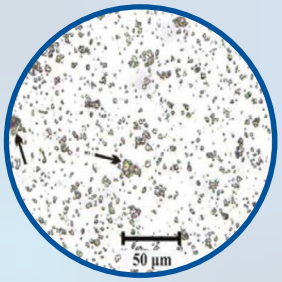

2 µm
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*Estudio realizado por el Dpto. de Farmacología Clínica y Farmacia Clínica, Universidad Nacional de Farmacia, Jarkov, Ucrania comparando dos productos similares a Daflon en dicho país.

DAFLON 1000 mg comprimidos recubiertos y DAFLON 1000 mg Suspensión Oral
Composición Daflon 1000 mg comprimidos recubiertos: Cada comprimido recubierto de Daflon 1000 mg contiene: Fracción flavonoide purificada y micronizada: 1000 mg (Correspondiendo a: Diosmina 90 %: 900 mg y Flavonoides expresados en hesperidina 10%: 100 mg). **Excipientes**: Carboximetilalmidón sódico, celulosa microcristalina, gelatina, estearato de magnesio, talco. **Recubrimiento:** dióxido de titanio (E 171), glicerol, laurilsulfato de sodio, macrogol 6000, hipromelosa, óxido de hierro amarillo (E 172), óxido de hierro rojo (E 172), estearato de magnesio. **Composición DAFLON 1000 mg Suspensión Oral:** Cada sachet de 10 ml de Daflon 1000 mg contiene: Fracción flavonoide purificada micronizada: 1000 mg (Correspondiendo a: Diosmina 90%: 900 mg y Flavonoides expresados en Hesperidina 10%: 100 mg). **Excipientes:** Malitol en polvo, goma xantan, benzoato de sodio, aromatizante de naranja, ácido cítrico, agua purificada. **Acción terapéutica:** Vasculoprotector. **Indicaciones:** Tratamiento de las manifestaciones de la insuficiencia venosa crónica de los miembros inferiores, funcional y orgánica. Sensación de pesadez, dolor, calambres nocturnos. Tratamiento de los signos funcionales relacionados con la crisis hemorroidal. Contraindicaciones: Hipersensibilidad a las sustancias activas o a alguno de los excipientes. **Advertencias y precauciones de empleo:** La administración de este producto no imposibilita el tratamiento específico de otras enfermedades anales. Si los síntomas no disminuyen rápidamente, debe practicarse un examen proctológico y el tratamiento debe ser revisado. Embarazo: No hay datos o estos son limitados relativos al uso de fracción flavonoide purificada micronizada en mujeres embarazadas. Los estudios realizados en animales no han mostrado toxicidad para la reproducción. Como medida de precaución, es preferible evitar el uso de Daflon durante el embarazo. Lactancia: Se desconoce si el principio activo/los metabolitos se excretan en la leche materna. No se puede excluir el riesgo en recién nacidos/niños. Se debe decidir si es necesario interrumpir la lactancia o interrumpir el tratamiento tras consideran el beneficio de la lactancia para el niño y el beneficio del tratamiento para la madre. **Reacciones adversas:** Trastornos del sistema nervioso: Raras: mareos, dolor de cabeza, malestar. Trastornos gastrointestinales: Frecuentes: diarrea, dispepsia, náuseas, vómitos. Poco frecuentes: colitis. Frecuencia no conocida: dolor abdominal. Trastornos de la piel y del tejido subcutáneos: Raras: erupción cutánea, prurito, urticaria. Frecuencia no conocida: edema aislado de la cara, labios y párpados. Excepcionalmente, edema de Quincke. P**osología y forma de administración:** Posología usual: un comprimido recubierto/ sachet por día preferiblemente por la mañana. Crisis hemorroidal: 3 comprimidos recubiertos/ sachets al día durante los primeros cuatro días y después 2 comprimidos recubiertos/sachets al día durante tres días. La ranura sirve únicamente para fraccionar y facilitar la deglución pero no para dividir en dosis iguales. MAMS Cert Nº 40.987. Daflon 1000 comprimidos: Elaborado en Les Laboratoires Servier Industrie, Gidy, Francia. Daflon 100 mg suspensión oral: Elaborado en 1-3 allée de la Neste - COLOMIERS Francia. Importado por: SERVIER ARGENTINA S.A. Av. Castañares 3222 (C1406IHS) C.A.B.A. - Tel.: 0800-777-SERVIER (7378437) Directora Técnica: Nayla D. Sabbatella - Farmacéutica. Versión: Enero/2020

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