



PORTUGUESE JOURNAL OF

# CARDIAC THORACIC AND VASCULAR SURGERY

Volume 28 - N.º 1 - January - March 2021

## **EDITORIAL**

- Reviewers are at the heart of the academic journals.

## **COMMENTS**

- Post-cardiotomy ECMO: time for hope or time for despair?
- The prognostic value of some neglected hematological parameters in carotid artery disease.

## **ORIGINAL ARTICLES**

- ECMO post-cardiotomy, a single centre experience.
- Extracorporeal membrane oxygenation support for postcardiotomy shock: single center experience.
- Thoracic sympathectomy: sedation experience.
- Video-assisted thoracoscopic surgery without chest drain placement.
- Mortality scores in surgical correction of abdominal aortic aneurysm in rupture.

## **REVIEW ARTICLE**

- The Impact of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in carotid artery disease.



# PORTUGUESE JOURNAL OF CARDIAC THORACIC AND VASCULAR SURGERY

Indexed on the Index Medicus and MEDLINE  
(Rev Port Cir Cardiotorac Vasc)

ÓRGÃO OFICIAL DA SOCIEDADE PORTUGUESA DE CIRURGIA CARDIO-TORÁCICA E VASCULAR  
FUNDADA EM 1984

## EDITOR-IN-CHIEF

Marina Dias Neto

## ASSOCIATE EDITORS

Nuno Carvalho Guerra (Cardiac Surgery), Cristina Rodrigues (Thoracic Surgery),  
João Rocha Neves (Vascular Surgery)

## REDATORIAL BODY

### Cardiothoracic Surgery

Álvaro Laranjeira, Cristina Rodrigues, Gonçalo Coutinho, Javier Galego, João Rocha Neves,  
Jorge Casanova, José Miranda, Nuno Costa, Pedro Antunes, Rui Rodrigues

### Vascular Surgery

Andreas Nicolaides, Augusto Ministro, Diogo Cunha e Sá, Emanuel Dias, João Vasconcelos,  
Leonor Vasconcelos, Luís Antunes, Michael Perrin, Paulo Dias, Pedro Almeida,  
Pedro Martins, Ricardo Gouveia, Timmy Toledo, Roberto Chiesa

### Other Areas

Ana Fonte Boa, André Lourenço, Cármen Brás Silva, Francisca Saraiva, Helena Donato, Hugo Vilela,  
Inês Falcão Pires, João Carlos Winck, João Viterbo, Manuela Vieira, Ricardo Fontes Carvalho,  
Roberto Roncon de Albuquerque Jr.

## SCIENTIFIC COUNCIL

### Cardiothoracic surgery

Adelino Leite Moreira, Ângelo Nobre, David Prieto, Fernando Martelo, Francisco Félix, João Carlos Mota,  
João Cravino, João Rodrigues, José Fragata, José Pedro Neves, José Roquete, Jorge Cruz, Luís Vouga,  
Manuel Guerreiro, Manuel Pedro Magalhães, Miguel Abecassis, Miguel Guerra, Miguel Sousa Uva,  
Paulo Pinho, Pedro Bastos, Pedro Magalhães, Teresa Godinho

### Vascular Surgery

Alexandra Canedo, Américo Dinis da Gama, Amílcar Mesquita, António Assunção, António Simões,  
Carlos Sarmiento, Duarte Medeiros, João Albuquerque e Castro, João Monteiro e Castro,  
Germano do Carmo, João Almeida Pinto, José Fernando Teixeira, José França, Luís Mota Capitão,  
Manuel Fonseca, Maria Emília Fonseca, Marina Dias Neto, Nuno Dias, Nuno Meireles,  
Oliveira Santos, Óscar Gonçalves, José A. Pereira Albino, R. Roncon de Albuquerque, Rui Almeida

## INTERNATIONAL SCIENTIFIC COUNCIL

Andrew Nicolaides, Carlos Vaquero, Claudio Muneretto, Christoph A. Nienaber,  
Diego Gonzalez Rivas, Francesco Maisano, Francesco Spinelli, Frank Vermassen, Hence Verhagen,  
Ignacio Lojo, Jean Paul de Vries, Jorge Fernandez Noya, José Galbis Carvajal, Martin Bjorck,  
Marzia Lugli, Nilo Javier Mosquera Arochena, Oscar Maleti, Roberto Chiesa,  
Tomas Centella, Vicent Riambau

Instructions for authors - [www.spctv.pt](http://www.spctv.pt)

**Proprietary and Administration:** Sociedade Portuguesa de Cirurgia Cardio-Torácica e Vascular  
Instituto Bento da Rocha Cabral - Calçada Bento da Rocha Cabral, 14 - 1250-047 Lisboa, Portugal  
[manuscritos@spctv.pt](mailto:manuscritos@spctv.pt)

The Portuguese Journal of Cardiac  
Thoracic and Vascular Surgery publishes  
four annual numbers, each number cost  
€ 10,00.

The annual subscription for Portugal and  
Spain is € 40,00. The Annual subscription  
for Angola, Brasil, Cabo-Verde, Guiné,  
Moçambique and S. Tomé is USA \$35.

For the other countries is USA \$40.  
For the members of the Portuguese  
Society of Cardio Thoracic and Vascular  
Surgery, Surgery and Cardiology the  
distribution is free.

PORTUGUESE JOURNAL OF  
CARDIAC THORACIC AND VASCULAR  
SURGERY 2012

Quarterly Publication  
ISSN - 0873-7215  
Depósito Legal nº60310/93

Sublinhado

Publicações e Publicidade Utopia  
Rua Prof. Vieira de Almeida, nº98 - 1.º A - Bloco B - Piso 0  
1600-371 LISBOA  
Tel.: 21 757 81 35





# TABLE OF CONTENTS

<b>PRESIDENT'S MESSAGE</b>	<i>Gonçalo Cabral</i>	5
<b>VICE-PRESIDENT'S MESSAGE</b>	<i>Miguel Sousa Uva</i>	7
<b>EDITORIAL</b>	My last editorial. <i>Miguel Guerra</i>	9
	Reviewers are at the heart of the academic journals. <i>Marina Dias Neto</i>	11
<b>EDITORIAL COMMENTS</b>	Post-cardiotomy ECMO: time for hope or time for despair? <i>Nuno Carvalho Guerra</i>	13
	The prognostic value of some neglected hematological parameters in carotid artery disease. <i>José Paulo Andrade</i>	15
<b>FOUNDERS</b>	Rui de Lima, Master and Pioneer in Portuguese Thoracic Surgery. <i>Vitor Sá Vieira</i>	17
<b>ORIGINAL ARTICLES</b>	ECMO post-cardiotomy, a single centre experience. <i>Daniela Gouveia, José Máximo, Nuno Costa, Soraia Moreira, Armando Abreu, Paulo Pinho, Jorge Casanova</i>	19
	Extracorporeal membrane oxygenation support for postcardiotomy shock: single center experience. <i>Manuela Silva, Carolina Rodrigues, Tiago Silva, Pedro Coelho, Nuno Banazol, Rui Rodrigues, Paulo Franco, José Fragata</i>	25
	Thoracic sympathectomy: sedation experience. <i>Maria Ribeiro, Marta Coelho, Teresa Monteiro, João Caldeira</i>	31
	Video-assisted thoracoscopic surgery without chest drain placement. <i>Patrícia M. Castro, Susana Lareiro, Joana Rei, José Miranda, Fátima Neves, Miguel Guerra</i>	35
	Mortality scores in surgical correction of abdominal aortic aneurysm in rupture. <i>Filipa Jácome, Marta Ribeiro, João Rocha-Neves, Sandrina Figueiredo-Braga</i>	39
<b>REVIEW</b>	The Impact of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio In Carotid Artery Disease. <i>António Pereira-Neves, Mariana Fragão-Marques, João Rocha-Neves, Luis Gamas, José Oliveira-Pinto, Alfredo Cerqueira, José Andrade, José Fernando-Teixeira</i>	45

<b>CASE REPORT</b>	<b>Right Ventricular myxoma in an asymptomatic patient.</b>	53
	<i>Hagen Kahlbau, Rita Carvalho, Valdemar Marques Gomes, Jorge Pinheiro Santos, José Fragata</i>	
	<b>Delayed presentation of foreign body aspiration in adults.</b>	57
	<i>Ana Catarina Moreira, Carolina Torres, Carlos Couto</i>	
	<b>Complex chest wall deformity causing cardiac arrest: a peculiar pediatric case.</b>	59
<i>Miguel Soares-Oliveira, Sofia Vasconcelos-Castro, Norberto Estevinho</i>		
<b>Pancoast Tumour with Spine Resection - Case Report.</b>	61	
<i>Daniel Cabral, Cristina Rodrigues, Carolina Torres, Wilson Teixeira, Sérgio Livraghi, Mariana Antunes, Francisco Félix</i>		
<b>Deep vein ultrasound-guided thrombolysis.</b>	65	
<i>Joana Ferreira, João Simões, Sandrina Braga, Pedro Sousa, Celso Carrilho, Amílcar Mesquita</i>		
<b>IMAGES IN MEDICINE / IMAGES IN SURGERY</b>	<b>Embolization of percutaneous left atrial appendage occlusion device: rescue surgery.</b>	69
	<i>Manuela Silva, Nuno Banazol, António Fiarresga, José Fragata</i>	
	<b>Varicosity of the communicating vein between the left renal vein and the left ascending lumbar vein.</b>	71
	<i>Luisa Amado Costa, André Peixoto, Luís Vitor, José Fonseca Santos</i>	

# PRESIDENT'S MESSAGE



**Gonçalo Cabral**  
Angiology and Vascular Surgery,  
Hospital Beatriz Ângelo, Loures

## Honoring our legacy, safeguarding the future, overcoming expectations

Dear Members,

The Sociedade Portuguesa de Cirurgia Cardíaca Torácica e Vascular (SPCCTV) is a unique scientific society in numerous aspects, dating back to its creation in 1984.

Since its inception, it has been bold, innovative and visionary, bringing together different specialties in the same institution.

After 37 years, history would enshrine the multidisciplinary as the path to excellence in Medicine, valuing the ideals that countless charismatic figures from national Cardiothoracic and Vascular Surgery had outlined.

This synergy has been throughout SPCCTV's history, simultaneously, its greatest challenge and its great strength. Such strength has allowed us to overcome numerous difficulties, and, I am sure, with the commitment of all the elements of the board that is now starting, we will continue to transform SPCCTV into a society closer to its members, more modern and more relevant to the community of Cardiac, Thoracic and Vascular Surgeons.

It is with great pride and sense of mission that I take on this challenge, aware of the arduous effort it entails, compounded by the pandemic context in which we live.

The purposes of scientific societies cannot be obscured by the constraints caused by the current public health situation. On the contrary, it is at this moment that, more than ever, our members need support in their training, which they see postponed daily by the overwhelming pressure of the care for the COVID-19 patients.

The SPCCTV clearly demonstrated its ability to adapt to this reality with the undisputed success of its 4DVisions 2020 congress, the first in online format of this scientific society.

The more than 400 subscribers, the quality of the work presented by specialists and residents and the enthusiastic discussion between speakers and moderators are the

proof that we are prepared for the challenges of the present and the future.

This event was the test balloon for a new model of interaction among our members, which we will cultivate throughout the 2020-2022 biennium. It is our goal that this interaction does not end at the annual congress, promoting regular events in an online format.

As such, we created a program of podcasts and webinars, dealing with themes from the various specialties, which will be made available on our website and advertised on our social networks. The contents presented are, for the most part, the responsibility of our Clubs of Cardiac, Thoracic and Vascular Surgery Trainees, a source of pride of this board.

This model of personalized training through the intervention of the main recipients - the residents in specific training - generates involvement, relevance and value.

Thus, we will continue to promote the Clubs of Cardiac, Thoracic and Vascular Surgery Trainees, stimulating their autonomous functioning, in synergy with the direction of the Society, ensuring their financial and scientific support for the desired training actions and, especially, ensuring that they actively participate in SPCCTV decisions and destinations.

We continue to believe that promoting the interaction between the trainees and the Society is the best way to ensure the future and relevance to SPCCTV.

Another guarantee of the relevance of society is its digital presence. Over the past 2 years, the SPCCTV website has undergone extensive remodeling, making it more appealing and easier to access. However, we know that there is room for great improvement, and this is one of the areas where intervention is ambitioned by the current board. The creation of links to the online platforms of our similar societies is currently in the operational phase, as well as to guidelines, clinical norms and consensus documents

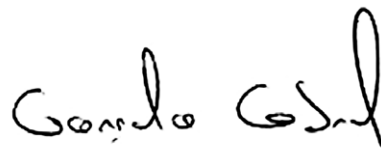
of the various specialties. We will incorporate on our page a space for information to the general population, thus fulfilling one of the purposes of scientific societies. This area of the citizen should include explanations about the main cardiac, vascular and thoracic pathologies and their forms of treatment.

With regard to the Revista da SPCCTV, the current board maintains the firm purpose of indexing the magazine in ISI Web of Science and obtaining an impact factor. The Revista da SPCCTV has, for this purpose, a privileged position in the panorama of the Thoracic, Cardiac and Vascular Surgery, thanks to the praiseworthy effort of all previous editors. It is our obligation to honor this legacy and raise the status of this intangible heritage of our society, making the journal an organ of scientific communication suitable for the publication and curricular enhancement of its authors. Such an objective implies making difficult decisions, which can be emotionally harsh for those who have laid the foundation for this magazine. These solid foundations will be useless if we do not finish a work that can last in time, as a relevant reference for generations of surgeons in training.

Finally, we will join efforts to finalize the National Registry of Cardiac Surgery and Thoracic Surgery, a project that began more than 6 years ago and which is essential to guarantee the quality of care and scientific publication in these areas.

Grateful for the legacy that has been transmitted to me, I will try to set a vision for the future of this society and with overcome all the challenges we face.

Because together, we are stronger!



Gonçalo Cabral | President of SPCCTV



# VICE-PRESIDENT'S MESSAGE



**Miguel Sousa Uva**

Service of Cardiac Surgery, Hospital da Santa Cruz, Carnaxide  
 Department of Surgery and Physiology, Faculdade de  
 Medicina da Universidade do Porto

The biennium of the new SPCCTV Board, which has now begun, under the leadership of its President, Dr. Gonçalo Cabral, is taking place in an environment of enormous uncertainty, caused by the situation of public health crisis. In this context, it is difficult to plan, predict and expect to fulfill all the goals that are part of our objectives: improve the support for the education of residents and young specialists, analyze, independently, and disseminate to our partners the developments of recent knowledge, in the three areas covered by our Society, collaborate with guardianships measuring what we do, inform the public and serve the best interests of our patients. Despite the difficulties, we will do everything, throughout this biennium, to meet the aspirations of personal and professional development of the youngest, to become more open and attentive to the needs of the population, through a renewed website and collaboration with health administrations and authorities.

We propose to review the model of the annual Congress of the Society, taking advantage of the experience acquired during the pandemic: incorporation of face-to-face, if possible, and virtual elements, associating previously recorded presentations and online discussion. In all crises we must find opportunities. The pandemic prevented the annual interaction between everyone, but it had at least one positive side effect, which was to allow discovering new ways of interacting, and at the same time reducing costs, through virtual connections with which we are familiarized, amplifying the voices of those less prone to intervene.

One of the focal points of a Scientific Society is its financial health. We must acknowledge and thank the

previous Direction, for having left us a relieved financial situation, which will allow us to support training courses / scholarships, cross training among our three specialties and other educational initiatives through the Journal of this society.

The National Registry of Cardiac Surgery is in a critical turning point. Three mainland services are in a good position to send data from 2019 or 2020. The obstacles in the other three services, of informatic nature, are currently being the target of a concerted intervention.

This is one of the objectives of the previous Direction, from which we take full responsibility, since it is of vital importance for the specialty and its credibility. We ask everyone to participate, proactively, in the insertion of their patients' data, at each of the patients' stages, in an action that becomes part of the daily routine. SPPCTV will not let this structuring objective "die on the beach" and counts on the collaboration of Sociedade Portuguesa de Cardiologia to achieve it.

Miguel Sousa Uva | Vice-president of SPCCTV



# EDITORIAL



**Miguel Guerra**

Cardiothoracic Surgery, Centro Hospitalar de Vila Nova de Gaia/Espinho  
Faculdade de Medicina da Universidade do Porto  
Casa de Saúde da Boavista, Porto

## My last editorial

The last issue of *Rev Port Cir Cardiotorac Vasc* (RPCCTV) of 2020 was the final one for which I was responsible as editor. The new editorial board will be taking full responsibility for the journal from the present issue on. I wish them every success, and as much pleasure from the journal as I have had in my 4 years of editorship. It has been very satisfying to be able to support – and shape – the development of national cardiac, thoracic and vascular surgery over these years.

Editorial responsibility for a leading scientific journal means that you need to cover a broad area, that is, research work from ‘bench to bedside’. My first step was actually to identify weaknesses in my own knowledge and invite experts in these areas as associate editors or editorial board members to fill these gaps of knowledge. These colleagues have all been extremely important for the increasing success of *RPCCTV* during the recent years.

The editorial process is a team work and I am very grateful for the important contributions from many people. The associate editors and the editorial board members have been essential both as advisors, second opinion assessors and reviewers. Thank you for your vision, hard work and commitment.

Although my formal editorship has come to an end, I will continue to be involved with the journal as an advisor

and reviewer over the coming years. I am also looking forward to the opportunity to give more time to my own research and practice.

In a world largely governed by financial and assertive concerns, publishing high-quality journals is a tough “business”, one that is under constant pressure and requires continuous changes. These changes include the need of the different views of different Editors, which will require new ideas adapted to the new information-acquisition behavior of our peers and readers, and specially of our authors. Your hard work and contributions to *RPCCTV* continue to move the field forward. We look forward to the coming years - the best is yet to come.

Thank you for the opportunity.

Sincerely,



Miguel Guerra | Past Editor-in-Chief



# EDITORIAL



**Marina Dias Neto**

Department of Angiology and Vascular Surgery CHUSJ, Porto  
Cirurgia e Fisiologia, Faculdade de Medicina  
da Universidade do Porto

## Reviewers are at the heart of the academic journals

Once we embrace medicine, we know that medical research is part of the deal. The accelerated technological development and the intensity of clinical research impose the constant need to dissect the medical literature in order to choose the best evidence-based decision.

Additionally, the exciting possibility of being part of the process, the responsibility and the intellectual honesty that are required, are challenges that some of us decide to pursue along with our clinical activity. The writing of a scientific article requires hard work, rigorous data collection and analysis and great network discussion.

The peer review process is a critical component of this creation, a bi-directional learning opportunity, the ultimate challenge the paper needs to face in order to be published.

Peer review of submitted manuscripts defines the process in which professional experts (peers) are invited to critically assess the quality, novelty, theoretical and empirical validity, and potential impact of research by others<sup>1</sup>. As pointed out before<sup>2</sup>, the term 'peer' is the key in this process. Peer means colleague, or equal. Authors and reviewers are essentially the same people with different tasks, taking the socratic method to its most refined form.

Peer review in forms that we would now recognize emerged in the early 19<sup>th</sup> century due to the increasing professionalism of science, and primarily through English scholarly societies<sup>1</sup>, but this process was systematically implemented in publishing only in the 1960s. It lends judgement of scientific integrity, respectability and scientific credibility to the journals. Blinding improves even more the quality and consistency of the reviewers, as well as the quality of the final manuscripts, by eliminating any source of bias in their evaluation<sup>3,4</sup>, something we are proud to adopt in our journal.

From the reviewers' point of view, the opportunity to validate academic work is a privilege and a growing process. By helping to improve the quality of the research

submitted to publication, we are also improving ourselves. Doing peer review makes us better writers, ask more and better questions and also increase networking possibilities within research communities.

At the same time, a great deal of duties are asked to the reviewers: read outside reviewing and think critically, master the subject matter, understand the data sources, read the whole paper, be specific and detailed in your comment, be on time, be respectful.

As such, editors today face a huge problem when trying to find peer reviewers for a manuscript. Frequent causes for reviewer's refusal include reviewer fatigue due to excessive invitations to evaluate manuscripts, lack of time or dissatisfaction with the editorial system.

Traditionally, this function is delegated to a group of persons who perform the task altruistically and without compensation. But we know that leads to lack of motivation in the long run. The global question arises as to how to attract, credit and incentivize reviewers to facilitate good publishing practice.

Having that in mind we would like to give more visibility to our reviewers, as we know they are the cornerstone of the scientific process, despite the lack of true academic recognition.

While other ways of retributing are pending, we would like to give full credit to our cooperating experts. In the last issue of each year, a full list of reviewers will be formally published as a way to recognize and acknowledge all the inputs we received to improve the scientific quality of the papers submitted to our journal.

We also would like to endorse specific platforms that are now emerging that allow reviewers to add reviews to a public profile, and have them verified to be used in promotion and funding applications. Reviewer Credits is one of these platforms ([reviewercredits.com](http://reviewercredits.com)). Reviews performed for partnered journals can be instantly added to the reviewers' profile as they do them. The Open Researcher

and Contributor ID (ORCID) initiative is integrated in the editorial management systems of large and small publishers, and is another platform that may provide a solution to this problem by tracking all academic contributions including records of reviews<sup>5</sup>. The peer review section of the ORCID record is for information about the reviewers' individual peer review contributions.

Although we know our efforts are still far from a true reward for the reviewers' precious time, we will keep track of reviewer rewards and incentives. In the meantime, we hope you stay linked and engaged in the quality and timely evaluations of our journal submissions'.



Marina Dias Neto | Editor-in-Chief

## REFERENCES

1. Tennant JP, Dugan JM, Graziotin D, Jacques DC, Waldner F, Mietchen D, et al. A multi-disciplinary perspective on emergent and future innovations in peer review. *F1000Res* 2017;6:1151.
2. Fernandez-Llimos F, Pharmacy Practice peer r. Scholarly publishing depends on peer reviewers. *Pharm Pract (Granada)* 2018;16:1236.
3. Laband DN, Piette MJ. A citation analysis of the impact of blinded peer review. *JAMA* 1994;272:147-9.
4. Fisher M, Friedman SB, Strauss B. The effects of blinding on acceptance of research papers by peer review. *JAMA* 1994;272:143-6.
5. Gasparyan AY, Akazhanov NA, Voronov AA, Kitas GD. Systematic and open identification of researchers and authors: focus on open researcher and contributor ID. *J Korean Med Sci* 2014;29:1453-6.

# EDITORIAL COMMENT

**Nuno Carvalho Guerra**  
Cardiothoracic Surgery Department  
Hospital de Santa Maria, Centro Hospitalar  
Universitário Lisboa Norte

## Post-cardiotomy ECMO: time for hope or time for despair?

Post-cardiotomy Low Cardiac Output Syndrome (LOCS) is a very severe life threatening situation that is responsible for a significant portion of cardiac surgery mortality, not to mention morbidity. It is defined by a reduced cardiac output that is not sufficient to offer enough oxygenation and ventilation to the tissues. It is estimated to happen in 1 -10% of cardiac surgeries, and also consumes very significant clinical resources. With standard medical therapy, estimated mortality of LCOS ranges from 2% to historically higher values of 38% in the most severe patients. In the cases of LOCS which are refractory to medical therapy and aortic counterpulsation balloon (IABP), Extra Corporeal Membrane Oxygenation (ECMO) is one of the final therapeutic options. We know from personal experience that mortality in these patients, in the absence of ECMO, exceeds 90% of cases. So, an obvious need for further mechanical support exists.

In this number of *Revista Portuguesa de Cirurgia Cardiorácica e Vasculár*, we offer two different Portuguese experiences of patients treated with ECMO in the setting of Post cardiotomy refractory LCOS. Gouveia et al. document their experience at Centro Hospitalar Universitário de São João, in Porto, which was started in 2007, but due to initial disappointing results, was abandoned up until more recently. This Hospital Center is renowned for its extensive use of non post-cardiotomy ECMO, and post-cardiac surgery patients have reaped some of the benefits of non surgical ECMO patients. After bleeding is controlled post surgery, the patients are transferred to a general ICU were ECMO is carried out until decannulation, more prolonged mechanical assistance, or death. Survival to discharge was 38,5% and one year survival was 25%, in patients unable to be weaned from cardiopulmonary bypass and who would have died a few hours after the index surgery.

We can also read Silva et al.'s experience, who publish their results with post-cardiotomy ECMO patients in Hospital de Santa Marta, Centro Hospitalar Universitário

Lisboa Central. This experience also shows satisfactory results, with a survival to discharge of 18% in adult patients. In this study, cannulation was more often central, and bleeding occurred in 45% of patients. No lower limb ischemia was documented. Survival to discharge and at one year was 18% in adult patients.

So, are post-cardiotomy ECMO outcomes dismal, bad, acceptable, or a reason to keep hoping and fighting for better? Should we forget about this technique, or keep using it and improving it? We know that contemporary results, when compared to historical ones, show that survival to discharge after post-cardiotomy ECMO has not improved, but the answer to this less than joyful finding is that we keep operating on sicker and sicker patients, and results of refractory LOCS patients who didn't receive ECMO are known to all.

ECMO has also undergone technical refinings in the last 11 years, that are nothing short of a revolution; this has been obtained through a constant effort of monitoring, improvement, and education from professional societies such as ELSO and medical professionals.

In the specific case of post-cardiotomy ECMO patients, vascular access depends on the operator's choice. On one hand post-sternotomy patients have a previous central vascular access, but bleeding and infection may complicate recovery. On the other, peripheral arterial disease is a common comorbidity of cardiac patients, and lower limb ischemia is a fearsome complication. Antegrade femoral perfusion may help diminish lower limb ischemia but it is not always straightforward to obtain, and appropriate thin cannulas may not be readily available.

Starting a post-cardiotomy ECMO program is always beset with difficulties and frequently initial results are dispiriting. We should remember that any patient with refractory LCOS will probably not survive more than a few hours, and also remember that putative ECMO patients who end up not receiving this therapy and end up not surviving would at least have had a chance, even if it is a 10

or 20% chance. We should all continue striving for better, even if survival to discharge is lower than we wished, since the alternative, not fighting for refractory LCOS patients, means death. These usual initial experiences will in the future undoubtedly give way to better results, since there is a lot of room for improvement in the acute mechanical support field. Further ways to improve results are related to a definite choice between cannulation placement (central or peripheral), ways to deal with lower limb ischemia (determining, in the acute setting, if any femoral artery is better suited for large-bore cannulation), using antegrade perfusion of lower limbs in a timely and safe fashion, and utilizing vascular access automatic suturing devices to prevent groin hematoma. Another situation that could definitely be improved is the left ventricle unloading strategy - none, IABP, or intra-cardiac unloading such as Impella, atrial septostomy, and other modalities. None is currently believed to be vastly superior to others, but in most post-cardiotomy ECMO patients IABP still offers the best compromise between invasiveness and efficacy.

Anticoagulation regimes and renal replacement therapy are two other aspects that will continue to be researched and that will be fine-tuned in the next years, improving short-term results.

If the patient survives to decannulation, a long road ahead still awaits him. Intra-hospital mortality after decannulation is still very significant, and neurological and infectious complications are very frequent and very frequently severe. A long period of rehabilitation is needed, both in the ward and as an ambulatory patient, and long-term quality of life after surviving ECMO is still unsatisfactory.

After hospital discharge, long term mortality varies; in these papers, at one year mortality seems to be stable, but at 5 years it is significantly low. Despite seemingly

disheartening, we should remember this very low survival concerns patients would not survive more than a few hours after the surgery, and have gone on to return home for a few more years.

We believe that ECMO is an invaluable tool to manage LCOS patients, and all moderate and large sized cardiac surgery departments should have this technique to offer these patients. We also believe that improving results of this very specialized technique should be an obligation, and improvement starts at outcome measuring and reporting. In this fashion, these patients who otherwise be dead have an opportunity to survive and return home. Continuous monitoring and improvement will allow even more of these patients to return home and live more years.

#### REFERENCES

1. Meani P, Matteucci M, Jiritano F, Fina D, Panzeri F, Raffa GM, Kowalewski M, Morici N, Viola G, Sacco A, Oliva F, Alyou-sif A, Heuts S, Gilbers M, Schreurs R, Maessen J, Lorusso R. Long-term survival and major outcomes in post-cardiotomy extracorporeal membrane oxygenation for adult patients in cardiogenic shock. *Ann Cardiothorac Surg.* 2019 Jan;8(1):116-122. doi: 10.21037/acs.2018.12.04.
2. Gouveia D, Máximo J, Costa N, Moreira S, Abreu A, Pinho P, Casanova J. ECMO Postcardiotomy, A single center experience. *Rev Port Cir Cardiorac Vasc Jan-Mar 2021*
3. Silva M, Rodrigues C, Silva T, Coelho P, Banazol N, Rodrigues R, Franco P, Fragata J. Extracorporeal Membrane Oxygenation Support for postcardiotomy shock: Single center experience. *Rev Port Cir Cardiorac Vasc Jan-Mar 2021*



# EDITORIAL COMMENT

**José Paulo Andrade**

Department of Biomedicine, Unit of Anatomy,  
Faculdade de Medicina da Universidade do Porto

## The prognostic value of some neglected hematological parameters in carotid artery disease

In 1988, when I was a young resident in the first year of the Clinical Pathology residency in the Emergency Laboratory, we had to perform parts of the complete blood count (CBC) manually. It took approximately 1 minute to have the blood ready to be introduced in a first-generation CBC automated analyzer. The analyzer would give us the basic CBC and hemoglobin values, and the white blood differential was performed in certain selected cases by identifying and counting the cells in a blood smear under a microscope. The values were expressed as relative percentages, and the morphology of the red blood cells and platelets was qualitatively reported. Fortunately, new CBC analyzers were introduced that same year in the Hematology and Emergency Laboratories. The new analyzers presented a series of new parameters, the RDW (red blood cell distribution width) and PDW (platelet distribution width). The word "width" in the RDW and PDW tests does not mean the size of individual red blood cells or platelets. Instead, it refers to the difference in size from the largest to the smallest cells. Most of the CBC counters calculate RDW as a coefficient of variation (CV), and it is expressed as a percentage (12-15%), thus reflecting the distribution curve of the corpuscular volume. I noticed that no one was looking at those still new parameters. At that time I designed some small studies about RDW and presented them in Internal Medicine meetings. One was called "The value of RDW in ferropenic anemias," presenting the classification of anemias based on the RDW and the mean corpuscular volume (MCV). Another was called "RDW is not related to reticulocyte count", where the reticulocyte count was performed manually. At that time, RDW was already seen as a strong marker of iron deficiency, as it often rises before the mean corpuscular volume falls, acting as an early diagnostic clue.

Fast forward to the 21<sup>st</sup> century. RDW is still a little neglected, but now, evidence has accumulated showing that there is a strong link between RDW and inflammation, and it may have prognostic value in nonhematological pathologies.<sup>1</sup> This is particularly prominent in cardiovascular

disorders, and RDW-CV was associated with the incidence of myocardial infarction and stroke.<sup>1</sup> It was also described as a good predictor of mortality in coronary artery disease in patients undergoing percutaneous coronary intervention and ischemic stroke.<sup>2,3</sup> Concerning RDW-CV and carotid atherosclerosis, an association between RDW-CV and carotid intimal thickness was found.<sup>4</sup> and the Tromsø Study found that increased RDW was a predictor of carotid plaque development and progression.<sup>5</sup> It was advanced that the high values of RDW may reflect deficiencies of the integrity of the cell membrane by inducing adhesion between RBCs and endothelium with effects on multiple organ systems and, consequently, associated with adverse outcomes.<sup>1</sup> With these data in mind, Duarte-Gamas et al. in a paper I also co-authored,<sup>6</sup> hypothesized that if there is a high prognostic value of RDW-CV in the aforementioned clinical situations, it could be used to predict long-term outcomes after carotid endarterectomy (CEA). It was found that RDW-CV was associated with MACE (major adverse cardiovascular events defined as a composite outcome of non-fatal myocardial infarction, acute heart failure, and all-cause mortality), myocardial infarction, and all-cause mortality in patients submitted to CEA. The associations were maintained for long-term all-cause mortality and MACE even after adjustment for hemoglobin levels, a potential confounding factor.

The role of inflammation and oxidative stress as culprits of atherosclerosis led Pereira-Neves *et al.*<sup>7,8</sup> to write a narrative review of the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) concerning their prognostic ability in patients with carotid artery disease. The review of these easily obtained hematological ratios included 18 papers with a total of 5339 patients. It was known that NLR was linked to prolonged low-grade inflammation presenting a positive correlation with high-sensitivity C-reactive protein,<sup>9</sup> and PLR was associated with cardiovascular diseases.<sup>10</sup> Both neutrophils and platelets have been implicated in pro-inflammatory status and repair, and there are suggestions of an active role in atherogenesis

due to activation of the complement cascade and cytokine production.<sup>10,11</sup>

As inflammation markers, it was not surprising to find that these hematological ratios revealed an ability to predict outcomes in patients presenting carotid artery disease. In detail, NLR and PLR may predict sub-clinical atherosclerosis and atherosclerosis progression in carotid artery disease. Moreover, they also predict the propensity for carotid stenosis to become symptomatic and morbidity after CEA and carotid stenting. More importantly, these hematological ratios may potentially identify patients with increased susceptibility to becoming symptomatic and with a higher likelihood of postoperative morbidity.

An important caveat: each clinical laboratory should estimate their own reference values as they are not only instrument-dependent but also population-dependent. The advantages of these hematological biomarkers (RDW, NLR, PLR) is that their quantification is fast, easy, inexpensive, and almost universally present and available in all automatic CBC counters. They can not provide definitive prognostic information, but they can supplement clinical decision-making to manage carotid artery disease when understood and used correctly. The information they can deliver is clinically valuable, and these markers can help assess patients who can benefit from CEA.

## REFERENCES

1. Tonelli M, Wiebe N, James MT, Naugler C, Manns BJ, Klarenbach SW, et al. Red cell distribution width associations with clinical outcomes: A population-based cohort study. *PLoS One*. 2019;14(3):e0212374.
2. Poludasu S, Marmur JD, Weedon J, Khan W, Cavusoglu E. Red cell distribution width (RDW) as a predictor of long-term mortality in patients undergoing percutaneous coronary intervention. *Thromb Haemost*. 2009;102(3):581-7.
3. Ye WY, Li J, Li X, Yang XZ, Weng YY, Xiang WW, et al. Predicting the One-Year Prognosis and Mortality of Patients with Acute Ischemic Stroke Using Red Blood Cell Distribution Width Before Intravenous Thrombolysis. *Clin Interv Aging*. 2020;15:255-63.
4. Ren D, Wang J, Li H, Li Y, Li Z. Red blood cell distribution width and carotid intima-media thickness in patients with metabolic syndrome. *BMC Cardiovasc Disord*. 2017;17(1):44.
5. Lappegard J, Ellingsen TS, Vik A, Skjelbakken T, Brox J, Mathiesen EB, et al. Red cell distribution width and carotid atherosclerosis progression. The Tromso Study. *Thromb Haemost*. 2015;113(3):649-54.
6. Duarte-Gamas L, Pereira-Neves A, Jacome F, Fragao-Marques M, Vaz RP, Andrade JP, et al. Red Blood Cell Distribution Width as a 5-Year Prognostic Marker in Patients Submitted to Carotid Endarterectomy. *Cerebrovasc Dis Extra*. 2020;10(3):181-92.
7. Pereira-Neves A, Fragão-Marques M., Rocha-Neves J., Gamas L., Oliveira-Pinto J., Cerqueira A., Andrade J.P., Fernando-Teixeira J. The Impact of Neutrophil-to-Lymphocyte Ratio and Platelet-To-Lymphocyte Ratio in arotid Artery Disease. *SPCCTV*. 2021.28(1)
8. Pereira-Neves A, Rocha-Neves J, Fragao-Marques M, Duarte-Gamas L, Jacome F, Coelho A, et al. Red blood cell distribution width is associated with hypoperfusion in carotid endarterectomy under regional anesthesia. *Surgery*. 2021.
9. Akpek M, Kaya MG, Lam YY, Sahin O, Elcik D, Celik T, et al. Relation of neutrophil/lymphocyte ratio to coronary flow to in-hospital major adverse cardiac events in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. *Am J Cardiol*. 2012;110(5):621-7.
10. Kim H, Conway EM. Platelets and Complement Cross-Talk in Early Atherogenesis. *Front Cardiovasc Med*. 2019;6:131.
11. Rosinska J, Ambrosius W, Maciejewska J, Narozny R, Kozubski W, Lukasik M. Association of platelet-derived microvesicles and their phenotypes with carotid atherosclerosis and recurrent vascular events in patients after ischemic stroke. *Thromb Res*. 2019;176:18-26.

# FOUNDERS

**Vitor Sá Vieira**

Former Senior Thoracic Surgery Consultant,  
Hospital Pulido Valente, Lisbon

## Rui de Lima, Master and Pioneer in Portuguese Thoracic Surgery



Rui Cândido de Figueiredo Lima is an unavoidable figure amongst the founding fathers of Portuguese Thoracic Surgery. He was born on the 25th of November 1910 in Lisbon where he studied and graduated in Medicine and Surgery on the 29th of July 1933.

Admitted to the Civil Lisbon Hospitals in November 1933, he began his clinical career in this prestigious public institution. In 1936 he was one of the applicants admitted to the General Surgery residency, in Dona Estefânia Hospital, under the guidance of the Senior Surgeon Luís Quintela, working alongside with the surgeons João Rafael Bello de Morais, Daniel Carreira and Martins de Queirós.

Hired as a General Surgery resident, he worked initially as a General Surgeon and later as a Thoracic Surgeon, participating in the first lung resections ever performed in Portugal, initiating his dedication to Thoracic Surgery from 1938 onward. After public exams where he was approved with "absolute merit", he attained the title of General Surgery Specialist by the Portuguese Medical Board, but still was not admitted on the Civil Hospitals payroll.

In 1941, a surgical department was created for tuberculosis treatment at Hospital Curry Cabral, headed by Luis Quintela, where he gained experience doing collapse therapy techniques (therapeutic pneumothorax and thoracoplasty) but also lung resections.

Seeking further knowledge he went to England in 1946 with a British Council scholarship, touring several hospitals for 6 months (Brompton Hospital, London Chest Hospital, and London Hospital) and finally working as a resident at the Harefield County Hospital in Uxbridge. He had firsthand experience cooperating with renowned Thoracic surgeons at the time: Price Thomas, Holme Sellors Thompson, Tubbs, Brock and Paterson among others. In Papworth (Cambridge) he came into contact with the cinesotherapy techniques, already vastly applied in the perioperative period, for the rehabilitation of tuberculosis patients.

Back in Lisbon, in the beginning of 1947, he went back to work as a general surgeon with Luis Quintela. By then he had accumulated a wide experience in Thoracic surgery, but was unable to exercise his chosen profession for the Lisbon Civil Hospitals had no posts for Thoracic surgeons, and the National Institute for Assistance to Tuberculous (I.A.N.T.) was not recruiting.

A window of opportunity presented itself when the I.A.N.T. opened two posts for Thoracic surgeons in 1950. Despite having roots in Lisbon, he ran for the D. Manuel II Sanatorium in Vila Nova de Gaia, being hired together with Esteves Pinto in July 1951.

An opening as Head of Department at the Flamenga Sanatorium, in Vialonga, brought him back to the Lisbon District in November 1951. His first action was to increase the treatment capacity from 60 to 130 beds, improving medical and surgical care, for tuberculosis was a social calamity. The creation of a pathology laboratory, a department of bronchoscopic intervention and improvements in the radiology department were other interventions that made an enormous difference in patient care.

The Flamenga Sanatorium referred patients for surgery to the D. Carlos I Sanatorium in Lisbon, but with a waiting list of many months, so he purchased surgical

instruments (some at his own expense) and founded a small Thoracic Surgery Department. In 1952 he performed the first successful lobectomy at the I.A.N.T. From December 1951 to June 1952 he operated 138 patients.

As a Thoracic Surgeon of the I.A.N.T., he also worked at the Encosta da Saúde Sanatorium, accumulating a total of 385 collapse therapies and lung resections surgeries from 1950 to 1961.

In July 1952 he transferred to D Carlos I Sanatorium. Initially he was authorized to operate on tuberculosis only. Later in 1954, due to the necessity to operate associated pathology in infectious tuberculosis patients he was authorized to perform general surgery in these patients at the Sanatorium.

From 1952 to 1955 he underwent several foreign fellowships, at Thoracic Surgery reference centers in Europe, where he contacted with the emerging techniques for lung resection.

At Edouard Herriot Hospital in Lyon he was with Paul Santy and Marcel Bérard in 1952 and 1954. In Sweden, in 1955, he contacted with Craaford and Bjork at the Karolinska. The same year he was in Paris at Broussais Hospital with D'Allaines and Dubost, at Laennec Hospital with J. Mathey, and in Holland at the Groningen University Hospital with Leendert Eerland.

In 1953 he was appointed as Head of Surgery of the I.A.N.T., and as such, Director of the Thoracic Surgery center of the South, at D Carlos Sanatorium. He went to Sousa Martins Sanatorium, in Guarda, on a regular basis every 15 days, to perform surgery but later, by his order, the patients that needed surgery were transferred to D. Carlos I Sanatorium where the patients received better post-operative care.

That same year, with the emergence of Cardiac Surgery, the Lisbon Center of Cardiovascular Surgery was created, within the Thoracic Surgery Center. He accumulated the post as Director of Cardiovascular Surgery until 1955, when a separation of pulmonary surgery and cardiovascular surgery occurred. He carried on as Director of the Thoracic Surgery Center, that grew and evolved under his leadership to become a national Thoracic Surgery reference center perpetuated by his followers.

From 1960 to 1963 he was a member of the Advisory Board for the I.A.N.T. and in 1972 he was appointed by the Secretary of State for a commission to reform the I.A.N.T. With the conversion of the so called "dispensários"s to primary care centers and the D. Carlos I and D. Manuel II Sanatoria into large Hospital Units, these would absorb the patients from some small sanatoria and other even smaller nursing shelters.

In 1975 the D. Carlos I Sanatorium was renamed as Hospital Pulido Valente, classified as a Central Hospital, where he continued as Head of Thoracic Surgery Department, the only surgical department in Portugal dedicated exclusively to non-cardiac Thoracic Surgery, until the present days.

That same year the Thoracic Surgery Department of Hospital Pulido Valente received the first General Surgery residents for the Thoracic Surgery fellowship, and from 1978 onwards, was recognized proficiency for Cardio-Thoracic Surgery training, receiving its first residents.

From 1976 until his retirement in November 1980, he taught General Surgery and Thoracic Surgery as an Invited Professor at the Faculdade de Ciências Médicas in Lisbon (now renamed "Nova Medical School").

On a personal level, I had the privilege of being a resident at his Department, working directly under his guidance, if only for a short time, from 1979 till 1980. He introduced me to the world of Thoracic Surgery from the treatment of tuberculosis and its sequels to the thoracic surgical oncology that was starting to emerge at that time.

His dedication to his patients, the respect for human life and the enthusiasm with which he taught and transmitted all his knowledge and life experience characterized his personality.

He performed the surgical technique with secure and weighted gestures, as a reflection of his vast experience of more than 4500 thoracic surgeries, not avoiding difficult cases but setting surgical indications for the best results with wisdom and talent.

He contributed for the evolution of Portuguese Thoracic Surgery with the publication of the modification of thoracoplasty and surgical treatment of Hydatid cysts techniques in "Variante da técnica de toracoplastia" and "Técnica pessoal de aspiração dos quistos hidáticos", as well as several publications on the technique of bronchoplasty from 1965 to 1980 ("A nossa experiência no tratamento dos adenomas brônquicos" and "Bronchial Adenoma: clinicopathologic study and results of treatment") and other personal unpublished technique modifications that he passed along to his followers.

Affiliated to several national and international scientific Societies, he was an effective member of the Board of Directors of the International Union Against Tuberculosis, and was elected as vice-president of the Portuguese Society of Respiratory Pathology from 1974 -1976.

After his initial experience as secretary to the medical Journal "Medicina Contemporânea" from 1935 to 1945, headed by Reynaldo dos Santos and Alberto Mac-Bride, he ended up publishing 44 papers in national and international medical journals, and was responsible for over 50 lectures in Thoracic Surgery both in Portugal and abroad.

It is unquestionable the way Dr. Rui Cândido de Figueiredo Lima's contribution brought prestige to Portuguese Thoracic Surgery, especially at D. Carlos I Sanatorium, latter, Hospital Pulido Valente.

In 2003 he passed beyond life and time, but his human and professional dimension will survive in the memory of all those who worked alongside him and had the privilege of his company. He was one of the most distinguished and significant pioneers and will go down in History as one of the Fathers of Portuguese Thoracic Surgery.

In conclusion I wish to express my uttermost pride and honor of having worked as his close assistant, on a daily basis, if only for one year, until his retirement at Hospital Pulido Valente

*The Author would like to thank Dr. Fernando Mendonça de Lima, Dr. Rui de Lima's son, for providing the documentation that made this small tribute possible.*

# ECMO POST-CARDIOTOMY, A SINGLE CENTRE EXPERIENCE

Daniela Gouveia<sup>\*1</sup>, José Máximo<sup>1</sup>, Nuno Costa<sup>1</sup>, Soraia Moreira<sup>1</sup>, Armando Abreu<sup>1</sup>, Paulo Pinho<sup>1</sup>, Jorge Casanova<sup>1</sup>

<sup>1</sup>Cardiothoracic Surgery Department - Centro Hospitalar Universitário de São João

\*Corresponding author: daniela.gouveia@gmail.com

## Abstract

**Objectives:** Our objective was to examine the results of ECMO post cardiectomy in Centro Hospitalar Universitário S. João (CHUSJ).

**Methods:** Between 2011 and 2019, 13 patients were cannulated for refractory cardiogenic shock post-cardiectomy; 8 (61,5%) male and 5 (38,5%) female. Patients under 18 years old were excluded.

Data was collected from hospital archives concerning preoperative comorbidities, open-heart surgery procedure, dates of ECMO cannulation and decannulation, postoperative complications, hospital mortality and cause of death. Follow-up was obtained by review of the last outpatient observation.

The outcomes investigated were hospital mortality and survival at 12, 36 and 60 months.

**Results:** After a median ECMO-VA therapy of 6 days (1-16 days), 7 (53,8%) patients were successfully decannulated; from these 2 succumbed from stroke and septic shock, one is still in intermediate care convalescing steadily and 4 were discharged. Overall 8 (61,5%) patients died. 5 (38,5%) survived, 4 were discharged home and 1 is still in intermediate care. Survival (after discharge) at 12, 36 and 60 months was respectively 25%, 16,7% and 8,3%.

Regarding postoperative complications, reoperation for bleeding was necessary in 5 (38,5%), stroke was diagnosed in 2 (15,4%), dialysis in 6 (46,2%), leg ischemia affected 5 (38,5%) and mediastinitis occurred in 1 (7,7%).

**Conclusions:** VA ECMO saves a life in each three patients suffering from refractory cardiogenic shock after cardiac surgery. Despite risks associated with advanced cardiopulmonary support, survivors maintain good health condition.

## INTRODUCTION

In selected patients in cardiogenic shock after heart surgery, venoarterial extracorporeal membrane oxygenation (VA ECMO) offers the possibility for heart recovery or a bridge to investigate other treatments.<sup>1</sup>

## OBJECTIVE

Our objective was to examine the results of post cardiectomy ECMO in Centro Hospitalar Universitário S. João (CHUSJ) in Oporto, Portugal, from 2011 to 2019.

## MATERIAL AND METHODS

We searched our registries for all adult patients treated with ECMO after open heart surgery. Therefore, between 2011 and 2019, 13 patients were cannulated for refractory post-cardiectomy cardiogenic shock: 8 (61,5%) males and 5 (38,5%) females.

Data was collected from hospital archives concerning preoperative comorbidities, open-heart surgery

procedure, dates of ECMO cannulation and decannulation, postoperative complications, hospital mortality and cause of death. Follow-up was obtained by review of the last outpatient observation.

Facing intraoperative failure to wean from cardiopulmonary bypass, eligibility for ECMO was decided by a multidisciplinary team, headed by the main surgeon and the ECMO expert on call. We emphasize that these difficult decisions are unsubstantiated by trials, information is scarce and consequently, absolute contraindications are not established. Type of cannulation was left at surgeon discretion; nonetheless peripheral cannulation was favoured, alongside distal perfusion catheter insertion.

After initial post-operative stabilization in the cardiothoracic unit, specially related to bleeding control in patients with central ECMO, according to the hospital policy all patients were transferred to a dedicated ECMO unit. In addition to regular ICU check-up, ECMO patients had head and peripheral tissue oxygenation near-infrared spectroscopy (NIRS) monitoring to detect ischemia. Moreover, right arm arterial pressure and oxygenation were mandatory to diagnose Harlequin syndrome. The



entire circuit was inspected daily for kinks, damage of tubes and presence of clots. Moreover, transmembrane pressure gradient ( $\Delta P$ ) trends and blood gas exchange analysis denoted oxygenator usability. Concerning anti-coagulation, after complete heparin reversal with pro-tamine, heparin was only initiated after the bleeding resolved and administered to maintain an activated pro-thrombin time (aPTT) 1,8-2 times normal. The objective in all patients was bridge to recovery.

The investigated outcomes were hospital mortality and survival at 12, 36 and 60 months.

**STATISTICAL ANALYSIS**

Descriptive analysis was performed for the entire cohort and data presented as percentage (%), mean and standard deviation, median, range or interquartile ranges (IQRs), according to its distribution. Intergroup analyses were conducted using chi-square tests or Fisher exact test for categorical variables and Student t-tests or Mann-Whitney for continuous variables, according to the dimension and distribution of the samples, respectively. Linear correlations were tested with the Pearson’s test. A stepwise logistic regression was conducted for the multivariate analysis of hospital mortality. The survival data was described with Kaplan Meyer curves and time related comparisons between groups using the log-rank test. The results were considered statistically significant if  $p < 0,05$  was computed.

**RESULTS**

The number of ECMO expanded with the absolute number of surgeries in our department (Fig.1) due to increased experience with the technique.

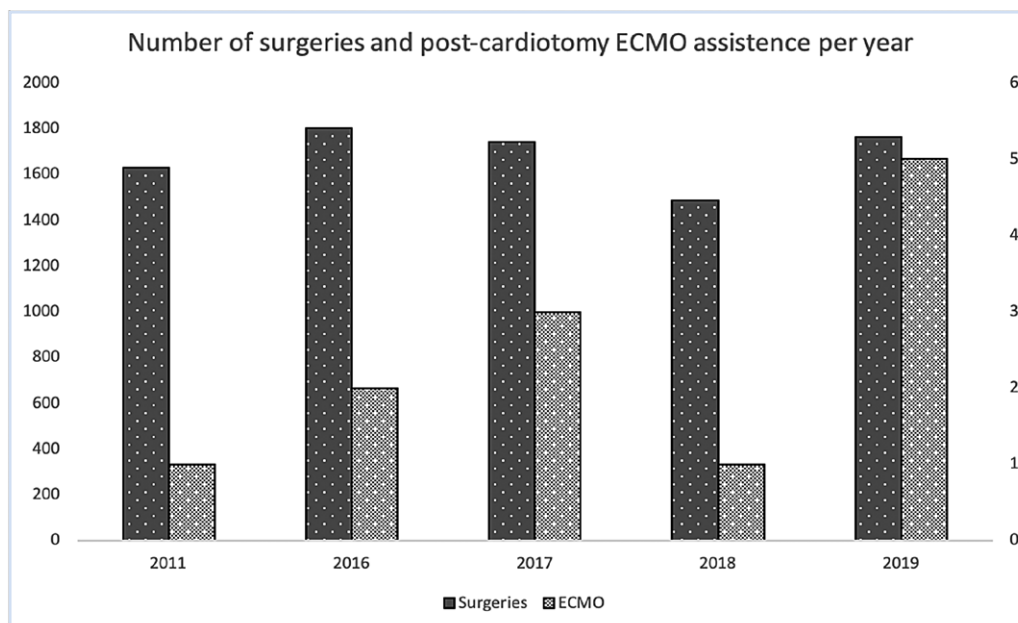
A total of 13 patients unable to wean from cardiopulmonary bypass were treated with VA-ECMO for a median of 6 days (1-16 days). Seven (53.8%) patients were successfully decannulated; from these 2 succumbed from stroke and septic shock, 4 were discharged and 1 was convalescing steadily at the time of writing. Overall, 8 (61,5%) patients died and 5 (38,5%) survived. Survival (after discharge) at 12, 36 and 60 months was respectively 25%, 16,7% and 8,3% (Fig. 2). Survivors remained in NYHA class I or II in follow-up appointment.

Regarding postoperative complications, reoperation for bleeding was necessary in 5 (38.5%), stroke was diagnosed in 2 (15,4%), dialysis in 6 (46,2%), leg ischemia in 5 (38,5%) and mediastinitis occurred in 1 (7,7%). (Table. 2)

**DISCUSSION**

The ECMO program was implemented in our hospital in 2010 through a dedicated team to address the H1N1 pandemic. Over the years experience grew, gradually encompassing sicker patients, namely the post cardiomy refractory cardiogenic shock ones. Although this group of patients is widely recognized as the ones having the worst outcomes with this technique, initial enthusiasm faded as the first patient died and the technique for post cardiomy shock was interrupted until 2017. However, as experience thrived with respiratory and non-respiratory ECMO, this technique was used more frequently and over time, initial worrisome results improved.

Refractory shock after cardiac surgery is more usual after technically challenging and lengthy operations, where the surgical team has put all its best, making the decision to use ECMO difficult. This difficulty is often increased by the emotional link between surgeon, patient



**Figure 1** Correlation of number of surgeries and ECMO per year.

**Table 1** Basic characteristics of the population

Covariates	Overall series (13 patients)
<b>Age (median)</b>	51 years (18-68)
<b>Gender</b>	Female 5 (38,5%) Male 8 (61,5%)
<b>Serum creatinine (μmol/L)</b>	84,9 (32,7-234,31)
<b>PAD</b>	0
<b>COPD</b>	1 (7,7%)
<b>Active endocarditis</b>	1 (7,7%)
<b>Critical state</b>	5 (38,5%)
<b>Insulin-dependent diabetes</b>	1 (7,7%)
<b>NYHA</b>	I – 2 (15,4%) II – 3 (23,1%) III – 2 (15,4%) IV – 6 (46,2%)
<b>CCS IV</b>	6 (46,2%)
<b>LVEF</b>	<21% - 3 (23,1%) 21-30% - 1 (7,7%) 31-50% - 6 (46,2%) >50% - 3 (23,1%)
<b>Recent myocardial infarction</b>	2 (15,4%)
<b>SPAP</b>	<31mmHg – 1 (7,7%) 31-55mmHg – 5 (38,5%) >55mmHg – 2 (15,4%) Unknown – 5 (38,5%)
<b>Urgency</b>	Elective – 7 (53,4%) Urgent – 4 (30,8%) Emergent – 2 (15,4%)
<b>Aorta surgery</b>	6 (46,2%)
<b>Euroscore II (median)</b>	8,7% (0,7-41,6)

PAD – pulmonary artery disease; COPD – chronic obstructive pulmonary disease; NYHA class – New York Heart Association classification; CCS-IV – Canadian cardiovascular society grade IV; LVEF – Left ventricle ejection fraction; SPAP – Systolic pulmonary artery pressure

and families, and by the surgical culture of success. Nonetheless, this decision demands good and objective clinical judgement. Scrutiny of factors identifying patients more likely to survive should warrant the establishment of guidelines.<sup>2</sup> However, until this moment no official recommendations about this topic were published, in particular contra-indications based in factors affecting survival or specific management strategies.

It is known that age is a decisive factor, since older patients have worse prognosis, particularly older than 70 years old.<sup>3</sup> Our oldest patient was 68 years old, nonetheless in this small series age per se did not affect survival ( $p=1,0$ ). Unambiguously, two patients over sixty survived, likewise one in thirties, one in twenties and a 22-year-old woman is

**Table 2** Operative characteristics of the population

Surgical procedure	Overall series (13 patients)
<b>Congenital (anomalous origin of coronary arteries)</b>	1 (7,7%)
<b>Isolated CABG</b>	2 (15,4%)
<b>Isolated valve</b>	2 (15,4%)
<b>Combined valve</b>	2 (15,4%)
<b>Valve &amp; CABG</b>	2 (15,4%)
<b>Heart transplantation</b>	4 (30,8%)
<b>Extracorporeal circulation time (min)</b>	169 (105-451)
<b>Aortic clamp time (min)</b>	97 (0-221)

currently admitted in intermediate care, after chest reconstruction for mediastinitis.

In addition to patient selection, other factors may influence outcomes, namely cannulation strategy. Despite easy conversion of cardiopulmonary bypass to central VA ECMO, since 2017 we favor peripheral cannulation, due to the excessive risk of bleeding and infection with the first. In our study, two out of three patients with central cannulation succumbed from septic shock and multiorgan failure. Recently a meta-analysis corroborated a positive association between central cannulation and hospital mortality in post-cardiotomy VA ECMO.<sup>4</sup>

Peripheral cannulation may be complicated with suboptimal venous drainage and unloading of the left ventricle. These difficulties may be surpassed by simple measures as flow diminution, inotropes or insertion of an IABP.<sup>5</sup> If preliminary measures fail, the preferred and most efficacious technique that has been utilized is atrial septostomy with a trans-atrial cannula placement as an additional inflow cannula to the system;<sup>6</sup> another valuable although more expensive option is Impella heart pump.<sup>7</sup> Surgical techniques have the drawback of invasiveness but permit insertion of large bore catheters to unload the left ventricle and rapidly reverse pulmonary edema. We point out that

**Table 3** Postoperative complications

Covariates	Overall series (13 patients)
<b>Reoperation for bleeding</b>	5 (38,5%)
<b>Stroke</b>	2 (15,4%)
<b>Dialysis</b>	6 (46,2%)
<b>Leg ischaemia</b>	5 (38,5%)
<b>Mediastinitis</b>	1 (7,7%)

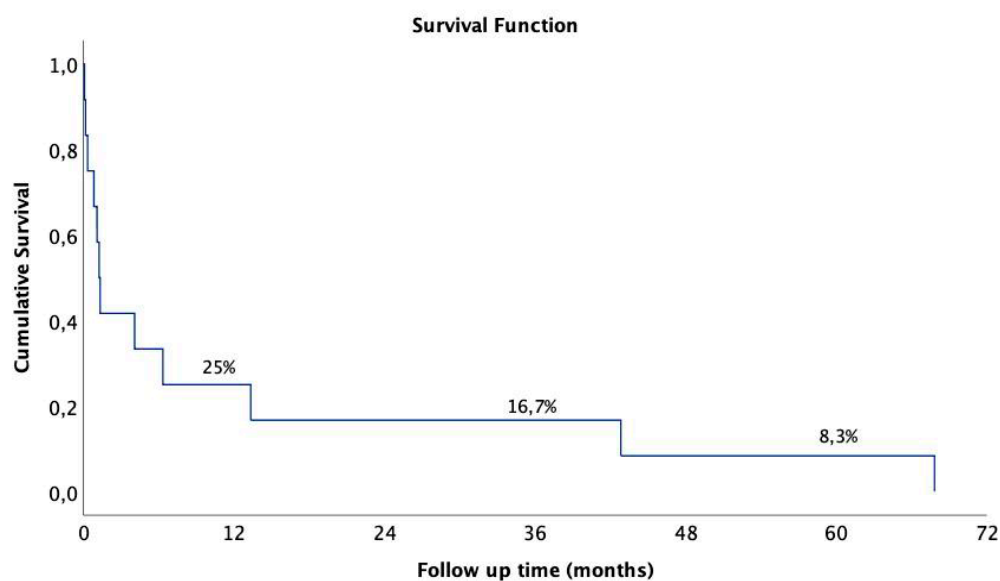


Figure 2

Survival after postcardiotomy ECMO.

patients with lowest ejection fraction often need efficient unloading to avoid irreversible damage.

Left ventricle unloading is controversial. In our study 3 (23,0%) patients had an IABP inserted before VA ECMO, which remained for purposes of left ventricle unloading. In the other nine patients, there was no evidence of severe left ventricle distension in the echocardiogram despite the adoption of conservative measures (no unloading). However, a recent meta-analysis demonstrated any unloading strategy in VA ECMO patients was associated with lower mortality as compared to no-unloading.<sup>8</sup> However, the role of residual left ventricular function remains elusive in these studies, as patients with better residual LV function will probably survive more and depend less on the strategy of unloading.

Four (33,3%) patients already discharged were in NYHA class I-II. In accordance with scientific literature, despite perioperative care improvement, hospital survival remains stable around 30%.<sup>9</sup> We emphasise that, despite this ominous results, VA ECMO salvages a third of patients in post cardiomy refractory cardiogenic shock and survivors can maintain a good health condition.<sup>10</sup> As expected, survival reduces over time as 25%, 16,7% and 8,3% patients are alive 12, 36 and 60 months after surgery.

Frequent complications ensue in patients requiring VA ECMO after heart surgery. We highlight the extended surgical extracorporeal circulation times, triggering coagulation disorders and bleeding, requiring transfusion with associated morbidity and mortality.

In this series, excessive haemorrhage was strongly associated with death, causing the demise of five (38,5%) patients. A meta-analysis showed comparable high rates of reoperation for bleeding (between 32,0-68,0%) in VA ECMO patients.<sup>11</sup> A recent observational study demonstrated association of low haemoglobin (< 9g/dL), fibrinogen (<2g/L), pH (<7,12) and BMI (<25) with early major

bleeding events.<sup>12</sup> Taking into account these findings, cannulation of severely acidotic or anemic patients may be futile, unless amenable to a speedy correction.

Peripheral cannulation may diminish leg perfusion, particularly in hemodynamically unstable patients with large arterial cannulas. Other factors related to ischemia are small femoral arteries, peripheral vascular disease, difficult cannulation<sup>1</sup> and vasoactive infusions.<sup>13</sup> We routinely monitor oxygenated blood in peripheral extremities, aiming for a perfusion pressure above 50mmHg and we perfuse the superficial femoral artery with a 5-7 Fr catheter, according to the patient's size.

In our small series, leg ischemia was a lethal complication, with only one survival of the five (38,5%) patients diagnosed. Wang et al reported an incidence of leg ischemia between 10,0-20,0%<sup>11</sup>, however parallelism of these results is challenging because of our small sample.

In our study, no patient suffered from peripheral artery disease; however vasoactive infusions were universally administered in these coagulopathic patients after long extracorporeal circulation runs.

Ischemic stroke and intracranial bleeding are major complication of VA ECMO. Ischemic stroke has no specific risk factors and does not appear to increase mortality, as opposed to intracranial bleeding, which is linked to female sex, central cannulation, thrombocytopenia and rapid CO<sub>2</sub> clearance.<sup>14</sup> In our analysis 2 (15,4%) patients succumbed to extensive ischemic stroke, but no case of brain hemorrhage was detected. This proportion is in line with recent studies.<sup>11</sup> Unsurprisingly, no case of Harlequin syndrome was diagnosed as in postcardiotomy VA ECMO patients it is uncommon that heart recovery happens before lung recovery.

Advanced circulatory support was maintained during a median of 6 days (1-16 days), without significant disparity between survivors and victims. Survivors were in



VA ECMO for 4-7 days besides a patient still admitted for mediastinitis who was decannulated at 16th day after surgery. Two patients died after more than 10 days of VA ECMO for aortic dissection and refractory right ventricle failure, which may be related to the diagnosis itself. One patient died of ischemic stroke after 10 days of VA ECMO, but one cannot ascertain if it was a complication directly related to ECMO. Biancari *et al* demonstrated prolonged VA ECMO therapy may achieve good results,<sup>15</sup> but Di Mauro recognized duration of circulatory support between 4-7 days achieves the best results.<sup>16</sup> In absence of recovery allowing weaning from ECMO, a patient deemed not having an irreversible clinical condition should maintain longer periods of circulatory support.

In these challenging patients, selection and optimization of perioperative care are vital to achieve good results. We hypothesize that the concentration of postcardiotomy patients in a single Department might improve the expertise and save more lives. As stated by Biancari *et al*, centers that treat more than 50 patients with postcardiotomy venoarterial extracorporeal membrane oxygenation have a significantly lower hospital mortality than lower volume centers.<sup>15</sup>

Despite the small number of this series, its results are in line with others reported<sup>15,11</sup> We understand better patient selection and improved perioperative care, namely improved hemostasis and less transfusions, will ultimately increase survival in our Department.

## CONCLUSION

VA ECMO saves a life in each three patients suffering from refractory cardiogenic shock after cardiac surgery. Despite risks associated with advanced cardiopulmonary support, survivors maintain good health condition.

Further studies in the field are required to better select and treat patients.

## STUDY LIMITATIONS

This study has limitations. It is a retrospective analysis of a very small sample of patients.

## ACKNOWLEDGMENTS

We recognise the proficiency, enthusiasm and readiness of ECMO team assisting us in difficult decisions. We acknowledge the perseverance of Health Professionals from the Intensive Care Department in taking care of these patients.

## REFERENCES

- Baldetti L, G. M. (2020). Strategies of left ventricular unloading during VA-ECMO support: a network meta-analysis. *Int J Cardiol.*, pp. 312:16-21.
- Bardia A, S. R. (2018). Postcardiotomy Venous Arterial Extracorporeal Membrane Oxygenation (VA ECMO) in Adult Patients - Many Questions, Few Answers, and Hard Choices. *J Cardiothorac Vasc Anesth.*, pp. 32(3):1183-1184.
- Biancari F, D. M. (2020). Multicenter study on postcardiotomy venoarterial extracorporeal membrane oxygenation. *J Thorac Cardiovasc Surg*, pp. 159(5):1844-1854.
- Biancari F, P. A. (2018). Meta-Analysis of the Outcome After Postcardiotomy Venous Arterial Extracorporeal Membrane Oxygenation in Adult Patients. *Cardiothorac Vasc Anesth*, pp. 32(3):1175-1182.
- Biancari F, S. D. (2019). Postcardiotomy Venous Arterial Extracorporeal Membrane Oxygenation in Patients Aged 70 Years or Older. *Ann Thorac Surg*, pp. 108(4):1257-1264.
- Di Mauro M, L. R. (2018). Time is your best friend, but it soon becomes your worst enemy: The conflict of venous arterial extracorporeal membrane oxygenation in cardiac surgery. *J Thorac Cardiovasc Surg*, pp. 155(6):2477-2478.
- Ellouze O, A. X. (12 de Mar de 2020). Risk Factors of Bleeding in Patients Undergoing Venous Arterial Extracorporeal Membrane Oxygenation. *Ann Thorac Surg*, pp. S0003-4975(20)30362-3.
- Le Guennec L, C. C. (2018). Ischemic and hemorrhagic brain injury during venous arterial-extracorporeal membrane oxygenation. *Ann Intensive Care*, p. 8(1):129.
- Mariscalco G, S. A. (2019). Peripheral versus central extracorporeal membrane oxygenation for postcardiotomy shock: Multicenter registry, systematic review, and meta-analysis. *J Thorac Cardiovasc Surg*, pp. S0022-5223(19)32376-1.
- Meani P, M. M. (2019). Long-term survival and major outcomes in post-cardiotomy extracorporeal membrane oxygenation for adult patients in cardiogenic shock. *Ann Cardiothorac Surg*, pp. 8(1):116-122.
- PL, M. (2019). The Role of Venous Arterial Extracorporeal Membrane Oxygenation in Postcardiotomy Cardiogenic Shock. *Crit Care Nurs Clin North Am*, pp. 31(3):419-436.
- Wang L, W. H. (2018). Clinical Outcomes of Adult Patients Who Receive Extracorporeal Membrane Oxygenation for Postcardiotomy Cardiogenic Shock: A Systematic Review and Meta-Analysis. *J Cardiothorac Vasc Anesth.*, pp. 32(5):2087-2093.
- Xie A, F. P. (2019). Left ventricular decompression in venous arterial extracorporeal membrane oxygenation. *Ann Cardiothorac Surg.*, pp. 8(1):9-18.



# EXTRACORPOREAL MEMBRANE OXYGENATION SUPPORT FOR POSTCARDIOTOMY SHOCK: SINGLE CENTER EXPERIENCE

Manuela Silva<sup>\*1</sup>, Carolina Rodrigues<sup>1</sup>, Tiago Silva<sup>1</sup>, Pedro Coelho<sup>1</sup>, Nuno Banazol<sup>1</sup>, Rui Rodrigues<sup>1</sup>, Paulo Franco<sup>1</sup>, José Fragata<sup>1</sup>.

<sup>1</sup>Department of Cardiothoracic Surgery, Santa Marta Hospital, Centro Hospitalar Universitário Lisboa Centro, Lisbon, Portugal

\*Corresponding author: manela\_silva@hotmail.com

## Abstract

**Objectives:** We aim to report our experience on venoarterial extracorporeal membrane oxygenation (VA-ECMO) for postcardiotomy shock (PCS).

**Methods:** Single center, retrospective study of all patients on VA-ECMO for PCS, from November 2006 to July 2019. Pediatric and adult patients were analysed separately. Primary outcomes were survival to discharge and one-year survival.

**Results:** Twenty-nine patients were included. Pediatric group (group PED) (62%, n=18): mean age  $1,3 \pm 2,1$  years and 39% male. Adults (group AD) (38%, n=11): mean age  $55,6 \pm 15,9$  years and 64% male. Indications in group PED were complex congenital heart surgery (94%) and heart transplant (6%), with 27% being reoperations; in group AD valvular surgery (45%), aortic surgery (21%), coronary artery bypass grafting (18%) and pulmonary endarterectomy (9%); 45% were reoperations. ECMO support was initiated intraoperatively due to failure to wean from cardiopulmonary bypass in 28% of group PED and 73% of group AD. Central cannulation was performed in all pediatric patients and 82% adults. Bleeding was the most common complication in both groups (group PED 39%, group AD 45%). Mean ECMO support time was respectively  $6,2 \pm 4,9$  and  $6,2 \pm 3,6$  days for group PED and group AD. Weaning rate was 44% in group PED (with 2 patients bridged to LVAD) and 45% in group AD. Survival to discharge as well as one-year survival were both 28% in group PED and 18% in group AD.

**Conclusion:** Despite low survival and high complication rates, VA ECMO support provides a survival benefit in refractory cases, with a dismal prognosis, that would otherwise die.

## INTRODUCTION

Cardiogenic shock following cardiac surgery is a life-threatening condition, causing severe myocardial contractile impairment and reduced organ perfusion.<sup>1</sup> Approximately 1% of patients on postcardiotomy shock (PCS) are refractory to inotropic support and/or intra-aortic balloon pump counter pulsation (IABP) support, have poor prognosis, and almost invariably die without urgent or emergent mechanical circulatory support (MCS).<sup>2,3</sup> Extracorporeal membrane oxygenation (ECMO) is a life-saving therapy for patients with unstable haemodynamics despite optimal loading and maximal dose of inotropes and it is increasingly used as the most advanced short-term therapy to promote cardiac recovery in PCS.<sup>2,4</sup> Venoarterial ECMO (VA-ECMO) provides both circulatory and respiratory support, allowing cardiopulmonary recovery.<sup>5</sup> Additionally, its immediate availability and ease of application not only enables timely rescue and

possible cardiopulmonary recovery, but also offers time for stabilization, identification of residual lesions or neurological compromise, and provides a bridge to decision, in which destination therapy with an upgrade to a ventricular assist device (VAD), heart transplantation, recovery or death will be the possible outcomes.<sup>6,7</sup> However, the exponential increase in ECMO use over the last decades has not been accompanied by improved early survival.<sup>8</sup>

We present our center's experience on VA-ECMO support for refractory PCS. This study aims to report and analyse the outcomes.

## METHODS

We retrospectively reviewed all patients on refractory PCS who were on VA-ECMO for temporary circulatory support from November 2006 to July 2019 in

our center. Pediatric (group PED) and adult (group AD) patients were analysed separately. All data, including patient demographics, ECMO support data, complications, in-hospital and one-year survival, were collected from the hospital clinical records and the department's database. Primary outcomes were survival to discharge and one-year survival.

## RESULTS

### Patients characteristics

A total of 29 patients required VA-ECMO support for PCS between November 2006 and July 2019. Group PED (62%, n=18) had a mean age of  $1,3 \pm 2,1$  years old (range 4 days - 8 years) and 39% were male. Group AD (38%, n=11) mean age was  $55,6 \pm 15,9$  years old (range 30 - 76 years) and 64% were male.

Indications for PC-ECMO in group PED were complex congenital heart surgery in 17 patient and post-heart transplant in one patient; 27% of patients had history of previous cardiac surgery. In group AD, indications were valvular surgery (n=5), aortic surgery (n=3), coronary artery bypass grafting (n=2) and pulmonary endarterectomy (n=1); 45% were reoperations. Other baseline characteristics are listed in Table 1.

### ECMO support characteristics

ECMO support was initiated intraoperatively due to failure to wean from cardiopulmonary bypass (CPB) – group PED 28%, group AD 73%; and due to refractory cardiogenic shock during the first postoperative day – group PED 50%, group AD 18%; between 24 and 48 hours after the surgery – group PED 11%, group AD 9%; and after 48 hours – group PED 11%. Central cannulation was performed in all pediatric patients and in 82% of the adults. ECMO support data is listed in Table 2.

### Postoperative outcomes

Inotropic support over 48 hours and prolonged mechanical ventilation were the most common complications in both groups. Bleeding (need for transfusion support and/ or total bleeding at 48 hours exceeding 10ml/kg, haemorrhagic dyscrasia and upper gastrointestinal bleeding) was 39% in group PED and 45% in group AD. Other complications were cerebrovascular injury (group PED 28%, group AD 9%), renal failure requiring dialysis (group PED 22%, group AD (45%), infection (group PED 39%, group AD 18%) and limb ischemia (group PED 6%, group AD 9% with limb amputation). The remaining outcomes are listed in table 2.

In group PED, two patients who were eligible for assistance upgrade were bridged to LVAD (11%). The

**Table 1** Baseline characteristics

	Group PED (n= 18)	Group AD (n= 11)
Age (years), mean $\pm$ SD <sup>a</sup>	1,3 $\pm$ 2,1	55,6 $\pm$ 15,9
Male gender (%)	7 (39)	7 (64)
Body mass index > 30 (%)	-	2 (18)
Arterial Hypertension (%)	-	7 (64)
Diabetes (%)	-	2 (18)
Hyperlipidemia (%)	-	4 (36)
Smoker (%)	-	5 (45)
Arrythmia	6 (33)	4 (36)
Myocardial infarction (%)	-	3 (21)
Congestive Heart failure (%)	4 (22)	6 (55)
Lung disease (%)	-	1 (9)
Renal disease (%)	-	2 (18)
Cerebrovascular disease (%)	-	-
Peripheral vascular disease (%)	-	1 (9)
Procedure		
Complex congenital heart surgery	17	-
Valvular surgery	-	5
CABG	-	2
Aortic surgery	-	3
Heart transplant	1	-
Pulmonary endarterectomy	-	1
Previous cardiac surgery (%)	5 (28)	5 (45)

<sup>a</sup>SD: standard deviation; <sup>b</sup>CABG: coronary artery bypass grafting.

**Table 2 ECMO data and postoperative outcomes**

	Group PED (n= 18)	Group AD (n= 11)
ECMO timing		
Intraoperative	5 (28)	8 (73)
Postoperative	13 (72)	3 (27)
ECMO <sup>a</sup> cannulation (%)		
Central	18 (100)	9 (82)
Peripheral	-	2 (18)
ECMO weaning (%)	8 (44)	5 (45)
ECMO duration (days), mean±SD <sup>b</sup>	6,2 ± 4,9	6,2 ± 3,6
ICU <sup>c</sup> stay (days), mean±SD	24,8 ± 35,3	11,6 ± 9,5
Hospital stay (days), mean±SD	32,6 ± 46,3	12,5± 9,3
<b>Complications (%)</b>		
Bleeding	7 (39)	5 (45)
Limb ischemia	1 (6)	1 (9)
Cerebrovascular events	5 (28)	1 (9)
Renal failure	4 (22)	5 (45)
Inotropic support >48h	18 (100)	11 (100)
Arrhythmias	3 (17)	1 (9)
MV > 24hd	18 (100)	11 (100)
Infection	7 (39)	2 (18)
Technical	1 (6)	-

<sup>a</sup>ECMO: extracorporeal membrane oxygenation; <sup>b</sup>SD: standard deviation; <sup>c</sup>ICU: intensive care unit; <sup>d</sup>MV: mechanical ventilation.

first patient was on ECMO support for 8 days and the second for 15 days, both for PCS following an atrial switch with coronary bypass grafting of the LAD due to ischemic injury. The first was on LVAD support for 14 days, complicated by intracranial haemorrhage and multiorgan dysfunction, and the other patient was one hour on LVAD, remaining refractory to any support. Both patients died in-hospital.

Mean ECMO support time was respectively 6,2 ± 4,9 and 6,2 ± 3,6 days in pediatric and adult groups. Mean ICU stay and mean hospital stay were 24,8 ± 35,3 and 32,6 ± 46,3 days in group PED, and 11,6 ± 9,5 and 12,5 ± 9,3 days in the group AD. Weaning rate was 44% in group PED and 45% in group AD.

### Survival

Survival to discharge as well as one-year survival were 28% in group PED and 18% in group AD (table 3). In group PED, the cause of death was multiorgan failure in 7 patients, refractory cardiogenic shock in 5 patients and one patient died from haemorrhagic shock. In group AD there were 5 deaths due to multiorgan failure, 4 patients died from refractory cardiogenic shock and one patient from septic shock.

### DISCUSSION

This retrospective study reports our center experience on VA ECMO as our first line MCS for patients on PCS refractory to optimized inotropic support and/or IABP support. Most reported data in the literature arise from retrospective series, mainly single-center experiences.<sup>1</sup> Recently, data from the Extracorporeal Life Support Organization (ELSO) Registry confirmed a substantial increase in PC ECMO use over the last 10 years.<sup>8</sup>

In our series, PC ECMO was performed in a total of 29 patients: 18 children and 11 adults. Survival to discharge was 28% in group PED and 18% in group AD, despite higher weaning rates of 44% (with 2 patients bridged to VAD, but neither of them survived) and 45%, respectively. Mean ECMO support time was respectively 6,2 ± 4,9 and 6,2 ± 3,6 days in pediatric and adult groups. These findings are in line with the literature. The latest expert consensus of EACTS/ELSO/STS/AATS reports a survival of 20-40%, despite a weaning rate of 40-60%; the duration of ECMO support necessary for adequate myocardial recovery is typically 5-7 days.<sup>9</sup> Successful weaning varies greatly within published series, ranging from 31% to 76%, with almost half of the reports showing a weaning rate at or slightly above 50%. Survival to discharge rates are far less, ranging

**Table 3**
**ECMO weaning, survival to discharge and one-year survival**

	Total Runs (n)	Weaning rate (%)	Survival to discharge (%)	One-year survival (%)
Group PED	18	44	28	28
Group AD	11	45	18	18

from 16% to 42%.<sup>10-16</sup> Biancari *et al*<sup>17</sup> showed a weaning rate of 60%, while hospital survival was 36%, probably owing to the combined impact of the underlying disease and the extent of the surgical procedure, along with further complications. Despite the technology improvements and increased experience in ECMO care management, survival has not improved in the last 20 years.<sup>11</sup> ELSO reported that has been a gradual decline in the survival after PC-ECMO.<sup>7</sup> This may be owing, at least in part, to more widespread application of this technology to higher risk patients.<sup>1</sup> Multiorgan failure, despite recovery from myocardial failure, is an important contributor to mortality.<sup>18</sup> In fact, the actual cause of death may be interpreted in a misleading fashion in ECMO patients, as reported by Rastan and colleagues who showed that in almost 30% of autopsies, an unexpected cause of death was found.<sup>19</sup> Another important finding in the present study is that all patients who survived the early postoperative period in both groups were alive at one-year follow-up. Although the follow-up period was short, it demonstrated that once successfully discharged from the hospital, the survivors remained alive. These results justify the use of aggressive treatment for patients with refractory PCS as confirmed by recent publications.<sup>20-22</sup>

The increased complication rate is due to both the ECMO circuit itself and the patients critical state, which can impact the immediate and remote outcomes.<sup>23</sup> Despite inotropic support over 48 hours and prolonged mechanical ventilation, bleeding was the most common complication (group PED 39%, group AD 45%). Other complications were cerebrovascular injury (group PED 28%, group AD 9%), renal failure requiring dialysis (group PED 22%, group AD 45%) and infection (group PED 39%, group AD 18%). The most common complication reported in the literature is bleeding.<sup>24</sup> Recently, Burrell *et al*<sup>25</sup> systematically reviewed 46 studies, encompassing 20375 patients. Likewise, bleeding occurred more frequently, followed by neurological and vascular complications. Intracerebral haemorrhage is a result of the challenging balance between adequate systemic anticoagulation therapy and thrombocytopenia induced by ECMO. Limb ischemia-related complications in peripheral ECMO cannulation can be avoided using a distal perfusion cannula, small femoral arterial cannula size and the use of a vascular graft anastomosed end-to-side to the femoral artery.<sup>9</sup> In our practise, the increased use of a distal perfusion cannula has contributed to minimize limb ischemia, with one case of amputation before its use. Comparable to our results, equipment failure is less reported.

Finally, severe ventricular dysfunction can lead to left ventricular (LV) distension, and VA ECMO may not be effective in decompressing the left side. The lack of evidence about the impact of LV venting on patient outcome, makes it impossible to provide conclusive recommendations for its use as a prophylactic procedure.<sup>9</sup> In our center, concomitant IABP is used to enhance LV unloading in selected cases of ineffective LV ejection with poor or absent aortic valve opening. In pediatric patients, our strategy for decompressing the LV consists in placing a vent through the right superior pulmonary vein.

In this study we reported our experience on PC ECMO and retrospectively analysed our outcomes. Regardless of the low survival rates and higher complication rate, these critical ill patients, from neonates to adults, would have had an even poorer prognosis and died without urgent or emergent rescue VA ECMO support. Increased MCS availability, advancements on ECMO equipment, care management and complication prevention are promising paths to improve the outcomes.

### Limitations

Our report shares the limitations of a single center, retrospective study. Moreover, the sample size is small and heterogeneous, with a short follow-up period, which may underpower the conclusions. Long term outcomes analysis on survival and quality of life would be valuable contributors to this study.

### REFERENCES

1. Lorusso R, Raffa GM, Alenizy K, Sluijpers N, Makhoul M, Brodie D, McMullan M, Wang IW, Meani P, MacLaren G, Kowalewski M, Dalton H, Barbaro R, Hou X, Cavarocchi N, Chen YS, Thiagarajan R, Alexander P, Alsoufi B, Bermudez CA, Shah AS, Haft J, D'Alessandro DA, Boeken U, Whitman GJR. Structured review of post-cardiotomy extracorporeal membrane oxygenation: part 1-Adult patients. *J Heart Lung Transplant*. 2019 Nov;38(11):1125-1143.
2. Meani P, Matteucci M, Jiritano F, Fina D, Panzeri F, Raffa GM, Kowalewski M, Morici N, Viola G, Sacco A, Oliva F, Alyousif A, Heuts S, Gilbers M, Schreurs R, Maessen J, Lorusso R. Long-term survival and major outcomes in post-cardiotomy extracorporeal membrane oxygenation for adult patients in cardiogenic shock. *Ann Cardiothorac Surg*. 2019 Jan;8(1):116-122.
3. Khorsandi M, Dougherty S, Sinclair A, Buchan K, MacLennan F, Bouamra O, Curry P, Zamvar V, Berg G, Al-Attar N. A 20-year multicentre outcome analysis of salvage mechanical circulatory support for refractory cardiogenic shock after cardiac surgery. *J Cardiothorac Surg*. 2016 Nov 8;11(1):151.
4. Rihal CS, Naidu SS, Givertz MM, Szeto WY, Burke JA, Kapur NK et al. 2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care: Endorsed by the American Heart Association, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. *J Am Coll Cardiol* 2015;65:e7-26.
5. Biancari F, Dell'Aquila AM, Mariscalco G. Predicting mortality after postcardiotomy venoarterial extracorporeal membrane oxygenation. *Ann Transl Med*. 2019;7(Suppl 3):S100.
6. Barge-Caballero E, Almenar-Bonet L, Gonzalez-Vilchez F, Lambert-Rodríguez JL, González-Costello J, Segovia-Cubero J, Castel-Lavilla MA, Delgado-Jiménez J, Garrido-Bravo IP, Rangel-Sousa D, Martínez-Sellés M, De la Fuente-Galan L, Rábago-Juan-Aracil G, Sanz-Julve M, Hervás-Sotomayor D, Mirabet-Pérez S, Muñoz J, Crespo-Leiro MG. Clinical outcomes

- of temporary mechanical circulatory support as a direct bridge to heart transplantation: a nationwide Spanish registry. *Eur J Heart Fail*. 2018 Jan;20(1):178-186.
7. Bellumkonda L, Gul B, Masri SC. Evolving concepts in diagnosis and management of cardiogenic shock. *Am J Cardiol* 2018;122:1104-10.
  8. Whitman GJR. Extracorporeal membrane oxygenation for the treatment of postcardiotomy shock. *J Thorac Cardiovasc Surg* 2017; 153:95-101.
  9. Lorusso R, Whitman G, Milojevic M, Raffa G, McMullan DM, Boeken U, Haft J, Bermudez CA, Shah AS, D'Alessandro DA. 2020 EACTS/ELSO/STS/AATS expert consensus on post-cardiotomy extracorporeal life support in adult patients. *Eur J Cardiothorac Surg*. 2021 Jan 4;59(1):12-53.
  10. Elsharkawy HA, Li L, Esa WAS, Sessler DI, Bashour CA. Outcome in Patients Who Require Venous Arterial Extracorporeal Membrane Oxygenation Support After Cardiac Surgery. *J Cardio-Thorac Vasc Anesth* 2010;24:946-51.
  11. Pokersnik JA, Buda T, Bashour CA, Gonzalez-Stawinski GV. Have changes in ECMO technology impacted outcomes in adult patients developing postcardiotomy cardiogenic shock? *J Card Surg* 2012;27:246-52.
  12. Mikus E, Tripodi A, Calvi S, et al. CentriMag venous arterial extracorporeal membrane oxygenation support treatment for patients with refractory postcardiotomy cardiogenic shock. *ASAIO J* 2013;59:18-23.
  13. Unosawa S, Sezai A, Hata M, et al. Long-term outcomes of patients undergoing extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. *Surg Today* 2013;43:264-70.
  14. Ariyaratnam P, McLean LA, Cale ARJ, Loubani M. Extra-corporeal membrane oxygenation for the post-cardiotomy patient. *Heart Fail Rev* 2014;19:717-25.
  15. Li CL, Wang H, Jia M, et al. The early dynamic behavior of lactate is linked to mortality in postcardiotomy patients with extracorporeal membrane oxygenation support: a retrospective observational study. *J Thorac Cardiovasc Surg* 2015;149:1445-50.
  16. Saxena P, Neal J, Joyce LD, et al. Extracorporeal membrane oxygenation support in postcardiotomy elderly patients: the Mayo Clinic experience. *Ann Thorac Surg* 2015;99:2053-60.
  17. Biancari F, Perrotti A, Dalén M, Guerrieri M, Fiore A, Reichart D et al. Meta-Analysis of the Outcome After Postcardiotomy Venous Arterial Extracorporeal Membrane Oxygenation in Adult Patients. *J Cardiothorac Vasc Anesth*. 2018 Jun;32(3):1175-1182.
  18. Hsu PS, Chen JL, Hong GJ, et al. Extracorporeal membrane oxygenation for refractory cardiogenic shock after cardiac surgery: predictors of early mortality and outcome from 51 adult patients. *Eur J Cardiothorac Surg* 2010;37:328-33.
  19. Rastan AJ, Lachmann N, Walther T, et al. Autopsy findings in patients on postcardiotomy extracorporeal membrane oxygenation. *Int J Artif Organs* 2006;29:1121-31.
  20. Unosawa S, Sezai A, Hata M, Nakata K, Yoshitake I, Wakui S et al. Long term outcomes of patients undergoing extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. *Surg Today* 2013;43:264-70.
  21. Rastan AJ, Dege A, Mohr M, Doll N, Falk V, Walther T et al. Early and late outcomes of 517 consecutive adult patients treated with extracorporeal membrane oxygenation for refractory postcardiotomy cardiogenic shock. *J Thorac Cardiovasc Surg* 2010;139:302-11, 11.e1.
  22. Po-Shun Hsu, Jia-Lin Chen, Guo-Jieng Hong, Yi-Ting Tsai, Chih-Yuan Lin, Chung-Yi Lee, Yu-Guang Chen, Chien-Sung Tsai, Extracorporeal membrane oxygenation for refractory cardiogenic shock after cardiac surgery: predictors of early mortality and outcome from 51 adult patients, *Eur J Cardiothorac Surg* 2010, Vol 37, Issue 2, 328-333.
  23. Lo Coco V, Lorusso R, Raffa GM, Malvindi PG, Pilato M, Martucci G et al. Clinical complications during venous-arterial extracorporeal membrane oxygenation in post-cardiotomy and non post-cardiotomy shock: still the achille's heel. *J Thorac Dis*. 2018 Dec;10(12):6993-7004.
  24. Extracorporeal Life Support Organization. Risks and complications. <https://www.else.org/Resources/RisksandComplications.aspx> (9 December 2020, date last accessed).
  25. Burrell AJC, Bennett V, Serra AL, Pellegrino V, Romero L, Fan E et al. Venous arterial extracorporeal membrane oxygenation: A systematic review of selection criteria, outcome measures and definitions of complications. *J Crit Care*. 2019 Oct;53:32-37.





# THORACIC SYMPATHECTOMY: SEDATION EXPERIENCE

Maria Ribeiro\*<sup>1</sup>, Marta Coelho\*<sup>1</sup>, Teresa Monteiro<sup>1</sup>, João Caldeira<sup>2</sup>

<sup>1</sup>Anesthesiology and

<sup>2</sup>Cardiothoracic Surgery, Centro Hospitalar Universitário  
Lisboa Norte, Lisboa, Portugal

\* This article was written in co-authorship by these two authors

\*Corresponding author: mariaribeiro@gmail.com

## Abstract

**Introduction/Study Goals:** Thoracic sympathectomy is considered to be the most effective treatment for hyperhidrosis, a procedure traditionally performed under general anesthesia. Nowadays it's a minimally invasive procedure, which makes it possible to perform under sedation with local anesthesia. The goal in this study was to assess the efficacy and safety of this anesthetic technique in video-assisted thoracic sympathectomy.

**Material and Methods:** The study took place in Centro Hospitalar Universitário Lisboa Norte, between June 2017 and September 2019. The anesthetic technique consisted in a propofol infusion titrated to achieve a moderate to deep sedation, in addition to local anesthesia with lidocaine 2% and ropivacaine 0,75% on surgical incisions. All patients were assessed subsequently for pain and anesthetic or surgical complications, with a 30-day follow-up.

**Results:** From a final sample of 63 patients, most were female (70%), with age ranging between 15 and 57 years old. There were no intra-operative complications. On the immediate postoperative period there were only two cases of poorly controlled pain.

**Conclusion:** Results showed efficiency and safety with sedation associated with local anaesthesia as an anaesthetic technique for video-assisted thoracic sympathectomy. This anaesthetic approach avoids possible complications associated with general anaesthesia and one lung ventilation, with good analgesic efficacy. However, there is still the need for a bigger sample to confirm the obtained results and to strengthen sedation as an anesthetic approach in thoracic sympathectomy.

## INTRODUCTION

Thoracic sympathectomy is presently considered the best treatment for localized hyperhidrosis, an idiopathic condition characterized by excessive sweating, not related to thermal regulation.<sup>1</sup> The estimated incidence ranges 0.6 to 1% and affects more often the palmar and axillary regions.<sup>2</sup>

In spite of not representing a serious health hazard, it impacts heavily on quality of life, with its emotional, social and professional implications of the mostly young working patients.

The pathophysiology underlying hyperhidrosis is not well established. Still, it is known that this condition is not associated to any structural or functional variant of the sweat glands, but to an autonomic nervous systems thermo-regulatory capacity dysfunction.<sup>1</sup>

Other clinical indications for sympathectomy include facial hyperhidrosis, regional algic syndromes, cardiac angina, congenital long QT syndrome and upper limb ischemia.

Conservative strategies have poor results and are limited in time, so the surgical alternative by thoracic sympathectomy is the therapy of choice.<sup>3</sup>

Surgical procedure consists in the interruption of the thoracic sympathetic chain between T2 and T4 levels, beneath the parietal pleura, near to the costovertebral joint.<sup>1,4</sup>

Surgery has the purpose of selectively interrupting sympathetic flow, and can be achieved by techniques such as cautery, resection or surgical clips placement, that allow for procedure reversal if these are removed in a second surgical intervention.

The extent of thoracic sympathectomy must be guided by the surgical indication and varies from center to center. In our center sympathetic flow is interrupted between T2 and T3 for palmar hyperhidrosis, T2-T4 for axillary Hyperhidrosis and T2-T5 for soles hyperhidrosis.

Traditionally, thoracic sympathectomy was performed under general anesthesia, with double-lumen selective intubation.<sup>5,6</sup> However, surgical progress now allow for a video-assisted thoracic sympathectomy, by carbon dioxide insufflation into the chest cavity as a way to create the

room for surgical manipulation. In this way it consists in a minimally invasive procedure, compatible with ambulatory surgery, using sedoanalgesia as an anesthetic technique, as long as the proper patient selection is performed.<sup>7</sup>

At our institution the use of sedoanalgesia for thoracic sympathectomy began in 2017. The objective of this paper is to evaluate the efficacy and safety of this approach as an anesthetic technique for thoracic sympathectomy.

## MATERIALS AND METHODS

The present study occurred at the Centro Hospitalar Universitário Lisboa Norte – Hospital Pulido Valente, from June 2017 to September 2019. To allow for thoracic sympathectomy, the anesthetic technique applied was sedation as an adjuvant to local anesthesia.

Intraoperative monitoring was the standard ASA monitoring. A facial mask or nasal goggles with the appropriate oxygen flow was used to maintain normoxemia. The patient was positioned in a sitting position with upper limbs abduction.

Just before starting surgery, a propofol perfusion was initiated after an initial bolus of 0.5-1 mg/Kg, titrated according to the patient's needs (25-100 mcg/Kg/min) with the objective of keeping a moderate to deep sedation.

For pain control, an alfentanil bolus of 10-20mcg/Kg anticipated the pain peaks- the trocars placement. In the absence of counter-indications, paracetamol 1g and ketorolac 30mg were administered intravenously.

Weight adjusted surgeon infiltration of the local surgical wounds with lidocaine 2% and ropivacaine 0,75% was done in all cases. To decrease the bias of surgical technique, all procedures were performed by the same main surgeon, with altering second surgeons.

Antiemetic prophylaxis was achieved by the administration of dexamethasone and ondansetron, according to the Portuguese Society for Ambulatory Surgery, using a risk score stratification (Apfel score).<sup>8</sup>

In the immediate post-operative period the patients were admitted to the Unidade de Cuidados Anestésicos Pós-Operatórios (UCAPO) until discharge criteria for phase II (infirmery) recovery was fulfilled.

## SELECTION CRITERIA

Eligibility for thoracic sympathectomy under sedoanalgesia in patients with hyperhidrosis was based in a rigorous multidisciplinary evaluation.

The patients were initially evaluated by the surgical team that clarified whether the complaints referred by the patients were caused by hyperhidrosis and if sympathectomy would be beneficial for the patients.

Patients to be treated by sympathetic trunk clipping were excluded from this study, as that technique requires complete immobility of the patient and should therefore be performed under general anesthesia.

After being considered as candidates by the surgical team, patients were observed by the Anesthetic team to insure that all anesthetic, surgical and social criteria for ambulatory surgery were met, and to exclude the presence of comorbidities that would exclude them from performing this procedure under sedoanalgesia.

Patients were informed of the risks and benefits of this intervention technique, assuring verbal and written consent from all candidates for treatment.

Patients were contacted by phone for the 30 day follow-up.

## VARIABLES

The technique efficacy was evaluated on the basis of global satisfaction of the patient and the surgeon in relation to the anesthetic technique used, as well as the postoperative pain evaluation on a numeric pain scale.

Safety was estimated by the number and type of intra and post-operative complications.

All patients underwent a chest X-Ray prior to discharge from the UCAPO.

## STATISTICAL ANALYSIS

In view of the sample size, a descriptive analysis was performed, without statistical conclusions.

## RESULTS

The final sample included 63 patients with a bilateral procedure in all cases.

The main diagnosis leading up to surgery were palmar hyperhidrosis or the association of palmar and axillary hyperhidrosis with a prevalence of 30 and 41% respectively.

Patient age ranged from 15 to 57 years, with a median of 30 years old. Most were females (70%). ASA classification varied between ASA I and II, with a similar distribution of 50.8 and 47.6%, respectively.

In relation to personal history, over half the patients had associated prior conditions, being the most frequent respiratory pathology like asthma (8%), enhanced by smoking habits in 24% of patients.

No intra-operative complications were registered.

Immediate post-operative pain was classified as grade 1-2 in the vast majority of patients (87.3%). Only 2 cases of grade 5 pain were reported, both solved with additional non-opioid analgesia.

## DISCUSSION

The results of our study seem to support the hypothesis that sedoanalgesia is a proper anesthetic approach for the performance of thoracic sympathectomies.

During the intra-operative period hemodynamic and respiratory stability were maintained as well as the adequate post-operative pain control and level of comfort of the patients. We highlight that the complications described were scarce in number and swiftly solved, with no future consequences.

This way, the efficacy and safety of the anesthetic technique here described seems to be confirmed for this surgical procedure.

It is essential to underline that the basis of this approach is an adequate patient selection. Considering the fact that most candidates for thoracic sympathectomy are young, relatively healthy patients, with little associated comorbidities, namely cardiorespiratory, this is the ideal population for the use of sedation. In this way, it is of utmost importance a careful pre-operative evaluation, in order to identify those patients that might not tolerate or be a candidate for the performance of the procedure under sedation only.

Critical analysis of the study concludes that the number of patients is small and enrollment of more patients for sedation thoracic sympathectomy is important to corroborate the preliminary results here reported.

## CONCLUSION

In comparison with general anesthesia, sedation offers some advantages, namely avoiding the need to approach the airway, the need for selective intubation with all the risks associated with it; on the other hand, allows for a faster patient recovery, less disturbing to their daily living.

This way, sedoanalgesia is an anesthetic technique with a good efficacy and safety profile for thoracic video-assisted sympathectomies.

To guarantee the success of this approach it is essential an adequate patient selection in the pre-operative period.

## REFERENCES

1. Thoracic sympathectomy for hyperhidrosis: from surgical indications to clinical results. Vannucci F, Araújo JA. 2017, *J Thorac Dis*, Vol. 9 (Suppl 3), pp. S178-S192. doi: 10.21037/jtd.2017.04.04 .
2. Single-port endoscopic thoracic sympathectomy with monitored anesthesia care: a more promising procedure for palmar hyperhidrosis. Ning Y, Wang Y, Tao X, et al. 2015, *World J Surg*, Vol. 39 (9), pp. 2269-2273.
3. One stage bilateral endoscopic sympathectomy under local anesthesia: Is a valid procedure for treatment of palmar hyperhidrosis? Awad MS, Elzefrawy A, Mansour S, Elshelha W. 2010, Vol. 6, pp. 11-5.
4. The pathophysiology of cervical and upper thoracic sympathectomy. Hasmonai M, Kopelman D. 2003, *Clin Auton Res*, Vol. 13, pp. 140-4.
5. Video-assisted thoracic surgery utilizing local anesthesia and sedation: 384 consecutive cases. Katlic MR, Factor MA. 2010, *Ann Thorac Surg*, Vol. 90(1), pp. 240-245. DOI: 10.1016/j.athoracsur.2010.02.113.
6. State of the art and perspectives in non-intubated thoracic surgery. E., Pompeo. 2014, *Ann Transl Med*, Vol. 2(11), p. 106. doi: 10.3978/j.issn.2305-5839.2014.10.01 .
7. Simpatectomia torácica bilateral R3 - R4 en um paciente sedado non intubado. JM., Mier-Odrizola. 2016, *Gac Med Mex*, Vol. 152, pp. 228-230.
8. Recomendações Portuguesas para a profilaxia e tratamento das náuseas e vômitos no pós-operatório em cirurgia de ambulatório. Vieira V, Marcos A, Patuleia D, Pinto J e Lança F. 2011, *Revista Portuguesa de Anestesiologia*, Vol. 20(2), pp. 11-17.



# VIDEO-ASSISTED THORACOSCOPIC SURGERY WITHOUT CHEST DRAIN PLACEMENT

Patrícia M. Castro<sup>\*1</sup>, Susana Lareiro<sup>1</sup>, Joana Rei<sup>1</sup>, José Miranda<sup>1</sup>,  
Fátima Neves<sup>1</sup>, Miguel Guerra<sup>1,2</sup>

<sup>1</sup>Cardiothoracic Surgery Department, Centro Hospitalar Vila Nova de Gaia/Espinho

<sup>2</sup>Faculdade de Medicina da Universidade do Porto

\*Corresponding author: p.monteiro.castro@gmail.com

## Abstract

**Background:** Placement of chest drain following thoracoscopic procedures has been the gold standard. Nevertheless, a drainless approach may be safe and feasible in selected patients and procedures. In this study we aim to report our clinical experience after drainless video-assisted thoracoscopic surgery.

**Methods:** We retrospectively analyzed data of all subjects submitted to drainless video-assisted thoracoscopic surgery at our centre between January 1, 2010 and December 31, 2019. The preoperative clinical and surgical data and the immediate postoperative data were retrospectively evaluated through the consultation of the clinical processes and the computer registry system. We used descriptive statistics: mean or median, according to data distribution, and absolute or relative frequencies.

**Results:** We included 161 patients, mean age of 31 years (min:15; max:78). We analyzed data from patients submitted to: thoracic sympathectomy(67.1%), wedge resection, for lung biopsy, metastasis or small nodules resection (21.7%), mediastinal cysts removal (6.2%), pleural lesions resection (3.7%) and emphysematous bullae resection (1.2%). The average length of stay was 1 day. Residual pneumothorax was noted in 15 patients (9.3%). Postoperative pleural drain placement due to pneumothorax occur in 4 patients (2.5%). There was no intra-hospitalar mortality.

**Conclusions:** Video-assisted thoracoscopic surgery without postoperative chest drain seems to be valid and safe according to our results.

**Keywords:** chest drain, thoracic surgery, video-assisted thoracoscopic surgery, drainless, sympathectomy, wedge resection.

## INTRODUCTION

Routine placement of an intercostal chest drain has been an established part of thoracic surgery, preventing postoperative accumulation of air, blood and/or fluid in the pleural space.<sup>1-4</sup>

Nevertheless, chest tubes are often reported as the main cause of postoperative pain and can induce morbidities such as immobilization and increase risk of wound infection.<sup>2,3,5</sup> The duration of chest tube insertion is known to be one of the main factors influencing hospitalization length of stay and consequently increasing medical costs.<sup>4,6,7</sup> Additionally, unnecessary chest tube placement is thought to reduce the potential advantages of thoracoscopic surgery.<sup>3,8</sup> Several studies have described that omission of chest tube placement after various thoracoscopic procedures is a safe and feasible approach that may help reduce postoperative pain and shorten hospital stay, allowing an earlier recovery.<sup>2,7,9</sup>

The purpose of this study is to determine the validity and feasibility of avoiding chest drain following video assisted thoracoscopic surgery (VATS).

## METHODS

This is a single-center and retrospective study including all subjects without pleural drainage following uniportal VATS at *Centro Hospitalar Vila Nova de Gaia/Espinho*, between January 1, 2010 and December 31, 2019. Procedures in which drain placement was waived include: thoracic sympathectomy, mediastinal cysts removal, pleural lesions, emphysematous bullae resection and wedge resection for lung biopsy, small peripheral lung nodules or metastasis. The preoperative, surgical and immediate postoperative data were retrospectively evaluated through the access of clinical files and computer registry system.

**Table 1**

Variables	Description
Age	in years, at the time of the surgery
Gender	female/male
Residual pneumothorax	yes/no, apical air is observed on postoperative X- Ray
Subcutaneous emphysema	yes/no, if air is detected beneath the skin
Postoperative chest drain placement	yes/no, chest drain placement after surgery
In hospital mortality	yes/no, at the hospital admission to surgery or up to 30 days after surgery

Demographic data were recorded. Postoperative early complications were evaluated, namely residual pneumothorax, subcutaneous emphysema and need of postoperative chest drain placement as well as results of the immediate postoperative period: hospitalization time and in-hospital mortality. Variables description is shown in Table 1.

Categorical variables are presented in absolute values and in valid percentage and the continuous variables as mean and standard deviation, or median and minimum and maximum, according to data distribution.

The IBM–SPSS Statistics version 26.0 (IBM, United States of America) program was used in data management and statistical analysis.

## RESULTS

During the study period, 161 surgeries were performed without chest drain placement following uniportal VATS at our center. Median age was 31.0 (15;78) years, 62.1% being female.

Most frequent procedure allowing drainless approach was sympathectomy (67.1%), following wedge resection either for lung biopsy, metastasis or small nodules resection (21.7%), mediastinal cysts removal (6.2%), pleural lesions resection (3.7%) and emphysematous bullae resection (1.2%). Procedures performed are detailed in Table 2.

Residual pneumothorax was noted in 15 patients (9.3%). Postoperative pleural drain placement due to pneumothorax occurred in 4 patients (2.5%). Subcutaneous emphysema was noted in 15 patients. None required reoperation. Postoperative early complications are detailed in Table 3.

Median length of stay was 1.0 (1;7) days. In-hospital mortality did not occur. Two patients required readmission after discharge, one due to pneumothorax and another due to hemothorax.

**Table 2**

Procedures	Frequency (%)
Sympathectomy	108 (67.1)
Wedge resection	35 (21.7)
Mediastinal cysts removal	10 (6.2)
Pleural lesions resection	6 (3.7)
Emphysematous bullae resection	2 (1.2)

**Table 3**

Postoperative early complications	Frequency (%)
Residual pneumothorax	15 (9.3)
Subcutaneous emphysema	15 (9.3)
Postoperative pleural drain placement	4 (2.5)
Reoperation	0 (0.0)

## DISCUSSION

Routinely, a chest tube is placed in the pleural cavity to monitor and treat any air leaks and to remove blood or fluid accumulation.<sup>8</sup> However, chest tube management is determined mainly by personal experience rather than standardized criteria. In 2011, the Society of Thoracic Surgeon, the American Association for Thoracic Surgery, European Society of Thoracic Surgeons, and the General Thoracic Surgery Club produced a consensus guidelines in order to unify management of chest tube.<sup>10</sup> Unfortunately, selection criteria for patients who do not require chest tube placement following VATS was not approached.

A plethora of studies had reported that the potential benefits of uniportal VATS might be undervalued by unnecessary chest drainage after surgery.<sup>5,7</sup> Postoperative chest tube itself may adversely impact on the respiratory system, since it contributes to increased postoperative pain, worsened ventilation capacity, preventing patient ambulation, increasing risk of infectious complications and thus, prolonging length of stay.<sup>1,5,11,12</sup> Furthermore, early chest drain removal is one of the strategies that is thought to prevent or reduce post-operative chronic neuralgia incidence.<sup>2</sup> Sienel *et al* conducted a prospective randomized study in which they confirmed that the need for analgesia is reduced in the absence of an intercostal drain.<sup>13</sup> Although the effect of avoiding chest tube placement on postoperative pain was not analyzed in our study, it is our belief that avoiding postoperative chest tube placement has several advantages with respect to pain management.



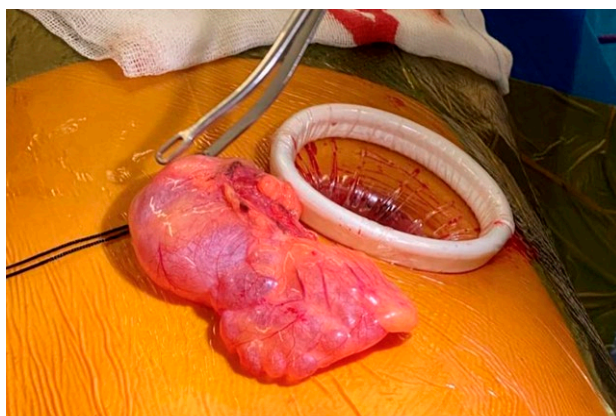


Figure 1

Uniportal VATS, mediastinal cyst removal without postoperative chest drain placement.

The concerns associated with omitting chest tube drainage after pulmonary resection refer to the risk of symptomatic pneumothorax, bleeding, and pleural effusions.<sup>2,7,8</sup> Due to notable improvements in recent years in instruments and devices used in VATS, there should be very few air leaks and little bleeding from the stapler line [8]. Nevertheless, residual pneumothorax was revealed on post-operative X-Ray in 15 patients (9.3%) and subcutaneous emphysema occurred in 15 patients (9.3%). The majority of these patients were asymptomatic and these findings had, therefore, no clinical impact. However, 4 out of 15 patients in whom residual pneumothorax was noted required chest tube placement: one after wedge resection, one after thoracic sympathectomy and two after emphysematous bullae resection due to primary pneumothorax.

In a study conducted by Watanabe *et al*, the presence of bullas or emphysema forbid drainless approach, because of an increased risk of postoperative development of new air leaks from the staple line.<sup>8</sup> Additionally, patients routinely received mechanical pleurodesis by pleural abrasion to prevent recurrence, and so, these patients probably need chest tube placement because of oozing of injured pleura.<sup>4</sup>



Figure 2

Postoperative X-ray after mediastinal cyst removal without postoperative chest drain placement.

On the other hand, in a prospective randomized trial, Park *et al* demonstrated that patients undergoing VATS wedge resection for primary pneumothorax can be treated without postoperative chest tube.<sup>7</sup> Further investigation on this field is needed. For instance, Zhang *et al*, conducted a study in which double-lumen catheter was inserted for prophylactic and remedial air-extraction in patients who have undergone thoracoscopic wedge resection, which can be an interesting strategy to reduce incidence of postoperative pneumothorax after drainless surgery.<sup>14, 15</sup>

According to our retrospective data review, the most frequent procedure allowing drainless approach was thoracic sympathectomy. In this surgery, sympathetic chain is interrupted (clipped, cut, or cauterized), theoretically without parenchymal lung injury. Rare complications include pneumothorax requiring chest tube drainage, pleural effusion, hemothorax, chylothorax, and persistent intercostal neuralgia.<sup>16,17</sup> As previously mentioned, within 4 patients (2.5%) who needed postoperative pleural drain placement due to pneumothorax, 1 was after sympathectomy. We hereby can conclude that drainless approach is safe and effective for this procedure.

Another potential advantage of omitting chest drain placement is reduction on postoperative length of stay and thus potential cost savings.<sup>1,2,9,11,18</sup> Our median length of stay was 1.0 (1;7) day. Post-operative management without a chest drain is thought to diminish morbidity and enhance recovery, with patients been discharged within less than 24 hours. Moreover, selective intercostal drain placement on the basis of air leak opens up for the possibility of outpatient surgery.<sup>19,20</sup> Omission of chest drain has even been described after major lung resection as segmentectomy or lobectomy by VATS in multiple studies. In these trials, careful pneumostasis with alveolar air leaks sealed with bioabsorbable mesh and/or fibrin glue allowed the omission of chest tube drainage in the majority of patients without increasing the risk of adverse events.<sup>5,6</sup>

Our data therefore, support that uniportal VATS without chest drain placement does not compromise postoperative length of stay and can be performed effectively without increased risk of major complication or death.

## STUDY LIMITATIONS

There are some limitations in our study: 1) retrospective, single center experience limiting external validity and 2) relatively small sample size. Our analysis lacked assessment on postoperative quality of life, pain management and patient satisfaction. Future investigations with more patients and a longer follow-up would be interesting to confirm potential improvement of these outcomes with drainless approach.

## REFERENCES

1. Satherley, L.K., et al., Routine placement of an intercostal chest drain during video-assisted thoracoscopic surgical lung

- biopsy unnecessarily prolongs in-hospital length of stay in selected patients. *Eur J Cardiothorac Surg*, 2009. 36(4): p. 737-40.
2. Liao, H.C., et al., Thoracoscopic Surgery Without Drainage Tube Placement for Peripheral Lung Nodules. *Ann Thorac Surg*, 2020. 109(3): p. 887-893.
  3. Cheng, K., et al., A chest tube may not necessary in children thoracoscopic lobectomy. *Medicine (Baltimore)*, 2019. 98(26): p. e15857.
  4. Lu, T.Y., et al., Evaluation of the necessity for chest drain placement following thoracoscopic wedge resection. *Surg Today*, 2017. 47(5): p. 606-610.
  5. Ueda, K., et al., Omitting chest tube drainage after thoracoscopic major lung resection. *Eur J Cardiothorac Surg*, 2013. 44(2): p. 225-9; discussion 229.
  6. Murakami, J., et al., The Validation of a No-Drain Policy After Thoracoscopic Major Lung Resection. *Ann Thorac Surg*, 2017. 104(3): p. 1005-1011.
  7. Park, J.B., et al., Postoperative chest tube placement after thoracoscopic wedge resection of lung for primary spontaneous pneumothorax: is it mandatory? *J Thorac Dis*, 2018. 10(8): p. 4812-4818.
  8. Watanabe, A., et al., Avoiding chest tube placement after video-assisted thoracoscopic wedge resection of the lung. *Eur J Cardiothorac Surg*, 2004. 25(5): p. 872-6.
  9. Lesser, T., et al., Lung Biopsy Without Pleural Drainage. *Dtsch Arztebl Int*, 2019. 116(19): p. 329-334.
  10. Brunelli, A., et al., Consensus definitions to promote an evidence-based approach to management of the pleural space. A collaborative proposal by ESTS, AATS, STS, and GTSC. *Eur J Cardiothorac Surg*, 2011. 40(2): p. 291-7.
  11. Nakashima, S., et al., Feasibility and safety of postoperative management without chest tube placement after thoracoscopic wedge resection of the lung. *Surg Today*, 2011. 41(6): p. 774-9.
  12. Holbek, B.L., et al., Thoracoscopic pulmonary wedge resection without post-operative chest drain: an observational study. *Gen Thorac Cardiovasc Surg*, 2016. 64(10): p. 612-7.
  13. Sieneel, W., et al., Early chest tube removal after video-assisted thoracoscopic surgery. Results of a prospective randomized study. *Chirurg*, 2005. 76(12): p. 1155-60.
  14. Zhang, J.T., et al., Prophylactic air-extraction strategy after thoracoscopic wedge resection. *Thorac Cancer*, 2018. 9(11): p. 1406-1412.
  15. Zhang, J.T., et al., Randomized Trial of an Improved Drainage Strategy Versus Routine Chest Tube After Lung Wedge Resection. *Ann Thorac Surg*, 2020. 109(4): p. 1040-1046.
  16. McConaghy, J.R. and D. Fosselman, Hyperhidrosis: Management Options. *Am Fam Physician*, 2018. 97(11): p. 729-734.
  17. Cerfolio, R.J., et al., The Society of Thoracic Surgeons expert consensus for the surgical treatment of hyperhidrosis. *Ann Thorac Surg*, 2011. 91(5): p. 1642-8.
  18. Luckraz, H., et al., Is an intercostal chest drain necessary after video-assisted thoracoscopic (VATS) lung biopsy? *Ann Thorac Surg*, 2007. 84(1): p. 237-9.
  19. Blewett, C.J., et al., Open lung biopsy as an outpatient procedure. *Ann Thorac Surg*, 2001. 71(4): p. 1113-5.
  20. Holbek, B.L., et al., Fast-track video-assisted thoracoscopic surgery: future challenges. *Scand Cardiovasc J*, 2016. 50(2): p. 78-82.



# MORTALITY SCORES IN SURGICAL CORRECTION OF ABDOMINAL AORTIC ANEURYSM IN RUPTURE

Filipa Jácome\*<sup>1</sup>, Marta Ribeiro<sup>2</sup>, João Rocha-Neves<sup>1,3</sup>, Sandrina Figueiredo-Braga<sup>4</sup>

<sup>1</sup>Centro Hospitalar Universitário de São João, EPE

<sup>2</sup>Escola de Medicina – Universidade do Minho

<sup>3</sup>Department of Biomedicine - Unit of Anatomy, Faculdade de Medicina da Universidade do Porto

<sup>4</sup>Hospital da Senhora da Oliveira de Guimarães, EPE

\*Corresponding author: filipajacome@gmail.com

This article was presented in SPCCTV 4Dvisions Congress (22/11/2019 – 24/11/2019)

## Abstract

**Introduction:** Ruptured abdominal aortic aneurysm's treatment relies on the emergent surgery, considering preoperative prognosis. There are several scores that estimate perioperative mortality of ruptured abdominal aortic aneurysm, however, the accuracy of such algorithms in some populations remains unknown.

**Objective:** Compare the prognostic validity of the Weingarten score with the Glasgow Aneurysm Score and the Vancouver Scoring System. Validation of three prognostic ruptured abdominal aortic aneurysms tools for the Portuguese population.

**Material and Methods:** A retrospective analysis of consecutive patients with ruptured abdominal aortic aneurysm surgically treated, in a peripheral and in a referral hospital between 2012 and 2016 was performed. The 30-day mortality discriminative power was analysed using each score.

**Results:** 120 patients were included. The mean Glasgow Aneurysm Score was  $98.53 \pm 19.57$ , the Vancouver Scoring System was  $3.64 \pm 1.43$ . The Weingarten score classified 51 (43.2%) patients as stable and 67 (56.8%) as unstable. The three scores demonstrated some predictive value concerning mortality, although Glasgow Aneurysm Score demonstrated the highest area under the ROC curve (0.74) and the best discriminatory capacity for cut-off points with higher specificity. Neither of the scores demonstrated clinically useful predictive value.

**Conclusions:** The Weingarten score did not present as a superior prediction model of preoperative mortality in ruptured abdominal aortic aneurysm. None of the scores, even when optimized for a higher specificity, could select which patients will not benefit from surgical intervention. The Glasgow Aneurysm Score was validated for the Portuguese population.

**Keywords:** Ruptured Abdominal Aortic Aneurysm, Mortality, Scores.

## 1. INTRODUCTION

Abdominal aortic aneurysm (AAA) estimated prevalence in men over 65 is 5% and rupture is considered a surgical emergency with an elevated mortality rate (80 to 90%), which makes this condition one of the ten most common causes of death.<sup>1-4</sup> In Portugal, an AAA prevalence of 2.4% was described<sup>5</sup>, and the survival rate of ruptured abdominal aortic aneurysms (rAAA) who reach the hospital alive is less than 50%.<sup>2</sup> The *European Society for Vascular Surgery* recommends the screening of AAA in men over 65<sup>6,7</sup>, notwithstanding, in Portugal, systematic screening has not yet been implemented.<sup>5</sup>

Due to the high surgical risk of correcting a ruptured AAA, some surgeons choose to select which patients

should be treated.<sup>4</sup> In 1994, Samy et al demonstrated that mortality in ruptured abdominal aortic aneurysms was influenced by age, preoperative shock (defined as blood pressure less than 80 mmHg), and personal history of heart disease, renal disease, and cerebrovascular disease, thus developing the Glasgow Aneurysm Score (GAS).<sup>8</sup> However, another variables also have been proposed as predictors of mortality, such as sex, low hematocrit or hemoglobin values, syncope or cardiac arrest.<sup>9-11</sup> Thus, several new scores have been presented<sup>12</sup>, nevertheless, GAS has frequently been shown to be a good predictor of mortality and the standard of comparison.<sup>13-15</sup> The Vancouver Scoring System (VSS) considers mainly preoperative variables that we can easily access, such as age, loss of consciousness and cardiac arrest.<sup>16</sup>

In April 2016, Weingarten et al proposed a new score based exclusively on the clinical presentation of the patient prior to surgery: hypotension (systolic arterial pressure <80 mmHg), loss of consciousness, cardiac failure and necessity of tracheal intubation.<sup>17</sup> Patients categorized as "unstable" presented higher mortality rates, correlating directly with higher GAS values.<sup>17</sup> Sutton *et al*<sup>18</sup> suggested that a risk assessment scoring system should be accurate, quick, easy to use bedside and should include a small number of variables, which were presented in these scores. Additionally, this scores consider preoperative characteristics, that turns it possible to use in immediately in admission, and is an advantage relatively to other scores.

In 2015, Abreu *et al* developed a study to evaluate the applicability of GAS in a Portuguese center.<sup>14</sup> They showed that it wasn't possible to identify a cut-off able to provide a guaranteed mortality so we could be refusing treatment to some patients, that could possibly survive.<sup>14</sup> However, to the extent of our knowledge, there are no further studies in Portugal or in other countries that try to prove the applicability of the Weingarten score.

The aim of this study was to compare the mortality predictive value of these scores. The secondary aim was to validate the scores to the Mediterranean population.

## 2. MATERIAL AND METHODS

All patients submitted to open or endovascular repair due to ruptured abdominal aortic aneurysm were evaluated. The sample was consecutively selected from the surgical database of two Portuguese hospitals, a peripheral (Hospital Senhora da Oliveira (HSO)) and a referral center (Centro Hospitalar Universitário de São João (CHUSJ)), between 2012 and 2016.

### 2.1. Procedure

The identification of patients submitted to ruptured abdominal aortic aneurysm repair by conventional or endovascular surgery was performed resorting to ICD 9 coding (HSO: Ruptured abdominal aorta aneurysm (441.3); Surgical correction of ruptured abdominal aortic aneurysm - 3952 | CHUSJ: ruptured abdominal

aortic aneurysm - 441.3; graft endovascular implant in the abdominal aorta (3971); Aneurism repair, ncop (3952); aorto-iliac femoral bypass (3925). A table was created by matching the patient's number to a tabulated number, to create the database. Three patients were excluded due to lack of data.

The scores were calculated according to the formulas described in table 1.

### 2.2. Statistical analysis

The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 25 (IBM Corp., released 2017. IBM SPSS Statistics for Windows, version 25.0, Armonk, NY, USA).

For the continuous variables, the mean and standard deviation (SD) were presented in those with normal or median distribution and interquartile ranges (AIQ) in those with normal distribution deviation, as well as maximum (max) and minimum (min) values of it. The normality of the variables was tested using the Shapiro-Wilk test or the analysis of asymmetry and kurtosis values, considering values between -1 and 1 as presenting a normal distribution.<sup>19</sup>

The Student's t-test for independent samples and the Mann-Whitney test were used to verify the relationship between the quantitative variables and perioperative mortality, depending on whether or not the normality assumptions were met, respectively.<sup>20</sup> The Chi-square test and the Fisher's exact test were used, when appropriate, for the categorical variables.<sup>21</sup> To discriminate the power of each score in predicting the mortality of patients with ruptured AAA, the Receiver Operating Characteristics (ROC) analysis was used, obtaining the area under the ROC (AUROC) as an effective measure of the inherent validity of the scores, as well as the values of sensitivity and specificity for the different cut-off points.<sup>22</sup> The R<sup>2</sup> with the Nagelkerke method was also calculated for each score.

## 3. RESULTS

The final sample consisted of 120 patients, patients' characteristics were listed in table 2. Table 3 shows the preoperative presentation of patients with ruptured AAA. Regarding the calculation of mortality scores, mean GAS was 96.<sup>30</sup>

**Table 1** Formulas to Glasgow Aneurysm Score and Vancouver Scoring System calculation

Glasgow Aneurysm Score <sup>12,25</sup>	Age (years) + 7 (if heart disease is present) + 10 (if cerebrovascular disease is present) + 17 (if shock is present) + 14 (if acute/chronic renal disease is present)
Vancouver Scoring System <sup>12</sup>	Mortality calculation predicted by Vancouver Score $\frac{e^x}{1 + e^x}$ in which "e" is the basis of the natural logarithm $x = -3.44 + 0.062 \times \text{age} +$ : <ul style="list-style-type: none"> <li>• loss of consciousness (yes "+ 1.14", no "- 1.14")</li> <li>• cardiac arrest (yes "+ 0.60", not "- 0.60")</li> </ul>

**Table 2** Patients characteristics and personal history

	HSO* n (%)	CHUSJ† n (%)	Total n (%)
Age (years)			
Mean ± SD‡	74.00 ± 3.00	73.00 ± 1.00	72,51 ± 9.34
min - max	61.00 – 91.00	51.00 – 96.00	5.10 – 96.00
Gender			
Male n (%)	11 (100.0)	98 (89.9)	109 (90.8)
Female n (%)	0 (0.0)	11 (10.1)	11 (9.2)
Personal History			
Smokers n (%)	3 (75.0)	55 (56.7)	58 (57.4)
Cardiac Disease n (%)	4 (36.4)	34 (35.8)	38 (35.8)
Renal Disease n (%)	5 (45.5)	57 (58.2)	62 (56.9)
Cerebrovascular Disease n (%)	2 (22.2)	14 (13.5)	16 (14.2)

\*HSO – Hospital Senhora da Oliveira; †CHUSJ – Centro Hospitalar Universitário de São João; ‡SD – standard deviation.

**Table 3** Preoperative clinical variables

	HSO* n (%)	CHUSJ† n (%)	Total n (%)
Hypotension	7 (63.6)	50 (47.2)	57 (48.7)
Cardiac arrest	2 (20.0)	11 (10.7)	13 (11.5)
Loss of consciousness	4 (36.4)	32 (30.8)	36 (31.3)
Intubation necessity	1 (91.0)	56 (58.3)	57 (53.3)

\*HSO – Hospital Senhora da Oliveira; †CHUSJ – Centro Hospitalar Universitário de São João

(SD ± 23.935, min 58 - max 184). The mean VSS was 3.64 (SD ± 1.43, min 1.48 - max 7.38). It was found that the Weingarten score ranked 51 patients (43.2%) as stable and 67 (56.8%) as unstable.

In the perioperative period (30 days), 6 patients died in HSO and 66 died in CHUSJ, corresponding to a mortality of 54.5% and 60.6%, respectively.

In the univariate analysis only renal disease (OR 2,78 95%; IC 1,26–6,14; p=0.011) and hypotension (OR 3,75;

95% IC 1,71–8,26; p=0.001) were considered statistically significant for 30 days mortality. Age was also considered significantly higher in the group of patients who died with a mean age of 74.97±9.4; min 51; max 96 (p <0.001).

The scores performance predicting mortality is described on Table IV.

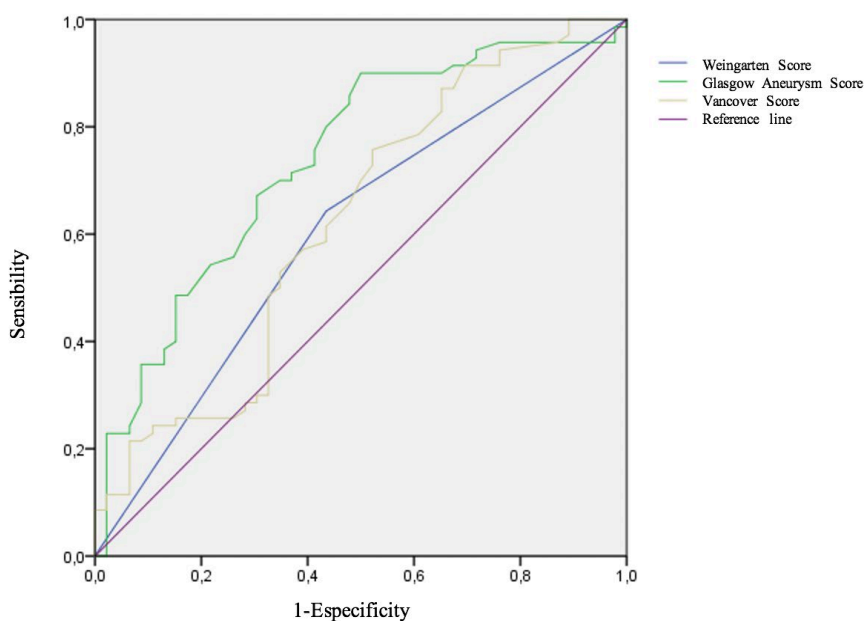
Regarding the ROC analysis, it was found, for all three scores, a linear increase in the risk of death (figure 1). GAS Area Under ROC (AUROC=0.74 [0.641-0.826],

**Table 4** Univariate analysis of mortality scores (\*GAS, †VSS and Weingarten)

	Death	Survival	p Value
GAS*			
Mean ± SD <sup>  </sup>	103.80 ± 17.653	90.79 ± 19.640	< 0.001 <sup>a,††</sup>
min <sup>  </sup> - max <sup>¶</sup>	58 - 141	59 - 184	
VSS†			
Mean ± SD <sup>  </sup>	3.83 ± 1,46	3.36 ± 1.34	0.060 <sup>b</sup>
min <sup>  </sup> - max <sup>¶</sup>	1.98 – 7.38	1.48 – 6.51	
Weingarten			
Unstable n (%)	46 (68.7)	21 (31.3)	OR** (95% CI <sup>#</sup> ) 2.28 (1.07 – 4.84) 0.031 <sup>c††</sup>
Stable n (%)	25 (49.0)	26 (51.0)	

a - Man-Whitney test  
b - T-student test  
c - Chi-square test  
†† Statistically significant p-value

\*GAS - Glasgow Aneurysm Score; †VSS - Vancouver Scoring; <sup>||</sup>IQR – Interquartile range; <sup>||</sup>SD - Standard Deviation; <sup>||</sup> minimum; <sup>¶</sup> maximum; <sup>#</sup> CI – Confidence interval; <sup>\*\*</sup>OR – Odds Ratio


**Figure 1**

ROC (Receiver Operating Characteristics) curve – comparison between Glasgow Aneurysm Score, Vancouver Scoring System and Weingarten Score.

$R^2$  0.154) demonstrated the best performance, followed by the Vancouver Score (VSS) with AUC=0.62 [0.526 – 0.738],  $R^2$  0.047. The Weingarten score had an AUROC of 0.60 [0.493 – 0.703],  $R^2$  0.05. A cutoff value for GAS above 87.5 was established, which had a sensitivity of 90% and a specificity of 50%. For the Vancouver score, the cut-off value was 2.76, with a sensitivity of 76% and a specificity of 48%. Thus, patients with scores on GAS and VSS scores higher than the defined cut-off points, twenty-four and twenty-six survived, respectively.

The agreement between Weingarten Score and GAS (cut-off: 98) was 28,6% ( $\pm$  8.7%), with  $p=0.02$ .

#### 4. DISCUSSION

Because of the high mortality of surgical correction of a ruptured AAA, some surgical groups select which patients should be submitted to surgical intervention.<sup>4</sup> Death risk estimates may be useful as a point of reference for the surgeon when this options are contemplated.<sup>10</sup>

In this study the demographics (sex, smoking status and age) are in agreement with the bibliography. It was also found that age, renal disease and hypotension were the only variables in our study that were related to mortality. Nevertheless, these results resemble those of Abreu et al who verified this same relationship.<sup>14</sup> They only differed in what concerns age of those who died: in their study patients who died were significantly younger, unlike our study, where they were significantly older (74 vs 68,  $p < 0.001$ ).<sup>14</sup> Mortality in both centers was estimated at 60%, similar to those obtained in another study.<sup>2</sup>

Of the three scores studied, GAS obtained consistently better results regarding correlation with mortality, presenting a higher AUROC (0.74), although it was not able to

predict the 95% probability cut off to 30 day death risk. The findings are consistent with those previously reported.<sup>13,15,23</sup> Relatively to VSS, a relation to mortality in the univariate analysis was not found, although presented an AUROC of 0.62. By 2015, Van Beek *et al* found an AUROC for this score of 0.72, but concluded that VSS overestimated death considerably.<sup>13</sup> Thus, this score is effective in identifying patients at high risk (> 90%), but it will not behave as well in patients with a lower mortality risk (>80%).<sup>4,24</sup> Despite the ease in obtaining the variables for the calculation of this score, the necessity of coefficients and mathematical calculations that are too complex make it impractical and, therefore, it has been seldom used.<sup>4</sup>

In spite of GAS and VSS were limited in their ability to identify patients at high risk and without survival benefit with surgical intervention<sup>13</sup>, these scores may be of value in comparative studies between different hospitals and surgeons, by allowing stratification of the patient's prognosis.<sup>4,13</sup> However, the necessity to know the patient's clinical data limits the applicability of these scores.<sup>25</sup>

In their study, Weingarten *et al* classified 85 patients as "unstable", with a mortality rate of 41% in these patients. In those classified as "stable", mortality was 13.0%.<sup>17</sup> Although, patients classified as "unstable" actually had a higher mortality rate (68.7%,  $p < 0.031$ ), approximately half (49.0%) of those considered "stable" died. Therefore, it is safe to say that in our study, the Weingarten score did not behave as a better predictor of mortality, nor did have a good discriminative power. Although the ease and rapid application in the emergency context, this score did not appear to be superior to the two previously known scores, GAS and VSS.

There is an agreement of 28.6% ( $p=0.02$ ) between Weingarten Score and GAS which means that the addition of both scores could have an additional predictive value, although adding complexity to the calculation.

The main limitation of this study is the retrospective data collection, especially those related to the preoperative presentation which, due to the emergency of the procedure, is sometimes conditioned. On the other hand, it becomes impossible to mimic the reality of urgency in the search for variables for the calculation of scores, which makes it hard to evaluate their real applicability in clinical practice.

In this study the three scores failed to predict mortality reliably, which is in accordance with the bibliography quoted.<sup>4,10,13,14,17,23,24</sup> Every recommendation is against the exclusive use of scores to select for surgery. Thus the score are effective as adjuvants for the surgical decision, and helping estimate the comparative balsa risks and results of each center.

## 5. CONCLUSION

GAS was found to be the best among the three scores studied, although it failed to discriminate the futility of surgery in patients at high risk. Nevertheless, the objective of validating the GAS score for the Portuguese population, represented by HSO and CHUSJ patients, was reached. The authors concluded that the Weingarten was not useful in clinical practice and that it did not supplant the GAS.

Nevertheless, this new score should not be set aside, but rather reformulated in future studies, so that, for each variable a quotation is attributed to increase the classification stratification and thus present a score that become more reliable in predicting mortality.

## REFERENCES

- Golledge J MJ, Daugherty A, Norman P. Abdominal Aortic Aneurysm: Pathogenesis and Implications for Management. *Arteriosclerosis, Thrombosis and Vascular Biology*. 26(12):2605–13.
- Castro-Ferreira R N-SM, Sampaio S, Gonçalves Dias P, da Costa-Pereira A, Freitas A. Dez anos de tratamento de aneurismas da aorta abdominal – exclusão endovascular vs. cirurgia aberta nas diferentes regiões portuguesas. *Angiologia e Cirurgia Vascolar*. 2015;11(2):51–60.
- Coelho A LM, Gouveia R, Sousa P, Campos J, Augusto R, et al. Aneurisma da aorta abdominal – estudo epidemiológico de doentes tratados num centro por um período de 8 anos com o objetivo de promover o rastreio populacional. Aneurisma da aorta abdominal – estudo epidemiológico de doentes tratados num centro por um período de 8 anos com o objetivo de promover o rastreio populacional. *Angiologia e Cirurgia Vascolar* [Internet]. 2016 Sep (Available from: <http://linkinghub.elsevier.com/retrieve/pii/S1646706X16300088>).
- Tambyraja AL MJ, Chalmers RTA. Prediction of outcome after abdominal aortic aneurysm rupture. *Journal of Vascular Surgery*. 2008;47(1):222–30.
- Castro-Ferreira R MP, Couto P, Barreira R, Peixoto F, Aguiar M, et al., realização. RpdadaaePoids. Rastreio populacional de aneurisma da aorta abdominal em Portugal – o imperativo da sua realização. *Angiologia e Cirurgia Vascolar*. 2016.
- Moll FL PJ, Fraedrich G, Verzini F, Haulon S, Waltham M, et al. Management of Abdominal Aortic Aneurysms Clinical Practice Guidelines of the European Society for Vascular Surgery. *European Journal of Vascular and Endovascular Surgery*. 2011.
- Chaikof EL BD, Dalman RL, Makaroun MS, Illig KA, Sicard GA, et al. The care of patients with an abdominal aortic aneurysm: The Society for Vascular Surgery practice guidelines. *Journal of Vascular Surgery*. 2009;50(4):S2–49.
- Samy AK MG, MacBain G. Glasgow aneurysm score. *Cardiovascular surgery (London, England)* [Internet]. 1994 Feb [cited 2016 Dec 7] (Available from: <http://www.ncbi.nlm.nih.gov/pubmed/8049922>):2(1):41–4.
- Prance S. WY, Cosgrove C., Walker A., Wilkins D., Ashley S. Ruptured Abdominal Aortic Aneurysms: Selecting Patients for Surgery. *European Journal of Vascular and Endovascular Surgery* [Internet]. 1999 Feb [cited 2017 Jun 13] (Available from: <http://linkinghub.elsevier.com/retrieve/pii/S1078588498907183>).
- Chen JC HH, Salvian AJ, Taylor DC, Strandberg S, Myckatyn TM, et al. Predictors of death in nonruptured and ruptured abdominal aortic aneurysms. *Journal of Vascular Surgery*. 1996;24(4):614–23.
- Tambyraja A MJ, Chalmers R. Predictors of Outcome After Abdominal Aortic Aneurysm Rupture: Edinburgh Ruptured Aneurysm Score. *World Journal of Surgery* [Internet]. 2007 Oct 17 [cited 2017 Jun 16] (Available from: <http://link.springer.com/10.1007/s00268-007-9181-5>):31(11):2243–7.
- Cornelis G. Vos M, PhDa, Jean-Paul P.M. de Vries, MD, PhD,\*, Correspondence information about the author MD, PhD Jean-Paul P.M. de Vries Email the author MD, PhD Jean-Paul P.M. de Vries, Debora A.B. Werson, MPAb, Eric P.A. van Dongen, MD, PhDc, Michiel A. Schreve, MDa, Çağdaş Ünlü, MD, PhDa. Evaluation of 5 different aneurysm scoring systems to predict mortality in ruptured abdominal aortic aneurism patients. December 2016; Volume 64, Issue 6: Pages 1609–16.
- van Beek SC RJ, Vahl AC, Wisselink W, Peters RJG, Legemate DA, et al. External Validation of Models Predicting Survival After Ruptured Abdominal Aortic Aneurysm Repair. *European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery* [Internet]. 2015 Jan [cited 2016 Nov 7] (Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25488513>):49(1):10–6.
- Abreu R MeCJ, Bastos Gonçalves F, Rodrigues G, Quintas A, Ferreira R, et al. Aplicação do Glasgow Aneurysm Score como modelo preditivo de mortalidade em doentes com rutura de aneurisma da aorta abdominal. *Angiologia e Cirurgia Vascolar*. 2016.
- Visser JJ WM, Kievit J, Bosch JL. Prediction of 30-day mortality after endovascular repair or open surgery in patients with ruptured abdominal aortic aneurysms. *Journal of Vascular Surgery* [Internet]. 2009 May [cited 2017 Jun 17] (Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0741521408022647>):49(5):1093–9.
- José Oliveira-Pinto MD1, Inês Carneiro1,3, Joel Sousa1,3, Sérgio Sampaio MD PhD1,4, Armando Mansilha MD PhD1,3. Preoperative mortality scores in ruptured aneurysms — bibliographic

- review. *Angiol Cir Vasc*. dez. 2017;vol.13 no.4.
17. Weingarten TN TL, Licatino LK, Bailey CH, Schroeder DR, Sprung J. Ruptured Abdominal Aortic Aneurysm: Prediction of Mortality From Clinical Presentation and Glasgow Aneurysm Score. *Journal of Cardiothoracic and Vascular Anesthesia*. 2016;30(2):323–9. .
  18. Sutton R B, Brooks M, Sarin S. The Surgical Risk Scale as an improved tool for risk-adjusted analysis in comparative surgical audit. *Br J Surg*. 2002;89:763–8.
  19. YH. C. Biostatistics 101: Data Presentation. *Singapore Medical Journal* [Internet]. 2003(Available from: <http://www.smj.org.sg/article/biostatistics-101-data-presentation>):44(6):280–5.
  20. YH C. Biostatistics 102: Quantitative Data - Parametric and Non-parametric Tests. *Singapore Medical Journal* 2003;44(8):391–6.
  21. YH. C. Biostatistics 103: Qualitative Data - Tests of Independence. *Singapore Medical Journal*. 2003;44(10):498–503.
  22. Kumar R IA. Receiver operating characteristic (ROC) curve for medical researchers. *Indian Pediatrics* [Internet]. (Available from: <http://link.springer.com/10.1007/s13312-011-0055-4>):48(4):277–87.
  23. Krenzien F WG, Hau H-M, Matia I, Benzing C, Atanasov G, et al. Risk Stratification of Ruptured Abdominal Aortic Aneurysms in Patients Treated by Open Surgical Repair. *European Journal of Vascular and Endovascular Surgery* [Internet]. 2016 Jan [cited 2017 Jun 17](Available from: <http://linkinghub.elsevier.com/retrieve/pii/S1078588415005213>):51(1):30–6. .
  24. Hsiang YN TR, Nicholls SC, McCullough K, Chen JC, Lokanthan R, et al. Predicting death from ruptured abdominal aortic aneurysms. *The American Journal of Surgery* [Internet] 2001 Jan [cited 2017 Jun 18];181(1):30–5. (Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0002961000005389>).
  25. De Rango P SG, Manzone A, Cieri E, Parlani G, Farchioni L, et al. Arbitrary Palliation of Ruptured Abdominal Aortic Aneurysms in the Elderly is no Longer Warranted. *Arbitrary Palliation of Ruptured Abdominal Aortic Aneurysms in the Elderly is no Longer Warranted. European Journal of Vascular and Endovascular Surgery* [Internet]. 2016 Jun [cited 2017 Apr 22](Available from: <http://linkinghub.elsevier.com/retrieve/pii/S107858841600099X>):51(6):802–9.



# THE IMPACT OF NEUTROPHIL-TO-LYMPHOCYTE RATIO AND PLATELET-TO-LYMPHOCYTE RATIO IN CAROTID ARTERY DISEASE

António Pereira-Neves<sup>\*1,2,3</sup>, Mariana Fragão-Marques<sup>2,4</sup>, João Rocha-Neves<sup>1,2,3</sup>, Luís Gamas<sup>2,3</sup>, José Oliveira-Pinto<sup>2,3</sup>, Alfredo Cerqueira<sup>3</sup>, José Andrade<sup>1</sup>, José Fernando-Teixeira<sup>3</sup>

<sup>1</sup>Department of Biomedicine – Unit of Anatomy and

<sup>2</sup>Department of Surgery and Physiology, Faculdade de Medicina da Universidade do Porto

<sup>3</sup>Department of Angiology and Vascular Surgery and

<sup>4</sup>Department of Clinical Pathology, Centro Hospitalar Universitário de São João, Porto

\*Corresponding author: antonio.hpneves@gmail.com

## Abstract

**Introduction:** Inflammation is a common underlying feature of atherosclerosis. Several inflammatory biomarkers have been reported to have prognostic value, in several areas, including in vascular surgery. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) may permit to identify patients at greater risk for cerebrovascular events, tailor patient management, improve preoperative status and possibly develop target anti-atherosclerotic therapy. However, studies reporting usefulness of these hematological biomarkers in the context of carotid artery disease are still scarce.

The aim of this study was to review the literature concerning the prognostic ability of NLR and PLR in the subpopulation of vascular patients with carotid artery disease.

**Methods:** A Medline search was performed in order to identify publications focused on the physiopathology of NLR and PLR and their impact in the management of patients with carotid artery disease.

**Results:** The study identified 18 articles with a total of 5339 patients. NLR is associated with carotid intima-media thickness, carotid plaques, carotid stenosis, symptomatic stenosis and intra-stent restenosis after carotid artery stenting and cognitive dysfunction after carotid endarterectomy. PLR is associated with carotid stenosis, symptomatic stenosis and predicts post-operative outcomes after carotid artery revascularization, including post-operative stroke, acute coronary syndrome and all-cause mortality.

**Conclusions:** The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have the ability to predict sub-clinic atherosclerosis, atherosclerosis progression in carotid artery disease and propensity for carotid stenosis to become symptomatic along with morbidity following CEA and carotid stenting. Consequently, these parameters may be considered to tailored therapy and improve patient management.

## INTRODUCTION

Carotid disease affects 3-4% of the general population with varying degrees according to age, gender and race.<sup>1</sup> In addition to cognitive decline, it is a major risk factor for ischemic stroke, with ipsilateral carotid atherosclerosis accounting for 20-30% of these events.<sup>2</sup> Patients with  $\geq 50\%$  carotid artery stenosis have an annual stroke risk of 0.34% and an annual transient ischemia attack (TIA) risk of 1.78%.<sup>1</sup> Despite the improved outcomes in recent years, stroke still poses a high burden of morbidity and mortality, leaving impaired half of those who survive.<sup>3</sup>

Thus, understanding carotid stenosis pathophysiology and progression and its crosstalk with sustained low-grade inflammation remains significant in identifying new disease predictors.<sup>4-7</sup> Several inflammation biomarkers have been reported, including new emerging complete blood count (CBC) related biomarkers, given its wide availability and prognostic value, which could allow closer monitoring of patients with expected negative outcomes, tailoring patient management or pre-operative status improvement and possibly the development of targeted anti-atherosclerotic therapy.<sup>8,9</sup> Platelets play a crucial role in the development and advance of atherosclerotic

disease by the secretion of proinflammatory cytokines.<sup>10,11</sup> Likewise, neutrophils promote plaque destabilization and subsequent rupture while stimulating thrombogenesis and increasing platelet aggregation.<sup>12,13</sup> Lymphopenia is associated with physiologic stress and immunodeficiency, cardiovascular complications, and mortality.<sup>14,15</sup> Two CBC markers with increasing relevance are the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), which have been suggested to predict outcomes in tumors, systemic lupus erythematosus, sepsis, and cardiovascular disease.<sup>15-23</sup> In the vascular field, these parameters have been associated with increased risk of death within two years of a major vascular surgery,<sup>24</sup> greater risk for progression or *de novo* chronic limb-threatening ischemia (CLTI)<sup>25</sup> and amputation rates in patients with CLTI,<sup>26-28</sup> poorer limb survival after embolectomy for acute limb ischemia,<sup>29</sup> higher risk of complications following surgical abdominal aortic aneurysm repair<sup>30</sup> and worse prognosis after acute mesenteric ischemia.<sup>31,32</sup> However, clinical relevance of these parameters in patients with carotid stenosis is scarcely described.

The aim of this study was to review the literature regarding the prognostic relevance of NLR and PLR in the subpopulation of vascular patients with carotid artery disease.

## METHODS

A Medline search was performed in order to identify articles focused on these hematological parameters and their pathophysiology and effects on outcomes in carotid artery disease. Keywords used for research included "carotid disease", "neutrophil-to-lymphocyte ratio", "platelet-to-lymphocyte ratio", "hematological parameters," and "carotid endarterectomy". Additional articles of scientific interest for the purpose of this non-systematic review were included by cross-referencing. Primary endpoints were to describe association between serologic markers and carotid disease progression. Association between ratios and demographic features was also assessed.

## RESULTS

The study identified 18 articles, including 5339 patients.

### NEUTROPHIL-TO-LYMPHOCYTE RATIO AND CAROTID ARTERY DISEASE

#### Clinical demographics

Higher values of NLR were associated with male gender ( $2.59 \pm 2.03$  vs  $2.09 \pm 0.86$ ,  $P=0.009$ ) in a retrospective study by Deser *et al*, which included 160 patients submitted to CEA for severe ICA stenosis and 201 patients without severe carotid stenosis,<sup>33</sup> a finding corroborated by another retrospective study enrolling 270 patients to

CEA ( $P=0.012$ ).<sup>34</sup> Additionally associated higher values of NLR with older age ( $P=0.006$ ). Increased body mass index (BMI) was associated with  $NLR < 5$  in a population of 432 patients that underwent CEA for high-grade carotid stenosis (both symptomatic and asymptomatic stenosis) ( $27.2 \pm 4.6$  vs  $25.7 \pm 3.5$ ,  $P=0.01$ ) [35].

#### Carotid intima-media thickness

In a cohort of patients with acute and subacute ischemic stroke, a significant positive correlation between NLR and increased carotid intima-media thickness (IMT) in male gender, after confounding adjustment (adjusted  $R^2=0.185$ , root mean squared error [MSE]=0.152).<sup>36</sup> Likewise, in a study by Suarez-Cuenca *et al*, patients awaiting bariatric surgery with known cardiovascular risk factors had a positive correlation between NLR and IMT ( $P=0.05$ ).<sup>37</sup> Both studies used carotid ultrasonography to evaluate IMT. Additionally, in patients with cardiac syndrome X and coronary artery disease, one also could verify association between NLR and IMT ( $P<0.05$ ),<sup>38</sup> while patients with diabetes mellitus type 2 an increased NLR revealed higher media thickness ( $P=0.005$  and odds ratio [OR], 140.89; 95% CI 1.71–11615.30,  $P=0.028$ , respectively).<sup>39,40</sup>

#### Carotid plaques

In order to evaluate subclinical atherosclerosis, Corriere *et al*.<sup>41</sup> recruited 384 patients  $\geq 65$  years who were submitted to carotid ultrasonography and found a statistically significant association between a higher value of NLR and the presence of carotid plaques, with  $NLR > 2.4$  revealing a prevalence of 80% and  $NLR > 3.68$  a prevalence of 97% of carotid plaques.

A prospective study enrolled 139 asymptomatic patients with intermediate carotid stenosis (50-70% stenosis), performing both carotid doppler ultrasonography and computed tomography angiography (CTA) to separate them in two groups: one with calcified plaques and another with non-calcified carotid plaques. This study found NLR to be significantly higher in the group with non-calcified plaques (OR, 5.686; 95% CI 2.498 – 12.944,  $P<0.001$ ).<sup>42</sup>

#### Carotid artery stenosis

Examining 105 consecutive patients with digital subtraction angiography (DSA) presenting with ischemic stroke, transient ischemic stroke or suspected carotid stenosis in a health check-up, Hong Jiang *et al*.<sup>43</sup> found NLR was independently associated with both maximal extracranial carotid stenosis and accumulated extracranial carotid stenosis (sum of right and left maximal carotid artery stenosis) (adjusted  $R^2=0.179$ ,  $P<0.001$  and adjusted  $R^2=0.183$ ,  $P<0.001$ , respectively). The suggested NLR cutoff of 1.89 was predictive of 50% maximal extracranial carotid stenosis or greater, with a 78.4% sensitivity and 77.4% specificity. Similarly, in the previously mentioned cohort by Deser *et al*.<sup>33</sup> NLR was significantly higher in patients with 70-99% carotid artery stenosis vs 0-50% ( $P<0.01$ ).



### Symptomatic carotid artery stenosis

Retrospectively analyzing 270 patients who underwent carotid endarterectomy (CEA) and grouping them in 4 different categories concerning NLR and PLR values, Nicolas Massiot *et al.*<sup>34</sup> found that increases in both ratios were significantly associated with symptomatic ICA stenosis ( $P=0.005$  and  $P=0.051$ , respectively). Erkan Köklü *et al.*<sup>44</sup> found similar results, with NLR being independently associated with symptomatic carotid plaque in intermediate carotid stenosis (50-70%) after multivariate logistic regression (OR, 7.779; 95% CI 3.685-16.424,  $P=0.001$ ) with an NLR cutoff value of  $\geq 2.6$  (73% sensitivity and 71% specificity).

### Post-operative outcomes of carotid artery revascularization

Zhengze Dai *et al.* in a study including 459 patients undergoing carotid stenting (164 for symptomatic carotid stenosis and 295 for asymptomatic stenosis), reported an overall rate of in-stent restenosis (ISR) of 15.7% at 14.6  $\pm$  19.1 months follow-up. ISR rate among asymptomatic patients was 16.9% and, specifically in this subgroup, an association between ISR and a baseline NLR value  $\geq 2.13$  after multivariate Cox regression analysis (HR, 2.74; 95% CI, 1.46-5.14) was found.<sup>45</sup> This association was not observed in patients submitted to CAS for symptomatic stenosis. Xiang Bao *et al.*,<sup>46</sup> who compared 108 patients submitted to CAS and had ISR vs 226 without IRS, also found a positive correlation with NLR and ISR (area under the curve [AUC]=0.703). A statistically significant association was not found for PLR.

Moreover, in a retrospective study, where 432 patients were submitted to CEA, NLR  $\geq 5$  was associated with a three-fold increased risk of cognitive dysfunction one day after surgery (OR, 3.38 [1.81-6.27],  $P<0.001$ ).<sup>35</sup>

## PLATELET-TO-LYMPHOCYTE RATIO AND CAROTID ARTERY DISEASE

### Clinical demographics

Nicolas Massiot *et al.*<sup>34</sup> studying patients submitted to CEA, found PLR increased with age ( $P<0.0001$ ), and that it was also linked to a subpopulation with a higher proportion of non-smokers ( $P<0.001$ ).

In a retrospective study enrolling 150 patients who underwent carotid CTA, higher levels of PLR were significantly associated with hypertension ( $P=0.022$ ) [47].

### Carotid artery stenosis

Higher PLR was significantly associated with a 90-99% CS (vs 0-50%,  $P<0.01$ ).<sup>33</sup> Retrospectively analyzing 150 patients with carotid stenosis submitted to CTA, the PLR value was correlated with the degree of stenosis ( $P<0.017$ ).<sup>47</sup> Ceyhun Varim *et al.*<sup>48</sup> divided 140 patients who underwent carotid CTA in 2 groups, one with critical carotid stenosis (symptomatic patients with  $>50\%$  carotid stenosis and asymptomatic patients with  $>80\%$  stenosis) and another one with non-critical carotid stenosis. The

study found PLR values were higher in the group with critical carotid stenosis ( $P<0.0001$ ), with a threshold of PLR  $> 117.1$  (89% and 68% sensitivity and specificity, respectively [95% CI, 0.043-0.159; AUC 0.101  $\pm$  0.03]).

### Symptomatic carotid stenosis

In a mentioned series of 150 patients with carotid stenosis, Soyulu *et al.* identified a higher PLR as a predictor of symptomatic stenosis (OR 1.012; CI 1.001-1.024,  $P=0.008$ ) with PLR  $> 119.43$  as the best threshold with 85.9% and 60.1% sensitivity and specificity, respectively.<sup>47</sup> Furthermore, the retrospective analysis of 270 patients submitted to CEA suggested an association between higher PLR values and symptomatic ICA stenosis ( $P=0.051$ ).<sup>34</sup>

### Postoperative outcomes of carotid artery revascularization and mortality

Deser *et al.* identified elevated PLR as an independent predictor of postoperative stroke for CEA (185.76  $\pm$  23.72 vs 115.80  $\pm$  43.39,  $P=0.035$ ). The threshold of 145.304 provided a sensitivity of 83.3% and a specificity of 73.8%, with a C-statistic of 0.862 (95% CI, 0.802-0.921,  $P=0.002$ ).<sup>33</sup>

In a cohort of 196 consecutive patients who underwent CEA, Aldo Bonaventura *et al.*<sup>49</sup> unveiled a positive correlation between PLR and acute coronary syndrome at 18 months follow-up with the cut-off being 153.6 (HR, 1.44; 95% CI, 1.08-1.92).

In a retrospective study, which included 146 patients submitted to selective carotid angiography, after multivariate analysis, only higher PLR predicted all-cause mortality in this cohort of patients with coronary artery disease (OR, 0.010; 95% CI, 1.002-1.018,  $P=0.009$ ).<sup>50</sup>

## DISCUSSION

This review highlights the ongoing interest in the study of these hematological ratios and their ability to predict outcomes in patients with carotid artery disease. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have the ability to predict sub-clinic atherosclerosis, atherosclerosis progression in carotid artery disease and propensity for carotid stenosis to become symptomatic along with morbidity following CEA and carotid stenting.

Atherosclerosis is a systemic vascular inflammatory disease, affecting medium and large-sized arteries, with inflammation playing an essential role in the initiation, progression, destabilization, and rupture of the atherosclerotic plaque, contributing to symptom onset and adverse outcomes. Plaques are composed of infiltrating inflammatory cells, namely monocytes, macrophages, T lymphocytes, and dendritic cells, in addition to smooth muscle cells, extracellular matrix proteins, lipids, and calcium deposits.<sup>51-53</sup>

NLR is linked to chronic low-grade inflammation, with high sensitivity C-reactive protein presenting a positive correlation with this ratio.<sup>54</sup> Although the role of NLR

is still not completely understood, evidence from a recent meta-analysis including 20 studies and 49097 patients suggested an association between IMT and serum levels of high sensitive C-reactive protein (hs-CRP), fibrinogen, and total leukocyte count.<sup>55</sup> Neutrophils have been implicated in cardiovascular inflammation and repair, as well as in atherosclerotic plaque invasion and instability through the production of proteolytic enzymes, arachidonic acid derivatives, and superoxide radicals.<sup>56,57</sup> Furthermore, neutrophils produce cytokines that have been suggested to increase plaque size and induce instability and rupture, such as IL-1b, IL-6, IL-18, and MCP-1.<sup>58</sup> These cytokines have been found in atherosclerotic plaques, including carotid atheromas,<sup>59</sup> and contribute with varying degrees to plaque formation and rupture. MCP-1 regulates migration and infiltration of monocytes/macrophages and the proliferation and migration of smooth muscle cells, migration of endothelial cells, and plaque neovascularization.<sup>51</sup>

The ratio PLR has been associated with cardiovascular disease and outcomes despite the incomplete understanding of the pathophysiology. Platelets have a central role in thrombus formation, although several molecular pathways that implicate them in atherogenesis have been suggested. Platelets induce a pro-inflammatory status through cytokine production and platelet-derived microvesicles, in addition to activating the complement system, an essential innate immunity component that contributes to vascular inflammation.<sup>60,61</sup> CCL5 secretion is one of the hallmarks of the initial inflammatory response to vascular injury, with platelets secreting a significant amount of this cytokine after their migration to the endothelial monolayer.<sup>62</sup> Platelets produce PDGF and MMPs, contributing to intimal thickening and atherosclerosis progression.<sup>63</sup>

Bochao D. Lin *et al*<sup>64</sup> have shown that NLR and, to an even a larger extent, PLR are influenced by heritability. Additionally, the authors revealed an association of both ratios with increased age, which was corroborated by others.<sup>34</sup> NLR has also been associated with an older population by other studies in the general population.<sup>65,66</sup> The authors argue that this correlation may be linked with underlying diseases present in the older population.<sup>34,65</sup> In fact, Basem Azab *et al*<sup>66</sup> reported higher values of NLR in patients with cardiovascular disease. Bochao D. Lin *et al*<sup>64</sup> also detected a higher mean level of NLR and PLR in men. Two other studies reported the same connection with higher NLR in men.<sup>33,34</sup> However, Bochao D. Lin *et al*<sup>64</sup> also had conflicting findings, describing a positive correlation with BMI, while Halazun *et al*<sup>35</sup> had a higher BMI in the cohort with NLR < 5. Nevertheless, what would be expected is a positive correlation as obesity generally reflects a chronic state of inflammation,<sup>67</sup> as described in previous studies.<sup>65,66,68,69</sup>

Interestingly, both NLR and PLR is positively correlated with carotid stenosis severity<sup>33,43,47,48</sup> and able to predict symptomatic stenosis.<sup>34,44,47</sup> Besides, it seems that both ratios are able to predict disease progression. Regarding NLR, it seems to provide a disease marker, being able to predict from higher IMT<sup>36-40</sup> to carotid plaques,<sup>41,42</sup> carotid stenosis<sup>33,43</sup> and symptomatic stenosis<sup>34,44</sup> while PLR is

able to predict both stenosis severity<sup>33,47,48</sup> and symptomatic stenosis.<sup>34,47</sup> However, NLR seems a better predictor of sub-clinic atherosclerosis, given the positive correlation demonstrated in several studies with NLR and IMT,<sup>36-40</sup> a proven marker of sub-clinic atherosclerosis.<sup>70</sup>

Furthermore, both ratios have a positive correlation with the severity of the outcomes, as the higher the threshold is settled, the greater the severity of the predicted outcome: NLR > 1.89<sup>43</sup> is predictive of a carotid stenosis > 50% while NLR > 2.6 is predictive of a symptomatic carotid stenosis.<sup>44</sup> Similarly, PLR > 117.1 predicts critical stenosis,<sup>48</sup> PLR > 119.43 predicts a symptomatic stenosis<sup>47</sup> while higher thresholds predict worse outcomes after CEA, with PLR > 145.304 as a predictor of stroke<sup>33</sup> and PLR > 153.6 as a predictor of acute coronary syndrome.<sup>49</sup> Therefore, there is a positive correlation between the above mentioned ratios and the grade of inflammation and atherosclerosis severity, with clinical findings supporting this association. Recognizing this serologic link can provide valuable information, namely to support the decision of which asymptomatic carotid stenosis most benefit from revascularization, still one of the main challenging decisions concerning carotid artery disease.<sup>44</sup> Accordingly, Yuksel *et al*<sup>42</sup> studied patients with asymptomatic carotid stenosis between 50% and 70% and found that patients with non-calcified carotid plaques presented higher values of NLR, permitting to identify the subset of patients with increased risk for cerebrovascular events.<sup>71</sup>

Zhengze Dai *et al*<sup>45</sup> and Xiang Bao *et al*<sup>46</sup> linked higher levels of NLR to ISR after carotid stenting, which is associated with an increased risk of late cerebrovascular events.<sup>72</sup> Also, in coronary artery disease, higher levels of NLR have proven to be able to predict restenosis after stent implantation.<sup>73,74</sup>

Anti-inflammatory therapy may emerge as an atherosclerotic treatment option and NLR and PLR can be used as inflammation markers and predictors of several postoperative outcomes.<sup>33,35,49,50</sup> There is a growing research interest, using hs-CRP as the control inflammatory biomarker, which correlates with NLR and PLR.<sup>75-77</sup> Anti-inflammatory therapies being tested include rosuvastatin<sup>78</sup> or canakinumab.<sup>79</sup>

This review has several limitations that warrant consideration. Firstly, it is possible that not all available data was captured, making publication bias possible. Additionally, most are single-center reports with limited populations. Finally, the interaction between serologic parameters and chronic atherosclerosis may have difficulty in establishing a causal relationship between serologic parameters and cerebrovascular events. Therefore, larger multicentric prospective, or ideally randomized controlled studies, should be pursued.

## CONCLUSION

This study highlights the increasing interest in NLR and PLR as inflammation/ atherosclerosis markers. These ratios are easily available markers and predict sub-clinic

atherosclerosis and atherosclerosis progression in carotid artery disease. This has clinical implications as may permit to identify patients with greater propensity to become symptomatic and even with greater post-operative morbidity. These potential abilities would allow tailored therapy such as dual antiaggregant therapy, anti-inflammatory therapy, or the preference of eversion technique rather than conventional endarterectomy in order to attempt the extraction of the whole plaque burden<sup>33</sup> and improve outcomes.

#### DECLARATION OF CONFLICTING INTERESTS

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

#### FUNDING

The author(s) received no financial support for the research, authorship, and/or publication of this article.

#### REFERENCES

- Aday, A.W. and J.A. Beckman, Medical Management of Asymptomatic Carotid Artery Stenosis. *Prog Cardiovasc Dis*, 2017. 59(6): p. 585-590.
- Bejot, Y., et al., Epidemiology of stroke in Europe and trends for the 21st century. *Presse Med*, 2016. 45(12 Pt 2): p. e391-e398.
- Naylor, A.R., et al., Editor's Choice - Management of Atherosclerotic Carotid and Vertebral Artery Disease: 2017 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg*, 2018. 55(1): p. 3-81.
- Ross, R., Atherosclerosis--an inflammatory disease. *N Engl J Med*, 1999. 340(2): p. 115-26.
- Taleb, S., Inflammation in atherosclerosis. *Arch Cardiovasc Dis*, 2016. 109(12): p. 708-715.
- Geovanini, G.R. and P. Libby, Atherosclerosis and inflammation: overview and updates. *Clin Sci (Lond)*, 2018. 132(12): p. 1243-1252.
- Libby, P., Inflammation in atherosclerosis. *Arterioscler Thromb Vasc Biol*, 2012. 32(9): p. 2045-51.
- Soeki, T. and M. Sata, Inflammatory Biomarkers and Atherosclerosis. *Int Heart J*, 2016. 57(2): p. 134-9.
- Moriya, J., Critical roles of inflammation in atherosclerosis. *J Cardiol*, 2019. 73(1): p. 22-27.
- Lievens, D. and P. von Hundelshausen, Platelets in atherosclerosis. *Thromb Haemost*, 2011. 106(5): p. 827-38.
- Huo, Y. and K.F. Ley, Role of platelets in the development of atherosclerosis. *Trends Cardiovasc Med*, 2004. 14(1): p. 18-22.
- Pircher, J., et al., Platelet-Neutrophil Crosstalk in Atherothrombosis. *Thromb Haemost*, 2019. 119(8): p. 1274-1282.
- Tavora, F.R., et al., Monocytes and neutrophils expressing myeloperoxidase occur in fibrous caps and thrombi in unstable coronary plaques. *BMC Cardiovasc Disord*, 2009. 9: p. 27.
- Ommen, S.R., et al., Usefulness of the lymphocyte concentration as a prognostic marker in coronary artery disease. *Am J Cardiol*, 1997. 79(6): p. 812-4.
- Bressi, E., et al., Impact of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio on 5-Year Clinical Outcomes of Patients with Stable Coronary Artery Disease Undergoing Elective Percutaneous Coronary Intervention. *J Cardiovasc Transl Res*, 2018. 11(6): p. 517-523.
- Mungan, I., et al., Does the preoperative platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio predict morbidity after gastrectomy for gastric cancer? *Mil Med Res*, 2020. 7(1): p. 9.
- Mady, M., et al., Neutrophil to lymphocyte ratio as a prognostic marker in metastatic gallbladder cancer. *HPB (Oxford)*, 2020.
- Vinal, D., et al., Prognostic value of neutrophil-to-lymphocyte ratio and other inflammatory markers in patients with high-risk soft tissue sarcomas. *Clin Transl Oncol*, 2020.
- Ma, L., et al., Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in patients with systemic lupus erythematosus and their correlation with activity: A meta-analysis. *Int Immunopharmacol*, 2019. 76: p. 105949.
- Huang, Z., et al., Prognostic value of neutrophil-to-lymphocyte ratio in sepsis: A meta-analysis. *Am J Emerg Med*, 2019.
- Zhao, C., et al., Prognostic value of an inflammatory biomarker-based clinical algorithm in septic patients in the emergency department: An observational study. *Int Immunopharmacol*, 2020. 80: p. 106145.
- Li, B., et al., Platelet-to-lymphocyte ratio in advanced Cancer: Review and meta-analysis. *Clin Chim Acta*, 2018. 483: p. 48-56.
- Guo, W., et al., Prognostic value of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio for breast cancer patients: An updated meta-analysis of 17079 individuals. *Cancer Med*, 2019. 8(9): p. 4135-4148.
- Bhutta, H., et al., Neutrophil-lymphocyte ratio predicts medium-term survival following elective major vascular surgery: a cross-sectional study. *Vasc Endovascular Surg*, 2011. 45(3): p. 227-31.
- Gary, T., et al., Platelet-to-lymphocyte ratio: a novel marker for critical limb ischemia in peripheral arterial occlusive disease patients. *PLoS One*, 2013. 8(7): p. e67688.
- Gonzalez-Fajardo, J.A., et al., Prognostic significance of an elevated neutrophil-lymphocyte ratio in the amputation-free survival of patients with chronic critical limb ischemia. *Ann Vasc Surg*, 2014. 28(4): p. 999-1004.
- Wang, Q., et al., Neutrophil-to-lymphocyte ratio is effective prognostic indicator for post-amputation patients with critical limb ischemia. *Saudi Med J*, 2017. 38(1): p. 24-29.
- Tasoglu, I., et al., Neutrophil-lymphocyte ratio and the platelet-lymphocyte ratio predict the limb survival in critical limb ischemia. *Clin Appl Thromb Hemost*, 2014. 20(6): p. 645-50.
- Tasoglu, I., et al., Usefulness of neutrophil/lymphocyte ratio as a predictor of amputation after embolectomy for acute limb ischemia. *Ann Vasc Surg*, 2014. 28(3): p. 606-13.
- Lareyre, F., et al., Association of Platelet to Lymphocyte Ratio and Risk of 30-Day Postoperative Complications in Patients Undergoing Abdominal Aortic Surgical Repair. *Vasc Endovascular Surg*, 2019. 53(1): p. 5-11.
- Wang, S., et al., Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio Are Effective Predictors of Prognosis in

- Patients with Acute Mesenteric Arterial Embolism and Thrombosis. *Ann Vasc Surg*, 2018. 49: p. 115-122.
32. Augene, E., et al., Platelet to lymphocyte ratio as a predictive factor of 30-day mortality in patients with acute mesenteric ischemia. *PLoS One*, 2019. 14(7): p. e0219763.
  33. Deser, S.B., et al., The association between platelet/lymphocyte ratio, neutrophil/lymphocyte ratio, and carotid artery stenosis and stroke following carotid endarterectomy. *Vascular*, 2019. 27(6): p. 604-611.
  34. Massiot, N., et al., High Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio are Associated with Symptomatic Internal Carotid Artery Stenosis. *J Stroke Cerebrovasc Dis*, 2019. 28(1): p. 76-83.
  35. Halazun, H.J., et al., Neutrophil-lymphocyte ratio as a predictor of cognitive dysfunction in carotid endarterectomy patients. *J Vasc Surg*, 2014. 59(3): p. 768-73.
  36. Hyun, S., et al., Can the Neutrophil-to-Lymphocyte Ratio Appropriately Predict Carotid Artery Stenosis in Patients with Ischemic Stroke?-A Retrospective Study. *J Stroke Cerebrovasc Dis*, 2015. 24(11): p. 2646-51.
  37. Suarez-Cuenca, J.A., et al., Neutrophil-to-lymphocyte ratio and its relation with pro-inflammatory mediators, visceral adiposity and carotid intima-media thickness in population with obesity. *Eur J Clin Invest*, 2019. 49(5): p. e13085.
  38. Demirkol, S., et al., Neutrophils/lymphocytes ratio in patients with cardiac syndrome X and its association with carotid intima-media thickness. *Clin Appl Thromb Hemost*, 2014. 20(3): p. 250-5.
  39. Kim, B.J., et al., The Combined Impact of Neutrophil-to-Lymphocyte Ratio and Type 2 Diabetic Mellitus on Significant Coronary Artery Disease and Carotid Artery Atherosclerosis. *J Cardiovasc Ultrasound*, 2016. 24(2): p. 115-22.
  40. Li, X., et al., High neutrophil-to-lymphocyte ratio is associated with increased carotid artery intima-media thickness in type 2 diabetes. *J Diabetes Investig*, 2017. 8(1): p. 101-107.
  41. Corriere, T., et al., Neutrophil-to-Lymphocyte Ratio is a strong predictor of atherosclerotic carotid plaques in older adults. *Nutr Metab Cardiovasc Dis*, 2018. 28(1): p. 23-27.
  42. Yuksel, I.O., et al., Association of Neutrophil/Lymphocyte Ratio with Plaque Morphology in Patients with Asymptomatic Intermediate Carotid Artery Stenosis. *Korean Circ J*, 2016. 46(5): p. 699-705.
  43. Jiang, H., et al., Neutrophil-to-Lymphocyte Ratio Correlates with Severity of Extracranial Carotid Stenosis-A Study Using Digital Subtraction Angiography. *J Stroke Cerebrovasc Dis*, 2017. 26(6): p. 1182-1190.
  44. Koklu, E., et al., Is Elevated Neutrophil-to-Lymphocyte Ratio a Predictor of Stroke in Patients with Intermediate Carotid Artery Stenosis? *J Stroke Cerebrovasc Dis*, 2016. 25(3): p. 578-84.
  45. Dai, Z., et al., Neutrophil to Lymphocyte Ratio as a Predictor of Restenosis After Angioplasty and Stenting for Asymptomatic Carotid Stenosis. *Angiology*, 2019. 70(2): p. 160-165.
  46. Bao, X., et al., Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio: novel markers for the diagnosis and prognosis in patients with restenosis following CAS. *Biomark Med*, 2020. 14(4): p. 271-282.
  47. Idilsoylu, A., et al., The correlation of the platelet-to-lymphocyte ratio with the severity of stenosis and stroke in patients with carotid arterial disease. *Vascular*, 2017. 25(3): p. 299-306.
  48. Varim, C., et al., Usefulness of the platelet-to-lymphocyte ratio in predicting the severity of carotid artery stenosis in patients undergoing carotid angiography. *Kaohsiung J Med Sci*, 2016. 32(2): p. 86-90.
  49. Bonaventura, A., et al., Platelet-to-lymphocyte ratio at the time of carotid endarterectomy is associated with acute coronary syndrome occurrence. *J Cardiovasc Med (Hagerstown)*, 2020. 21(1): p. 80-82.
  50. Tek, M., et al., Platelet to lymphocyte ratio predicts all-cause mortality in patients with carotid arterial disease. *Rom J Intern Med*, 2019. 57(2): p. 159-165.
  51. Koenig, W. and N. Khuseynova, Biomarkers of atherosclerotic plaque instability and rupture. *Arterioscler Thromb Vasc Biol*, 2007. 27(1): p. 15-26.
  52. Ammirati, E., et al., Markers of inflammation associated with plaque progression and instability in patients with carotid atherosclerosis. *Mediators Inflamm*, 2015. 2015: p. 718329.
  53. Tabas, I., G. Garcia-Cardena, and G.K. Owens, Recent insights into the cellular biology of atherosclerosis. *J Cell Biol*, 2015. 209(1): p. 13-22.
  54. Akpek, M., et al., Relation of neutrophil/lymphocyte ratio to coronary flow to in-hospital major adverse cardiac events in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. *Am J Cardiol*, 2012. 110(5): p. 621-7.
  55. Willeit, P., et al., Inflammatory markers and extent and progression of early atherosclerosis: Meta-analysis of individual-participant-data from 20 prospective studies of the PROG-IMT collaboration. *Eur J Prev Cardiol*, 2016. 23(2): p. 194-205.
  56. Eriksson, E.E., et al., Direct viewing of atherosclerosis in vivo: plaque invasion by leukocytes is initiated by the endothelial selectins. *FASEB J*, 2001. 15(7): p. 1149-57.
  57. Silvestre-Roig, C., et al., Neutrophils as regulators of cardiovascular inflammation. *Nat Rev Cardiol*, 2020.
  58. Tecchio, C., A. Micheletti, and M.A. Cassatella, Neutrophil-derived cytokines: facts beyond expression. *Front Immunol*, 2014. 5: p. 508.
  59. Alloza, I., et al., RNAseq based transcriptomics study of SMCs from carotid atherosclerotic plaque: BMP2 and ID3 proteins are crucial regulators of plaque stability. *Sci Rep*, 2017. 7(1): p. 3470.
  60. Kim, H. and E.M. Conway, Platelets and Complement Cross-Talk in Early Atherogenesis. *Front Cardiovasc Med*, 2019. 6: p. 131.
  61. Rosinska, J., et al., Association of platelet-derived microvesicles and their phenotypes with carotid atherosclerosis and recurrent vascular events in patients after ischemic stroke. *Thromb Res*, 2019. 176: p. 18-26.
  62. Suffee, N., et al., RANTES/CCL5-induced pro-angiogenic effects depend on CCR1, CCR5 and glycosaminoglycans. *Angiogenesis*, 2012. 15(4): p. 727-44.
  63. Song, I.S., et al., Chebulinic acid inhibits smooth muscle cell migration by suppressing PDGF-Rbeta phosphorylation and inhibiting matrix metalloproteinase-2 expression. *Sci Rep*, 2017. 7(1): p. 11797.
  64. Lin, B.D., et al., Causes of variation in the neutrophil-lymphocyte

- and platelet-lymphocyte ratios: a twin-family study. *Biomark Med*, 2016. 10(10): p. 1061-1072.
65. Li, J., et al., Neutrophil-to-Lymphocyte Ratio Positively Correlates to Age in Healthy Population. *J Clin Lab Anal*, 2015. 29(6): p. 437-43.
  66. Azab, B., M. Camacho-Rivera, and E. Taioli, Average values and racial differences of neutrophil lymphocyte ratio among a nationally representative sample of United States subjects. *PLoS One*, 2014. 9(11): p. e112361.
  67. Cox, A.J., N.P. West, and A.W. Cripps, Obesity, inflammation, and the gut microbiota. *Lancet Diabetes Endocrinol*, 2015. 3(3): p. 207-15.
  68. Aydin, M., et al., Neutrophil/lymphocyte ratio in obese adolescents. *North Clin Istanbul*, 2015. 2(2): p. 87-91.
  69. Bozkus, F., et al., Does the neutrophil-to-lymphocyte ratio have any importance between subjects with obstructive sleep apnea syndrome with obesity and without obesity? *Tuberk Toraks*, 2018. 66(1): p. 8-15.
  70. Braicu, M.D., et al., The assessment of subclinic atherosclerosis objected through IMT in normal and dyslipidemic patients with various degrees of glucose tolerance. *Rom J Intern Med*, 2009. 47(3): p. 257-65.
  71. Gorelick, P.B., Carotid endarterectomy : where do we draw the line? *Stroke*, 1999. 30(9): p. 1745-50.
  72. Lal, B.K., et al., Restenosis after carotid artery stenting and endarterectomy: a secondary analysis of CREST, a randomised controlled trial. *Lancet Neurol*, 2012. 11(9): p. 755-63.
  73. Bolca, O., et al., The neutrophil-to-lymphocyte ratio is associated with bare-metal stent restenosis in STEMI patients treated with primary PCI. *Coron Artery Dis*, 2015. 26(5): p. 402-8.
  74. Turak, O., et al., Usefulness of the neutrophil-to-lymphocyte ratio to predict bare-metal stent restenosis. *Am J Cardiol*, 2012. 110(10): p. 1405-10.
  75. Ozturk, Z.A., et al., Is increased neutrophil lymphocyte ratio remarking the inflammation in sarcopenia? *Exp Gerontol*, 2018. 110: p. 223-229.
  76. Akboga, M.K., et al., Increased Platelet to Lymphocyte Ratio is Related to Slow Coronary Flow. *Angiology*, 2016. 67(1): p. 21-6.
  77. Soliman, W.M., et al., Neutrophil to Lymphocyte and Platelet to Lymphocyte Ratios in Systemic Lupus Erythematosus: Relation With Disease Activity and Lupus Nephritis. *Reumatol Clin*, 2018.
  78. Ridker, P.M., et al., Reduction in C-reactive protein and LDL cholesterol and cardiovascular event rates after initiation of rosuvastatin: a prospective study of the JUPITER trial. *Lancet*, 2009. 373(9670): p. 1175-82.
  79. Ridker, P.M., et al., Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease. *N Engl J Med*, 2017. 377(12): p. 1119-1131.





# RIGHT VENTRICULAR MYXOMA IN AN ASYMPTOMATIC PATIENT

Hagen Kahlbau\*<sup>1</sup>, Rita Carvalho<sup>2</sup>, Valdemar Marques Gomes<sup>1</sup>, Jorge Pinheiro Santos<sup>1</sup>, José Fragata<sup>1</sup>

<sup>1</sup>Department of Cardiothoracic Surgery – Hospital de Santa Marta, Lisbon, Portugal  
<sup>2</sup>Department of Clinical Pathology – Centro Hospitalar Lisboa Central, Lisboa, Portugal

\*Corresponding author: hkahlbau@gmx.com

## Abstract

*Myxomas are the most common cardiac tumors; however right ventricular myxomas are very rare. We present the case of an asymptomatic 74 year old female with a right ventricular myxoma originating from the interventricular septum diagnosed during a routine echocardiographic examination.*

*Initially the patient refused surgery due to being asymptomatic, but agreed to be operated two months later. Surgical removal was uneventful, as was the postoperative course.*

*Histopathological analysis confirmed the suspected diagnosis of cardiac myxoma.*

**Keywords:** Cardiac tumor, Myxoma.

## INTRODUCTION

Cardiac myxomas are the most common tumors of the heart, accounting for 75-80% of all cardiac tumors, and 90% of the patients are aged 30 – 60 years when diagnosed.<sup>1</sup> In more than 90% of cases myxomas are located in the left atrium, followed by right atrial and left ventricular locations.<sup>2</sup> Ventricular myxomas are rare and among those right ventricular (RV) myxomas are reported with an incidence of only 1,7 % of all cardiac myxomas.<sup>3</sup> Associated syndromes such as Carney's complex and family history should always be considered.<sup>4</sup> Symptoms can be related to embolism which occurs in 30-40% of all cases<sup>5</sup> or to right ventricular outflow tract (RVOT) obstruction and include syncope, dyspnea or peripheral edemas. Surgical resection is indicated and should not be delayed.

## CASE REPORT

We present the case of an asymptomatic 74 year old female, when a 43 x 25 mm right ventricular, mobile mass originating from the interventricular septum and protruding through the pulmonary valve in systole was diagnosed during a first time performed routine echocardiography. The patient had neither family history for cardiac tumors nor any associated comorbidities. For further diagnostic purposes a magnetic resonance tomography was performed (Figure 1).

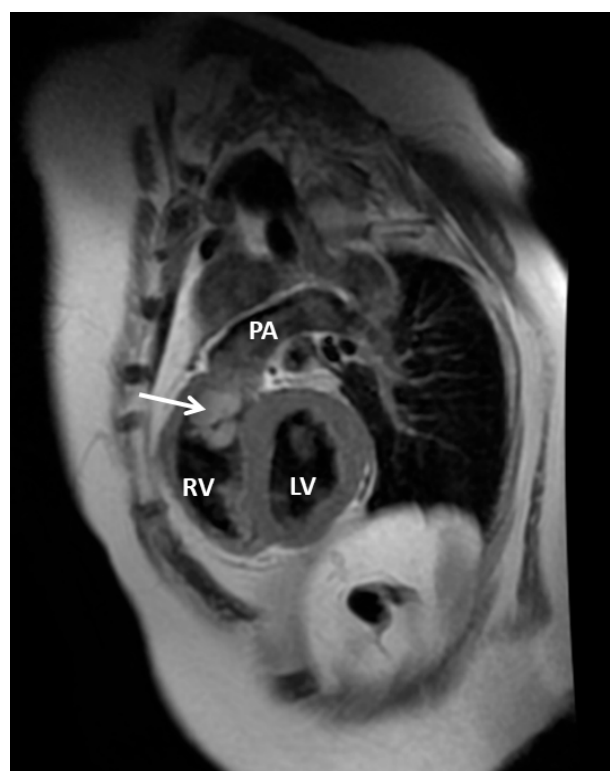


Figure 1

Preoperative Magnetic Resonance Tomography showing a right ventricular (RV) mass (white arrow) protruding into the right ventricular outflow tract. PA = Pulmonary artery; LV = Left ventricle.

The patient initially refused surgery due to her asymptomatic status, but two months later, after reconsidering during follow up consultation, she accepted surgical removal of the RV mass.

The routine preoperative laboratory analysis was normal, as was the coronary angiogram.

The surgical procedure was performed through a median sternotomy and cardiopulmonary bypass (CPB) with central aortic and bicaval cannulation. After aortic cross clamping and administration of antegrade cardioplegic blood solution, the RV was opened through a longitudinal ventriculotomy and the RVOT, interventricular septum and tricuspid valve were inspected (Figure 2 A). A mass was detected in the RVOT extending from the interventricular septum to the RVOT. A complete mass resection was performed using scissors and electrocautery (Figure 2 B). The right ventriculotomy was closed with a double prolene 4/0 suture. The postoperative course was uneventful and the pre discharge echocardiography was normal.

Histopathological analysis of the mass revealed a cardiac myxoma with cells positive for CD 31 and CD 34 (Figure 2 C).

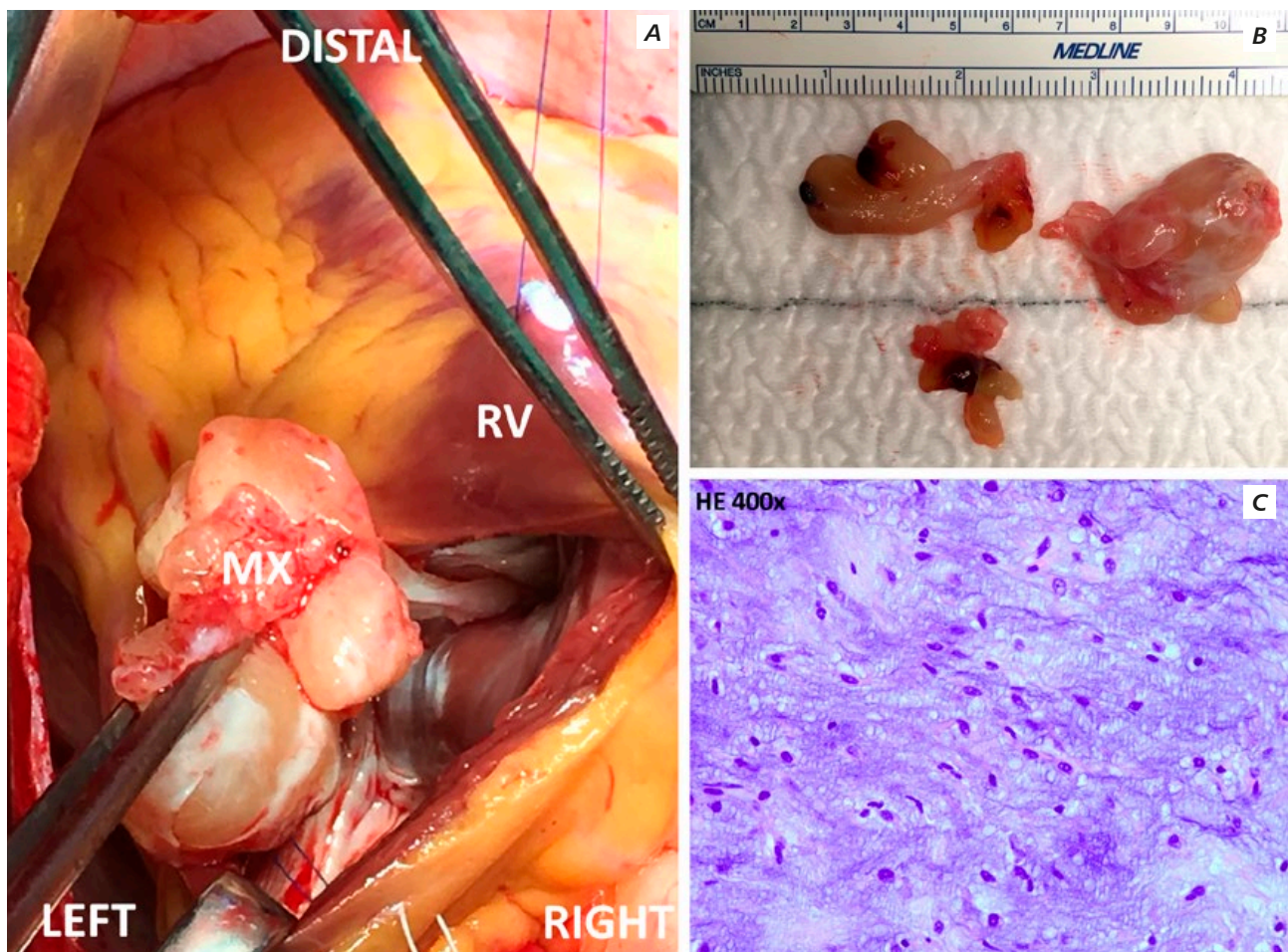
The patient was discharged at postoperative day eight. During regular postoperative consultations the patient kept asymptomatic and the one year postoperative echocardiography showed no signs of tumor recurrence.

## DISCUSSION

Right ventricular myxomas are uncommon benign cardiac tumors, which usually present with typical RVOT obstruction-related symptoms. In our case the patient was asymptomatic and the diagnosed right ventricular mass a coincidental find on a routine echocardiographic examination.

Due to the lack of symptoms the patient initially refused surgery. Previous publications have underlined that myxomas have a high documented embolization rate, which can lead to further complications when surgery is delayed.

Recurrence rate of RV myxomas is not well documented in the literature due to its rarity, but cardiac myxomas in general have an overall recurrence rate of less than 3%, but can be as high as 22% in familial cases.<sup>5</sup>



**Figure 2** A - Intraoperative image showing the opened Right Ventricle (RV) with the mass formation (MX); B - Completely resected right ventricular mass; C - Hematoxylin and eosin stain study of the RV myxoma.



*ACKNOWLEDGEMENTS: We thank Eugénia Pinto, MD for the image of the hematoxylin and eosin stain study and the department of anesthesiology (Ana Ferro, MD and Isabel Fragata, MD) for intraoperative echocardiography assessment.*

#### REFERENCES

1. Butany J, Nair V, Naseemuddin A, Nair GM, Catton C, Yau T. Cardiac tumours: diagnosis and management. *Lancet Oncol.* 2005; 6: 219-28.
2. Pemberton J, Raudkivi P. Right ventricular myxoma causing pulmonary outflow tract obstruction. *Interact Cardiovasc Thorac Surg.* 2012; 14:362-3.
3. Kuon E, Kreplin M, Weiss W, Dahm JB. The challenge presented by right atrial myxoma. *Herz.* 2004; 29:702-9.
4. Satitthummanid S, Tumkosit M, Benjacholamas V, Chattranukulchai P, Boonyaratavej S, Puwanant S. Right ventricular myxoma. *J Am Coll Cardiol.* 2011; 57: 630.
5. Assaf Y, Nasser M, Jneid H, Ott D. Pulmonary Embolism Following Incomplete Resection of a Right Ventricular Myxoma: A Case Report and Review of the Literature. *Cardiol Ther.* 2018; 7: 107-117.29-34



# DELAYED PRESENTATION OF FOREIGN BODY ASPIRATION IN ADULTS

Ana Catarina Alves Moreira\*<sup>1</sup>, Carolina Cintra Torres<sup>2</sup>, Carlos André Ribeiro da Silva Couto<sup>1</sup>

<sup>1</sup>Pulmonology Department, Hospital Garcia de Orta, EPE Almada

<sup>2</sup>Thoracic Surgery Department, Centro Hospitalar Universitário Lisboa Norte - Hospital Pulido Valente

\*Corresponding author: catarina\_icbas@hotmail.com

## Abstract

Foreign body (FB) aspiration in adults is usually associated with predisposing risk factors. Clinical manifestations are immediate but less frequently it could lead to insidious lung damage, as demonstrated by the presented case. We present a case of unsuspected FB aspiration, mimicking an infection vs lung tumour. After left lower lobectomy, pathology revealed a foreign body (animal bone) at the origin of the lingular bronchus.

## INTRODUCTION

Tracheobronchial foreign body (FB) aspiration is not uncommon, though the incidence in pediatric age is higher.<sup>1,2</sup> The clinical manifestations range from acute asphyxiation, when FB obstructs the main airway, whereas in more distal airway obstruction, signs of a recurrent infection with insidious lung damage are more common. A delayed diagnosis is frequent in cases where FB aspiration is not overt, so it should be considered as one of the causes of persistent post-obstructive pneumonia.<sup>3,4,5</sup> Symptoms are usually nonspecific, so a high level of clinical suspicion is needed, as its presentation mimics other respiratory tract pathologies.<sup>6</sup> The predisposing factors in adults are male sex, old age, CNS dysfunction, psychiatric illness, alcohol and/or sedative abuse, trauma intubation, dental procedure and pulmonary disease.<sup>7,8</sup> Because of the anatomical features of the bronchial tree, foreign body is commonly lodged in the right, especially in the right intermediate bronchus.<sup>9</sup> According to the literature, based in case series, it was reported that 50.1% of aspirated foreign bodies were in the right bronchial system, 46.5% were in the left bronchial system, and 3.6% were in the trachea.<sup>10</sup>

## CASE REPORT

We present a case of delayed presentation and unsuspected FB aspiration in an adult in whom a lobectomy was performed. A 63 years-old Caucasian man, former smoker, with past medical history of COPD, hypertension, dyslipidemia and acute myocardial infarction in 2005, without history of alcohol or sedatives abuse presented in the Outpatient

Clinic of Pneumology in January. He reported a history of weight loss starting 9 months before and vigorous cough episodes leading to syncope in the last 6 months. He also reported haemoptysis since 2 months before. He denied history of fever, chest pain or aspiration. Pulmonary auscultation revealed crackles in the left hemithorax. On investigation, chest- RX showed an opacification of the middle left hemithorax and chest-CT revealed a lingular consolidation with atelectasis (figure 1). A bronchoscopy was performed, with evidence of a white and necrotic plaque in the left upper division bronchi with signs of obstruction and bronchial lumen reduction, and also signs of mucosal edema and infiltration

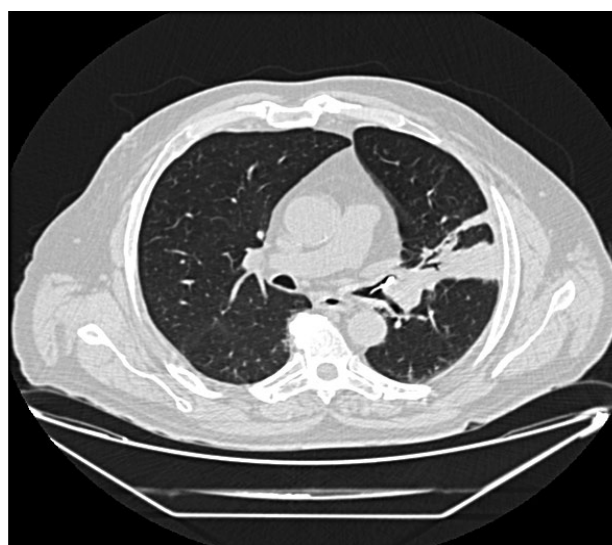
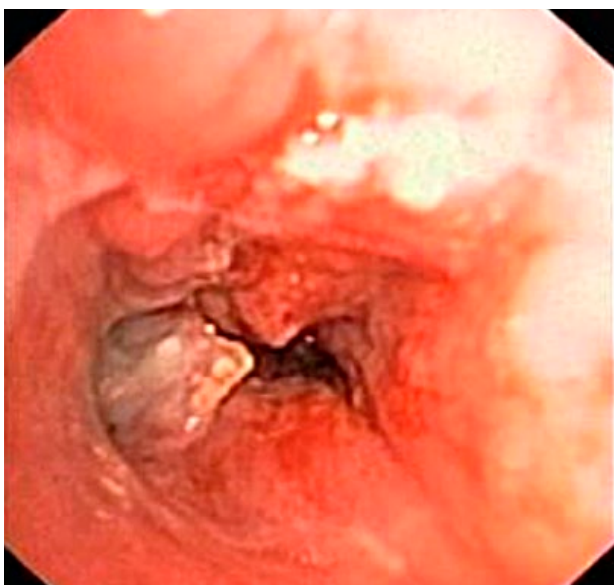


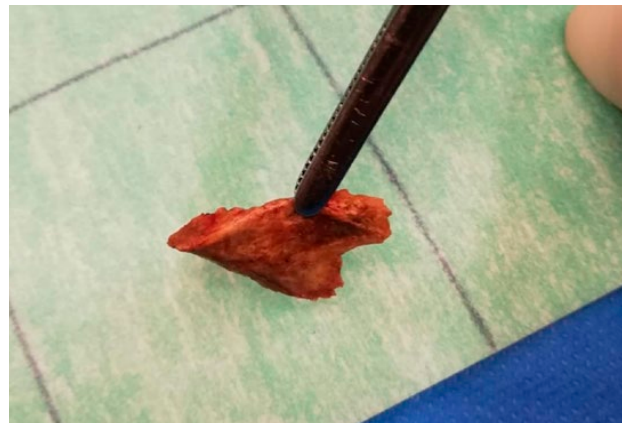
Figure 1 Chest CT- lingular consolidation and atelectasis.



**Figure 2 and 3**

*Endoscopic images from flexible bronchoscopy- white and necrotic plaque in the left upper division bronchi with signs of obstruction and bronchial lumen reduction, as also signs of mucosal edema and infiltration.*

(figures 2, 3) Biopsies were negative for malignancy. The patient kept the recurrent symptoms initially described along the next 6 months, and there was a radiological impairment in sequential chest-CT scan, with a higher extension of the lingular consolidation. A PET-CT scan was performed, with signs of increased metabolic activity in the lingular consolidation (SUV maximum of 8,4). Considering the insidious clinical evolution, the persistence of symptoms and radiological impairment, the suspicion was infectious or malignant aetiology. The patient underwent a left upper lobectomy, where a foreign body was removed - animal bone- located at the opening of the lingular bronchus (figure 4). The histological result showed an inflammatory infiltrate surrounding the foreign body (chicken bone).



**Figure 4** *Foreign body - animal bone- removed in lobectomy.*

This case demonstrates the potential diagnostic challenges of FB aspiration. There was neither an obvious predisposing risk factor nor a history suggestive of aspiration, what have led to a lack of suspicion and consideration of other causes as most probable.

An accurate and timely diagnosis and appropriate treatment is crucial to prevent long-term complications.

#### REFERENCES

1. Roda J, Nobre S, Pires J, et al. Foreign bodies in the airway: A quarter of a century's experience. *Rev Port Pneumol* 2008. 14(6); 787-802.
2. Cho HK, Cho KY, Cho SY, et al. Bronchial foreign body aspiration diagnosed with MCDT. *Korean J Pediatr*. 2007. 50; 781-784.
3. Bhana BD, Gunaselvam JG, Dada MA. Mechanical airway obstruction caused by accidental aspiration of part of a ballpoint pen. *Am J Forensic Med Pathol*. 2000. 21;362-5.
4. Al-Majed SA, Ashour M, Mobeireek AF, et al. Overlooked inhaled foreign bodies: late sequelae and the likelihood of recovery. *Respir Med*. 199 (91); 293-6.
5. Baharloo F, Veyckemans F, Francis C, et al. Tracheobronchial foreign bodies: presentation and management in children and adults. *Chest*. 1999. 115; 1357-62.
6. L. Lin, L. Lv, Y. Wang, X. Zha, F. Tang, and X. Liu. The clinical features of foreign body aspiration into the lower airway in geriatric patients. *Clinical Interventions in Aging*. 2014. 9;1613-1618.
7. J. C. Kam, V. Doraiswamy, J. F. Dieguez et al. Foreign Body Aspiration Presenting with Asthma-Like Symptoms. *Case Reports in Medicine*, vol. 2013, Article ID 317104, 4 pages, 2013.
8. Marquette CH, Martinot A. Foreign body removal in adults and children. In: Bolliger CT, ed. *Interventional bronchoscopy*. Basel: S Karger AG 2000: 96-107
9. Dong YC, Zhou GW, Bai C, et al. Removal of tracheobronchial foreign bodies in adults using a flexible bronchoscope: experience with 200 cases in China. *Intern Med* 2012. 51; 2515-9
10. Özdemir C, Sökücü SN, Karasulu L. Foreign Body Aspiration in Adult: Analysis of 28 Cases. *Eurasian J Pulmonol* 2015; 17: 29-34

# COMPLEX CHEST WALL DEFORMITY CAUSING CARDIAC ARREST: A PECULIAR PEDIATRIC CASE

Miguel Soares-Oliveira\*<sup>1</sup>, Sofia Vasconcelos-Castro<sup>1</sup>, Norberto Estevinho<sup>1</sup>

<sup>1</sup>Department of Pediatric Surgery, Centro Hospitalar Universitário São João, Porto, Portugal

\*Corresponding author: castro.sofia.v@gmail.com

## Abstract

**Introduction:** Congenital chest wall deformities are common in children, causing self and parental concern mainly due to cosmesis. These defects rarely cause severe symptoms in patients.

**Case report:** 11-year-old girl with a complex chest wall deformity and severe scoliosis causing progressive neurological loss of function. When mobilized to prone position for orthopedic surgery, she suffered sudden hypotension immediately followed by a cardiac arrest, that reverted after moving the child back to supine position. The cardiac arrest was interpreted as a result of a decrease in venous blood return secondary to heart and great vessels compression. She was then proposed and submitted to a modified Ravitch procedure with retrosternal metal bar placement in order to allow ventral positioning. This was successfully achieved, and the patient underwent scoliosis correction 3 months later. After more than a year of follow up, she reduced the need for non-invasive ventilation and tolerates prone positioning.

**Conclusion:** This case report alerts medical community that beyond cosmesis concerns, severe chest wall deformities can cause life-threatening events if not correctly managed.

## INTRODUCTION

Chest wall deformities are common, affecting nearly 1% of the population. Most of them just cause cosmetic concerns and it is rare to cause any cardiac or respiratory symptoms.<sup>1</sup> Cardiac arrest is a very rare complication of any surgical procedure for correction of a chest wall deformity.<sup>2</sup> However, cardiac arrest secondary to external compression of a chest wall deformity was never described before. Herein we describe the first case of a child with a complex chest wall deformity that suffered a sudden cardiac arrest just by chest wall compression while in prone position.

## CASE PRESENTATION

A 11-year-old girl with neurofibromatosis and a severe dorsal scoliosis was admitted for orthopedic scoliosis correction due to gradual loss of motor function on her lower limbs and urinary incontinence. She also showed a severe chest wall deformity, mainly with pectus carinatum component (figure 1) and was dependent on non-invasive ventilation. She showed no cardiac anomaly on echocardiography nor arrhythmias on electrocardiography. In the operating room, when positioned in prone position for the posterior

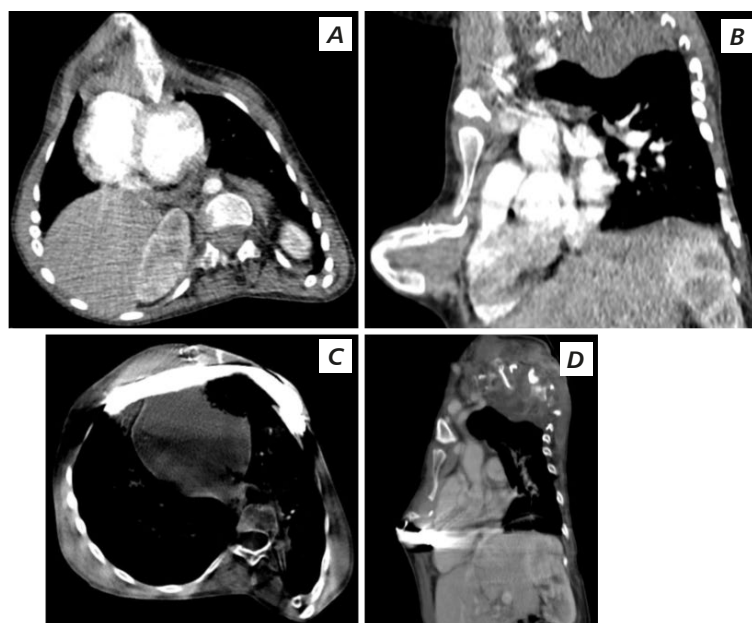
approach, she suffered cardiac arrest that was immediately reverted when mobilized back to dorsal decubitus. It was rather obvious that this condition was due to a positional component of her chest wall deformity. A chest computed tomography (CT) scan showed a severe sternal deformation: the manubrium-sternum articulation showed a 90-degree angle, with apparent compression of the left ventricle and probable cardiac/great vessels kinking when in ventral decubitus (figure 2A and B).

After a multidisciplinary discussion with Orthopedics, Anesthesiology, Pediatric Cardiology and Pediatric



Figure 1

Profile patient view of pectus carinatum component.


**Figure 2**

CT scan imaging. A and B- preoperative heart compression by sternal deformity. C and D- postoperative image showing retrosternal bar.

Surgery, it was concluded that: scoliosis correction was necessary in order to prevent further neurologic impairment; the prone position was mandatory for the orthopedic correction; heart and great vessels compression happened directly caused by the sternal deformity; there was no structural cardiac abnormality responsible for the cardiac arrest. On this wise, the girl was proposed for chest wall correction first, in order to tolerate the prone position necessary for the orthopedic surgery afterwards.

She was submitted to a modified Ravitch intervention, with partial sternal and rib cartilage resection and insertion of a retrosternal metal bar to enhance chest wall stability (figure 2C and D). The postoperative course was uneventful.

Scoliosis correction was done nearly 3 months after thoracic surgery, and the patient tolerated the prone position without any complication, namely cardiac dysfunction. Transesophageal echocardiogram was performed during the entire procedure and no sign of diminished blood return was noted.

After a year of follow up, the patient showed an improvement in lung function (non-invasive ventilation only during the night), stable cardiac function and can moderately tolerate ventral decubitus.

## DISCUSSION

Chest wall deformities are common among otherwise healthy children. The majority of the cases are classified as pectus excavatum or pectus carinatum, and a combination of both is seen in nearly 6% of all patients.<sup>3</sup>

The majority of patients refer aesthetic intolerance, but some may complain of minor symptoms, such as chest pain, shortness of breath or intolerance to exercise. However, there are some reports of life-threatening events, most

of them as a consequence of chronic heart compression that may lead to various types of arrhythmias.<sup>4</sup> Surgical correction of these deformities may also lead to serious complications, such as heart contusion and/or perforation.<sup>2</sup> Zou *et al* reported a case of cardiac arrest during a Nuss procedure without physical cardiac injury during the intervention and suggested it may have happened due to slight rotation of the heart.<sup>5</sup>

To our knowledge, this is the first described case of a pediatric patient that suffered cardiac arrest due to external compression of the heart by a complex chest wall deformity. The carinatum and excavatum components of this case make it unique and should raise awareness to the medical community: life-threatening events can occur in patients with chest wall deformities merely by their positioning.

## REFERENCES

1. Williams AM, Crabbe DCG. Pectus deformities of the anterior chest wall. *Paediatric Respiratory Reviews* 2003;4(3):237-42.
2. Hebra A, Kelly RE, Ferro MM, Yüksel M, Campos JRM, Nuss D. Life-threatening complications and mortality of minimally invasive pectus surgery. *Journal of pediatric surgery* 2018;53(4):728-32.
3. Goretsky MJ, Kelly RE, Jr., Croitoru D, Nuss D. Chest wall anomalies: pectus excavatum and pectus carinatum. *Adolescent medicine clinics* 2004;15(3):455-71.
4. Li T, Bishop-Rimmer E, Shieh M, Kreiger P, Felberbaum M, Heller M. Pectus excavatum: a cause of serious cardiac dysfunction and dysrhythmia. *The American Journal of Emergency Medicine* 2015;33(9):1333.e1-e2.
5. Zou J, Luo C, Liu Z, Cheng C. Cardiac arrest without physical cardiac injury during Nuss repair of pectus excavatum. *J Cardiothorac Surg* 2017;12(1):61-.



# PANCOAST TUMOUR WITH SPINE RESECTION - CASE REPORT

Daniel Cabral\*<sup>1</sup>, Cristina Rodrigues<sup>1</sup>, Carolina Torres<sup>1</sup>, Wilson Teixeira<sup>2</sup>, Sérgio Livraghi<sup>2</sup>, Mariana Antunes<sup>1</sup>, Francisco Félix<sup>1</sup>

<sup>1</sup>Thoracic Surgery Department, Centro Hospitalar Universitário Lisboa Norte

<sup>2</sup>Neurosurgery Department, Centro Hospitalar Universitário Lisboa Norte

\*Corresponding author: dmacedocabral@mail.com

## Abstract

*Pancoast tumours are defined as tumours arising from the upper lobe and invading the thoracic inlet, representing less than 5% of all lung cancers. Clinical features depend on the involved structures. For many years invasion of the spine was considered unresectable and fatal. Due to the progress in spine surgery, en bloc resection including the spine is nowadays possible.*

*We report the first case of a successful en bloc vertebral resection of a Pancoast tumour in a 66 year-old male, with a squamous cell carcinoma, treated at our department in a multidisciplinary setting, after induction chemoradiotherapy.*

*An en bloc resection including the left upper lobe, the first three ribs and the vertebral body of D2, was performed through a Paulson incision after posterior cervico-dorsal arthrodesis.*

*A complete R0 resection was confirmed on the pathology specimen.*

*Currently, one year after surgery, although no local recurrence has occurred, the patient is being treated with immunotherapy due to disease progression in the right acetabulum which was irradiated (20Gy) and then submitted to iliac resection and prosthesis reconstruction.*

## INTRODUCTION

Pancoast tumours were first described in 1838, however they only became a more clear entity after the reports of Henry Pancoast in 1924 and Tobias in 1932.<sup>1,2,3,4</sup> They represent less than 5% of all lung cancers, being defined as tumours that arise from the upper lobe and invade the thoracic inlet.<sup>1,3,4</sup> Clinical features depend on the involved structures. The combination of severe and unrelenting shoulder and arm pain along the distribution of the eighth cervical and first and second thoracic nerve trunks, Horner's syndrome (ptosis, miosis, and anhidrosis) and atrophy of the intrinsic hand muscles comprises a clinical entity named as "Pancoast-Tobias syndrome".

Spine involvement has long been considered to be a contraindication for surgery.<sup>4</sup>

## CASE REPORT

We report the case of a 66 year-old male, former heavy smoker. He mentioned the presence of cough and left ptosis and miosis in the previous six months.

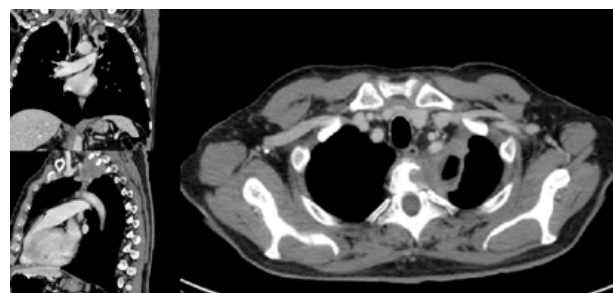
Chest CT showed a 6 cm long-axis mass in the left upper lobe, invading the first and second ribs and the

vertebral body of D2, with increased uptake on FDG-PET. There were no further uptake locations.

The diagnosis was obtained by fiberoptic bronchoscopy. Pathology revealed a squamous cell carcinoma (PD-L1 > 50%).

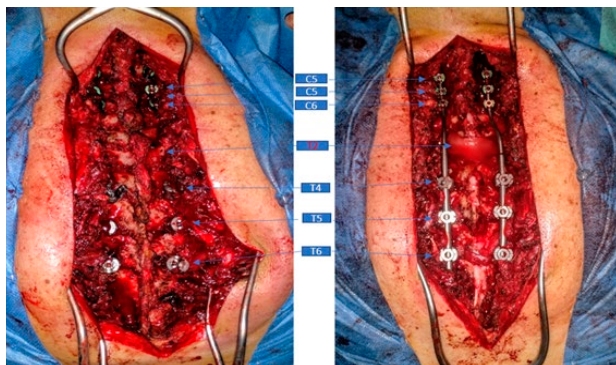
The case was discussed at a multidisciplinary meeting, including the neurosurgery team, and neoadjuvant chemotherapy (vinorelbine/cisplatin) and radiotherapy (50Gy) was decided.

Five weeks after the last radiotherapy session, the patient was admitted for a joint surgical procedure between thoracic surgeons and neurosurgeons.



**Figure 1** Initial diagnostic Chest CT.





**Figure 2** Cervico-dorsal arthrodesis.

### SURGICAL TECHNIQUE

The intervention was divided into four stages. In the first one, the patient was positioned in ventral decubitus and then instrumentation of C4-C7 and T4-T6 was performed and bilateral screws were placed. At last D2 posterior neural arch was removed and the roots of D2 were sectioned bilaterally.

After this the patient was rotated onto a right lateral decubitus and a *Paulson* thoracotomy was made to allow for a left upper lobectomy, anterior section of the first three ribs and posterior disarticulation of the first and third ribs. A left lower lobe wedge resection removed a small peripheral nodule.

In the third part a D1-D2 and D2-D3 discectomy took place, allowing the *en bloc* resection of the full specimen, including the vertebral body of D2. Then a XRL® implant was placed in order to replace the vertebral body.



**Figure 3** Operative field after left upper lobectomy with 1st to 3rd ribs, the vertebral body of D2 (arrow on the body of D2) and the specimen.

In the last part the thoracic surgery team completed a mediastinal lymphadenectomy and hemostasis control.

### AFTER SURGERY/FOLLOW-UP

He stayed in the ICU for eleven days, being weaned off mechanical ventilation on the fifth day after surgery. The patient developed ventilator associated pneumonia and partial left lung atelectasis, which slowly improved.

He was discharged on day 25<sup>th</sup>.

Pathology analysis of the specimen confirmed squamous cell carcinoma with free margins. TNM 8th edition: ypT4N0.

The patient had an early progression, or a previously undiagnosed oligometastasis to the right acetabulum, which was irradiated (20Gy) and then submitted to iliac resection and prosthesis reconstruction.

Currently, one year after surgery he is under immunotherapy, with no signs of local or systemic recurrence.



**Figure 4** Chest X-ray at discharge.

### DISCUSSION

Squamous cell carcinoma, as in our case, is the most frequent histology of Pancoast tumours.<sup>1</sup>

For many years spine invasion was considered a contraindication for surgery.<sup>3,5,6,7</sup> However, progress in spine surgery and instrumentation changed the game. Nowadays *en bloc* tumour resection with curative intent can be performed in selected patients.<sup>2,5</sup>

In 1989, DeMeester *et al* reported the first case series, including 12 patients, of *en bloc* resection of the lung and a tangential portion of the involved vertebral body after induction RT, reporting an overall survival of 42% after 5 years.<sup>8</sup> Seven years later, in 1996, Grunenwald *et al* described the first total vertebrectomy.<sup>9</sup>

Later on, Collaud *et al* performed a systematic literature review including a total of 135 patients submitted to *en bloc* resection of lung, chest wall and spine, as part of a multimodality approach. They reported overall survivals of 57%, 43%, and 26% at 3, 5, and 10 years, respectively. In the subgroup of patients with microscopic complete resection the results were slightly better with survivals of 62%, 48%, and 29% at 3, 5, and 10 years, respectively.<sup>5</sup> This shows the real relevance of an R0 resection.

The extent of spine resection does not seem to impact overall survival, so the length of spine invasion by itself should not be a contraindication for surgery if complete resection is feasible.<sup>5</sup>

Bolton *et al*, in their study reported overall survivals of 47% and 27% at 2 and 5 years, respectively.<sup>3</sup>

Trimodality treatment, including chemotherapy, radiotherapy and surgery, is the gold standard. Preoperative radiotherapy allows a reduction of the tumour size and viable cells in order to improve the R0 resection rates.

Furthermore, chemotherapy concurrent to RT improve resection rates and can limit the risk of distant metastasis due to occult systemic disease.<sup>4,10</sup>

Our patient was treated with induction chemoradiotherapy followed by surgery. An R0 resection was obtained.

Knowing that incomplete resection leads to tumour recurrence, *en bloc* resection has become the gold standard for this kind of tumour.<sup>7,10</sup>

Free-margins resection, as well as the nodal status and T status are the most important prognostic factors.<sup>4</sup>

Due to the extent of the resection important complication rates are associated with these procedures, ranging from 28% to 52%. Some of the most common, as experienced in our case, are atelectasis and pneumonia.<sup>4</sup>

## CONCLUSIONS

Spine invasion is no longer a contraindication for Pancoast tumour surgery.

*En bloc* resection of tumours invading the spine is feasible as part of a multidisciplinary and multimodality approach in experienced centers and carries a good overall survival.

## REFERENCES

1. Panagopoulos et al. Pancoast tumors: characteristics and preoperative assessment. *J Thorac Dis.* 2014;6(S1):S108-S115.
2. Rush V. Management of Pancoast Tumours, *The Lancet* 2006; 7: 997-1005
3. Bolton et al. Superior sulcus tumors with vertebral body involvement: A multimodality approach. *J Thorac Cardiovasc Surg.* 2009;137:1379-87.
4. Fahed Zahir et al. Single Posterior Approach for En-Bloc Resection and Stabilization for Locally Advanced Pancoast Tumors Involving the Spine: Single Centre Experience. *Asian Spine J.* 2016;10:1047-1057.
5. Collaudet al. En Bloc Resection of Pulmonary Sulcus Non-small Cell Lung Cancer Invading the Spine, A Systematic Literature Review and Pooled Data Analysis. *Annals of Surgery* 2015;262: 184-188.
6. Rush et al. Induction Chemoradiation and Surgical Resection for Superior Sulcus Non-Small-Cell Lung Carcinomas: Long-Term Results of Southwest Oncology Group Trial 9416 (Intergroup Trial 0160). *J Clin Oncol.* 2007, 25:313-318.
7. Grunenwald et al. Radical en bloc resection for lung cancer invading the spine. *J Thorac Cardiovasc Surg* 2002;123:271-9.
8. Albertucci et al. Management of tumor adherent to the vertebral column. *J Thorac Cardiovasc Surg.* 1989;97:373-378.
9. Grunenwald et al. Total vertebrectomy for en bloc resection of lung cancer invading the spine. *Ann Thorac Surg.* 1996;61:723-25.
10. Jain et al. Posterior midline approach for single-stage en bloc resection and circumferential spinal stabilization for locally advanced Pancoast tumors. *J Neurosurg Spine* 2008; 9:71-82.



# DEEP VEIN ULTRASOUND-GUIDED THROMBOLYSIS

Joana Ferreira<sup>\*1,2</sup>, João Simões<sup>2</sup>, Sandrina Braga<sup>2</sup>, Pedro Sousa<sup>2</sup>, Celso Carrilho<sup>2</sup>, Amílcar Mesquita<sup>2</sup>

<sup>1</sup>Life and Health Science Research Institute (ICVS), School of Medicine, Universidade do Minho, Guimarães/Braga, Portugal;

<sup>2</sup>Vascular Surgery Department- Hospital da Senhora da Oliveira, Guimarães; Portugal

\*Corresponding author: Joana222@gmail.com

## Abstract

Catheter directed thrombolysis is a minimally invasive procedure that results in a significant reduction in venous obstruction after deep vein thrombosis. The technique implies the performance of phlebographies to monitor the thrombolysis progression. The objective of this paper is to describe the use of vascular ultrasound to follow the thrombus lysis and to adjust the catheter position according to the progression of the thrombolysis. This is the first case reported describing the application of ultrasound to monitor the thrombolysis. A 36-year woman was admitted ilio-femoral vein. The ipsilateral great saphenous vein was the percutaneous access to perform the anterograde thrombolysis. The procedure, including the control of thrombus lysis, as well as catheter progression was performed under ultrasound guidance. The thrombolysis took 52 hours. The patient has two years of follow-up without any complaint. The use of vascular ultrasound to monitor the thrombolysis has several theoretical advantages in patients with adequate biotopes. It minimizes the number of venograms and can be performed at the bedside. It is effective and inexpensive.

**Keywords:** vascular ultrasound; deep vein thrombosis; catheter-directed thrombolysis.

## INTRODUCTION

Catheter-directed thrombolysis (CDT) consists in the percutaneous placement of a catheter into a thrombosed vein followed by infusion of a thrombolytic agent directly into the clot.<sup>1,2</sup> The continuous infusion of the thrombolytic usually continues for at least 24 hours.<sup>1</sup> When compared to systemic thrombolysis, CDT minimizes the systemic drug exposure, reducing the risk of bleeding and the dose of thrombolytic.<sup>1,2,3</sup>

The subgroup analysis of the ATTRACT trial showed that the CDT may have a benefit in patients with iliac vein thrombosis.<sup>4</sup> Camerota concluded that CDT reduced the severity of post-thrombotic syndrome and reduced the proportion of patients who developed moderate-or-severe post-thrombotic syndrome.<sup>5</sup> The CDT also reduces risk of recurrent deep vein thrombosis.<sup>1,2,3</sup>

Long life expectancy patients with acute venous ilio-femoral thrombosis have the greatest benefit from CDT.<sup>1,2</sup>

Ideally the thrombolysis should be performed in the first 2-3 weeks following the onset of deep vein thrombosis symptoms.<sup>1</sup> In order to maintain the catheter in direct contact with the thrombus and to monitor the efficacy of thrombolysis, venograms are usually recommended every 8 to 24 hours.<sup>1</sup> Using ultrasound for monitoring in the place of venograms has several advantages.

## CASE REPORT

A 36 years old woman was admitted due to deep vein thrombosis in the right limb with 24 hours of evolution. The thrombus was localized at the common femoral vein, external and common iliac veins. The great saphenous, femoral and the deep femoral veins were spared.

A hip oedema was evident (hip diameter was 52 cm 17 cm above to the patella). A CDT was performed. The procedure, including the control of thrombus lysis, as well as catheter progression was performed under ultrasound guidance.

After 52 hours of treatment oedema disappeared (hip diameter was 50 cm). The control phlebography demonstrated repermeabilization of the right ilio-femoral deep vein. The patient completed 6 months of direct oral anticoagulation. A thrombophilic condition was excluded by appropriate testing. She stopped smoking and taking oral contraceptives. She has 2 years of follow-up without complaints and a computed tomographic scan showed that the deep venous system remains permeable.

## Technical description

The patient was positioned supine with the foot externally rotated. The skin was prepared with betadine and local anesthesia was applied (1% lidocaine). Ipsilateral great

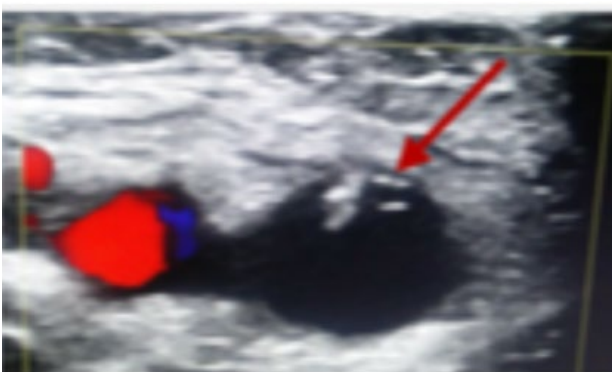


**Figure 1** Great saphenous vein with a 4 Fr multiperforated straight catheter to perform thrombolysis.

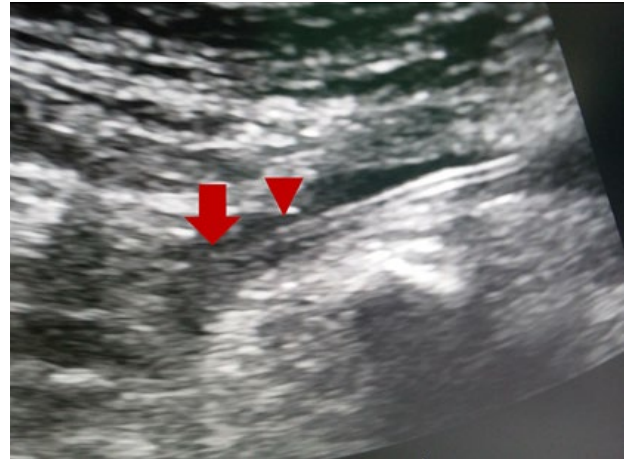
saphenous vein was punctured with ultrasound guidance. A 5 Fr sheath was positioned and 4 Fr multiperforated straight catheter was inserted on a guidewire Terumo angled type (Figure 1). The antegrade progression of the guidewire and the catheter was monitored with ultrasound until the catheter tip was in direct contact with the distal end of the thrombus, at the common femoral vein. Heparin (500-1000U/h- aPTT target: 50-90 seconds) was infused into the sheath while the thrombolytic- alteplase (0,01mg/kg/h) was simultaneously infused into the catheter. The patient was evaluated clinical, analytically (hemoglobin, platelets, APTT, fibrinogen) and with ultrasound twice a day. She used compression stockings.

8 hours after the procedure, ultrasound controlled showed that the common femoral vein was patent (Figure 2). With ultrasound control the catheter was proximally moved until the tip reached the distal end of the thrombus at the external iliac vein, 10 cm above the inguinal ligament. Twice a day the thrombolysis was monitored using doppler ultrasound, instead of phlebography.

52 hours after the procedure the ultrasound control showed permeability of deep vein system (Figure 3). To confirm the result a phlebography was performed. The phlebography showed small filling defects at the external iliac vein without compromising the venous return. We decided to not deploy a stent. The CT scan performed at follow-up showed the permeability of deep vein system (Figure 4 and 5).



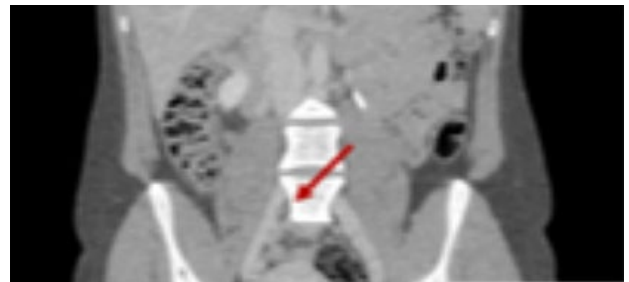
**Figure 2** Transverse vascular ultrasound image showing the catheter tip (arrow) in the right common femoral vein.



**Figure 3** Longitudinal vascular ultrasound image showing the thrombus (arrow) and the catheter tip (triangle) in the right external iliac vein.



**Figure 4** CT scan (performed two years after the thrombolysis) showing the permeability of common femoral right vein (arrow).



**Figure 5** CT scan (performed two years after the thrombolysis) showing the permeability of right common iliac vein (arrow).

## DISCUSSION

To our knowledge this is the first case reported in the literature about the use of vascular ultrasound to monitor the efficacy of thrombolysis and to adjust the catheter position according to the lysis of the clot.

The ATTRACT trial concluded that there was no difference in the incidence of post-thrombotic syndrome in patient treat with CDT when compared to patients on anticoagulation.<sup>4</sup> However, this study included patients with acute deep vein thrombosis in the femoropopliteal segment alone as well



as those with proximal iliac thrombosis. The iliofemoral cases are known to be higher risk for late post-thrombotic syndrome.<sup>4</sup> The subgroup analysis of the ATTRACT trial showed that the CDT may have a benefit in patients with iliac vein thrombosis.<sup>4</sup>

Lin considered that catheter direct thrombolysis should be performed in younger, healthier patients, with more to gain from prevention of post-thrombotic syndrome later in life.<sup>6</sup> In this report the patient was 36 years old, healthy, with a low risk of bleeding, so we judged that she could benefit from CDT. We decided to use the vascular ultrasound during the procedure minimizing the number of phlebographies.

Ultrasound was used to obtain venous access, as recommended.<sup>1,3,7</sup> It is necessary due to the variable vessel course, to avoid puncturing the thrombosed vein and the nearby structures (arteries and nerves), to minimize the bleeding risk and to preserve the integrity of the access.<sup>1,3,7</sup>

In this case the great saphenous vein and antegrade approach were used as an access to thrombolysis. Fiengo demonstrated that the use of great saphenous vein is a valid, safe and easy alternative to the deep vein system, with less risk of haematoma and venous lesion. <sup>8</sup> This access can be performed in supine position, while the popliteal vein (the alternative access in this case) would be approached in prone position.<sup>9</sup> In a randomized control study comparing the popliteal, great and small saphenous vein as an access to CDT thrombolysis, the authors concluded the great saphenous vein was the most efficacious.<sup>9</sup> The antegrade approaches chosen during catheterization reduce the risk of damage to the valve leaflets.<sup>9</sup>

In this case report, the vascular ultrasound was performed every 6 hours to monitor the thrombolysis and when indicated to advance the catheter into the clot. To our knowledge this technique has not been described in the literature. It has several advantages in a patient with a favorable biotype. It can be performed at the bedside, minimizing the patient movement and the risk of catheter displacement.<sup>10</sup> The number of phlebographies can be minimized, avoiding the radiation and contrast exposition which is a particular advantage in younger patients.<sup>10</sup> In a study published by Madsen during thrombolysis a daily venography was performed requiring a median of three invasive procedures.<sup>11</sup> The injection of contrast material, during phlebographies can disrupt the thrombus.<sup>12</sup> The thrombolysis and the contrast exposition can cause nephropathy. <sup>7</sup> With the use of ultrasound, the thrombolysis follow-up can be frequently performed with a constant reposition of the catheter improving the thrombolysis efficacy. In this case the thrombolysis was performed in 52 hours, the thrombolytic protocols range from 12-72 hours.<sup>7</sup>

## CONCLUSION

The use of vascular ultrasound to monitoring the venous thrombolysis has theoretical advantages. Avoids

radiation and contrast exposition, can be performed at the bedside is inexpensive, do not cause discomfort. It will be necessary to increase the number of study patients to validate this approach.

## REFERENCES

1. Fleck D, Albadawi H, Shamoun F, Knuttinen G, Naidu S, Oklu R. Catheter-directed thrombolysis of deep vein thrombosis: literature review and practice considerations. *Cardiovascular Diagnosis and Therapy* 2017;7(3):S228–S237.
2. Jenkins JS, Michael P. Deep Venous Thrombosis: An Interventionalist's Approach. *The Ochsner Journal* 2014;14(4):633–640.
3. Gogalniceanu P, Johnston CJC, Khalid U, Holt PJE, Hincliffe R, Loftus IM, Thompson MM. Indications for Thrombolysis in Deep Venous Thrombosis. *European Society for Vascular Surgery* 2009;39:192–198.
4. Marston WA, Hill C. Results of the ATTRACT trial do not change the management of acute deep vein thrombosis. *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 2018;6(1):5–6.
5. Comerota AJ, Kearon C, Julian JA, Goldhaber SZ, Kahn SR, Jaff MR, Razavi MK, Kindzelski AL, Bashir R, Patel P, Sharafuddin M, Sichel MJ, Saad WE, Assi Z, Hofmann LV, Kennedy M, Vedantham S. Endovascular Thrombus Removal for Acute Iliofemoral Deep Vein Thrombosis. *Circulation* 2019;139:1162–1173.
6. Lin M, Hsieh JCF, Hanif M, McDaniel A, Chew DK. Evaluation of thrombolysis using tissue plasminogen activator in lower extremity deep venous thrombosis with concomitant femoral-popliteal venous segment involvement. *Journal of Vascular Surgery: Venous and Lymphatic Disorders* 2017;5(5):613–620.
7. O'Connor P, Lookstein R. Endovascular Interventions for Venous Disease. *Techniques in Vascular and Interventional Radiology* 2018;21(2):55–64. Doi: 10.1053/j.tvir.2018.03.010
8. Fiengo L, Bucci F, Khalil E, Salvati B. Original approach for thrombolytic therapy in patients with Ilio-femoral deep vein thrombosis : 2 years follow-up. *Thrombosis Journal* 2015;13:1–5. Doi: 10.1186/s12959-015-0070-0.
9. Duan P, Ni C. Randomized study of different approaches for catheter-directed thrombolysis for lower-extremity acute deep venous thrombosis. *Journal of the Formosan Medical Association* 2016;115(8):652–657. Doi: 10.1016/j.jfma.2015.07.001.
10. Conte MS, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, Mills JL, Ricco J-B, Suresh KR, Murad MH, GVG Writing Group. Global vascular guidelines on the management of chronic limb-threatening ischemia. *Journal of Vascular Surgery* 2019;69(6):3S–125S.e40. Doi: 10.1016/j.jvs.2019.02.016
11. Madsen CP, Gesla J, Vijdea RL, Serifi MA, Christensen JK, Houliand K. Results of catheter-directed thrombolysis for acute ilio-femoral deep venous thrombosis- A Retrospective cohort study. *JRSM Cardiovascular* 2018;7:1–8. Doi:10.1177/2048004018766801
12. Kohi MP, Kohlbrenner R, Koli KP, Lehrman E, Taylor AG, Fidelman N. Catheter directed interventions for acute deep vein thrombosis. *Cardiovascular Diagnosis and Therapy* 2016;6(6):599–611.





# EMBOLIZATION OF PERCUTANEOUS LEFT ATRIAL APPENDAGE OCCLUSION DEVICE: RESCUE SURGERY

Manuela Silva\*<sup>1</sup>, Nuno Banazol<sup>1</sup>, António Fiarresga<sup>2</sup>, José Fragata<sup>1</sup>

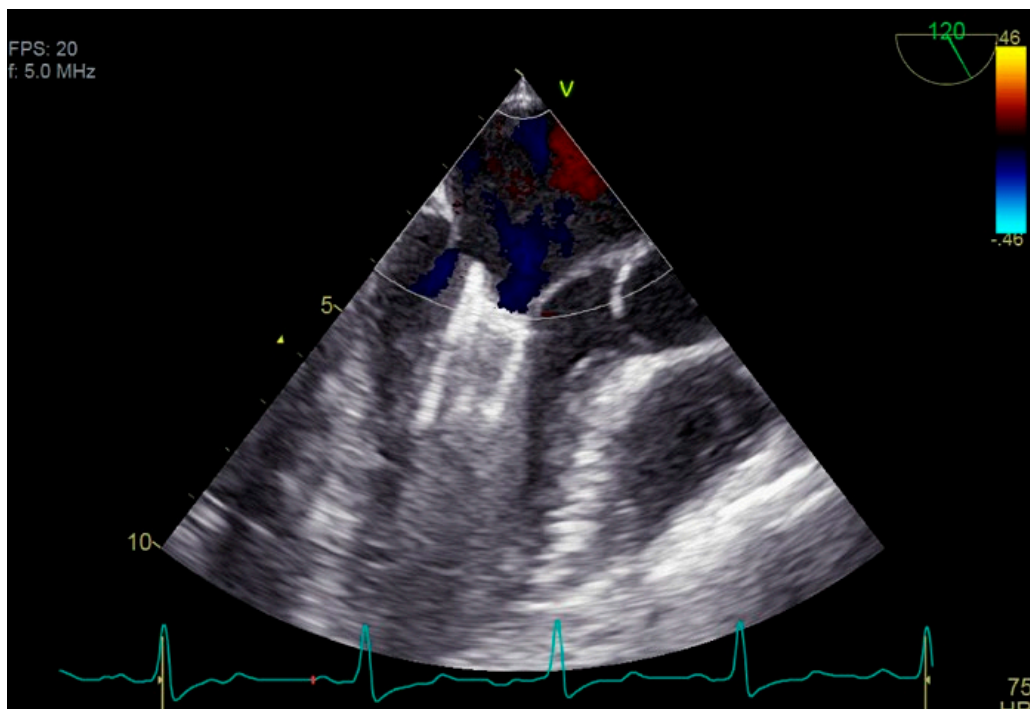
<sup>1</sup>Department of Cardiothoracic Surgery and

<sup>2</sup>Department of Cardiology, Hospital Santa Marta, Centro Hospitalar Universitário de Lisboa Central, Lisboa

\*Corresponding author: manela\_silva@hotmail.com

59-year-old woman with permanent atrial fibrillation and previous haemorrhagic stroke was admitted for percutaneous left atrial appendage occlusion. Shortly after, Amplatzer™ device migration into the left

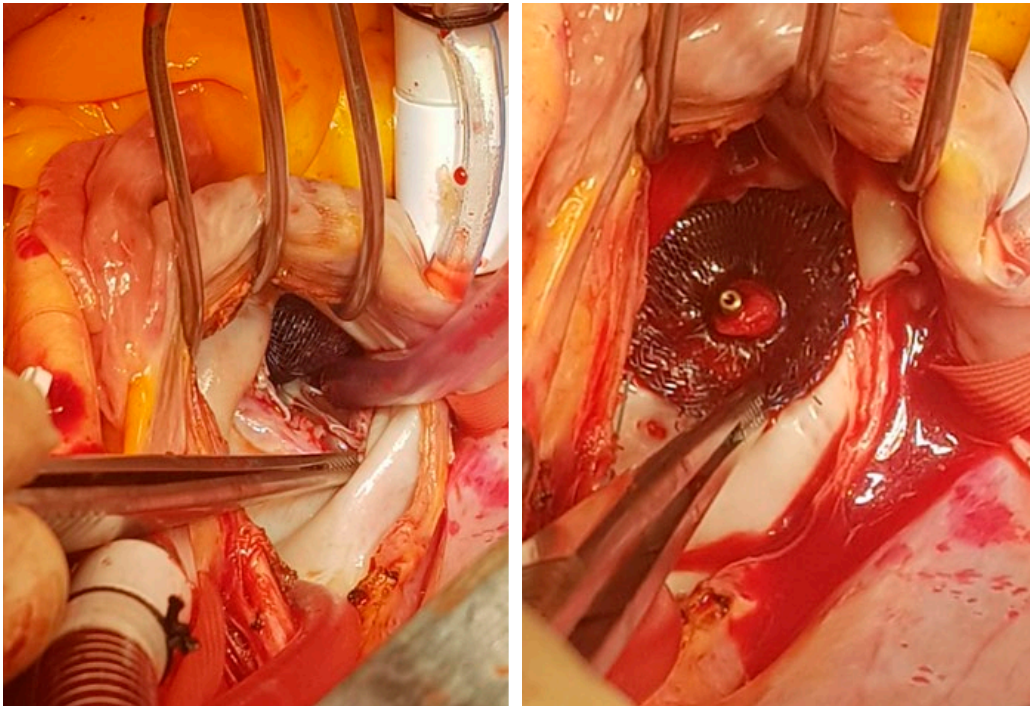
ventricular outflow tract was confirmed. Unsuccessful transcatheter mobilization led to an emergent surgery for device retrieval and LAA closure. No events at 6-month follow-up.



**Figure 1**

*Intraoperative transesophageal echocardiography showing device migration into the left ventricular outflow tract, entrapped in mitral subvalvular apparatus.*





**Figure 2** *Amplatzer™ device retrieval by left atriotomy.*

# VARICOSITY OF THE COMMUNICATING VEIN BETWEEN THE LEFT RENAL VEIN AND THE LEFT ASCENDING LUMBAR VEIN

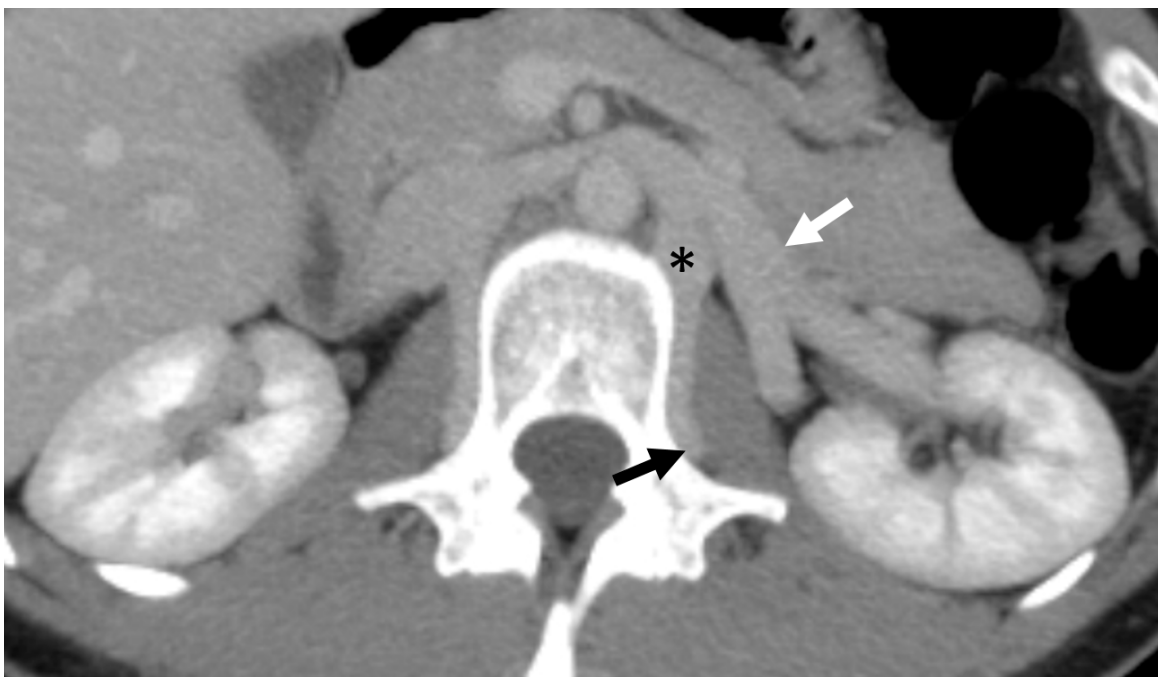
Luísa Amado Costa<sup>\*1</sup>, André Peixoto<sup>1</sup>, Luís Vítor<sup>1</sup>, José Fonseca Santos<sup>1</sup>

<sup>1</sup>Service of General Image, Centro Hospitalar Universitário Lisboa Norte, EPE

\*Corresponding author: al30costa@gmail.com

32 years-old female patient presented with lumbar pain. Computed tomography revealed varicosity of the communicating vein between the left renal vein and the left ascending lumbar vein. This entity may pose

technical difficulties during aortoiliac surgeries and renal surgeries as iatrogenic injury of this vessel may cause life-threatening retroperitoneal hemorrhage.



**Figure 1**

Axial contrast-enhanced computed tomography image shows the ectatic communicating vein (\*) between the left renal vein (white arrow) and the left ascending lumbar vein (black arrow).





**Figure 2**

*Sagittal contrast-enhanced computed tomography image shows the ectatic communicating vein (\*) between the left renal vein (white arrow) and the left ascending lumbar vein (black arrow).*



