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Executive Summary of the Thesis

Topological Data Analysis of the topology of the Abdominal Aortic Aneurysm through the use of Persistent Homology

Laurea Magistrale in Mathematical Engineering - Ingegneria Matematica

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1. Introduction

Abdominal Aortic Aneurysm (AAA) is a vascular disease that affects the aorta, the biggest artery of the human body, in its abdominal portion.
It is considered the most common aortic pathology and is characterized by a dilatation of the vessel caused by the haemodynamical stress and chronical inflammation processes in its inner layers.
AAA is a dangerous pathology that, in an asymptomatic way, can evolve towards the progressive enlargement of the aortic diameter up to leading to its rupture, with fatal consequences if left untreated [1].

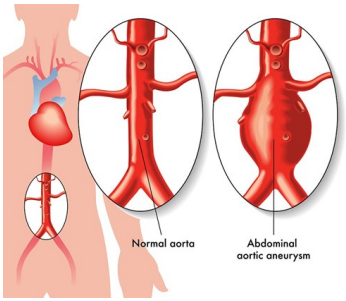


Figure 1: Comparison between a healthy and an aneurysmatic aorta. Image from [2].

AAA often presents with two main wall characteristics: thrombus and calcification. The former being an aggregation of platelets, blood particles and necrotic debris, the latter caused by deposit of calcium causing stiffening of the wall. Both affects negatively the aorta, altering its normal functioning.

2. Context

Although AAA is still not fully understood, there is a vast literature aimed to study it.
Among the large amount of scientific papers, mainly relegated to the medical and biological field, there is an increasing interest among the engineering community.
Yet, given the quantity of available studies, a statistical analysis of AAA's variability seems to be little considered, especially when compared to the huge number of mechanical and haemodynamical studies. The latters provide important results about the connection between the abnormal geometry of the vessel affected by the pathology and the haemodynamical and mechanical indexes that can quantify the risk of rupture such as the Wall Shear Stress (WSS) [3] and thrombus deposition with the Oscillatory Shear Index (OSI) [4].

This thesis aims at filling the main gaps in statistical literature with two different kinds of approaches regarding the AAA's morphology.

3. Exploratory Analysis

As a first exploratory study, a cluster analysis has been performed to group patients affected by AAA using morphological features, in order to have an insight on the shapes' variability and start to approach the clinical problem with geometrical descriptors of the AAA, which are the most common available data.
The data used belong to a dataset taken from [5] and consist of 255 patients described by 3 different types of numerical features:

- Global descriptors of the abdominal aorta: length of the first healthy portion under the renal arteries (i.e., aortic neck) and its mean diameter, aortic length, tortuosity and maximum diameter. The dataset contains also features related to the iliac arteries such as their maximum diameter.
- Normalized global descriptors: the previous descriptors divided by aortic mean neck diameter. This class of features is particularly important, enclosing the information on how much the aorta has grown compared to its healthy state, something that the raw dimensions above can not provide.
- Angles: the last category of features used in this analysis consists of aortic and iliac 3D angles. The importance of angles, besides giving insights on the general shape of the aorta, is supported by various studies [6]. These claim that the complexity of the aortic geometry can bring to an unsteady blood flow resulting in irregular secondary flow patterns altering the aorta's normal functioning.

The complete list of variables used can be seen in Figure 3 below.
Among the methods used, it was decided to use one of the most common statistical tools: Hierarchical Clustering. It works by progressively aggregating the patients together (e.g., observations) using specified criterion (e.g., linkages and distances).
Analysis have been performed on *R* version 4.2.0.
The most satisfying results have been found using Ward D2 linkage dividing patients in five different groups. The results found are robust to a change of distance, always providing similar results.
The groups found have been interpreted, with the clinician's help, looking at the expected AAA severity. The five colors used to name the groups are: Blue, Green, Grey, Orange and Red. Blue and Green clusters are the largest groups (respectively 83 and 78 patients) characterized by the presence of a small aneurysm. They are differentiated by aortic neck's diameter and consequently normalized dimensions. In fact, Green cluster's patients have a bigger healthy aortic diameter compared to the ones in the Blue one but are otherwise similar with respect to AAA's dimensions and angles.

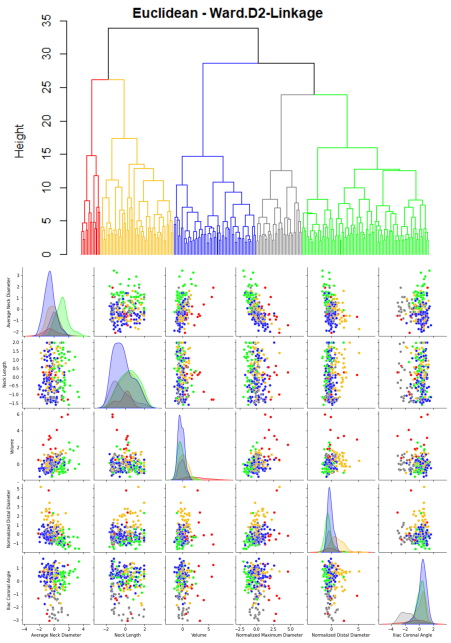


Figure 2: Here it is possible to see the final groups' distribution for the variables considered most characterizing along with the associated dendrogram.

Grey cluster is a small group of 22 patients that, having similar AAA dimensions to the Blue and Green groups, is characterized by acute iliac angles and an unusual aortic shape.
The remaining two groups can be considered representative of the more complicated cases. The Orange group presents aneurysms that involve the lower portion of the abdominal aorta even extended, in some cases, to the iliac arteries. Lastly, the Red cluster, that is composed by only 6 patients, refers to the most concerning

cases with bigger diameters and higher volumes. To refine the clusters, discarding unused features and to see the most important ones, an univariate permutational Analysis of Variance (ANOVA) with 5000 permutations has been performed. The choice to opt for a permutational ANOVA rather than its standard counterpart has been driven by the lack of Gaussianity of the univariate populations. It was chosen to discard only the features whose associated p-value was higher than 0.01, that is many of the angles initially considered. See Figure 3 for further details.

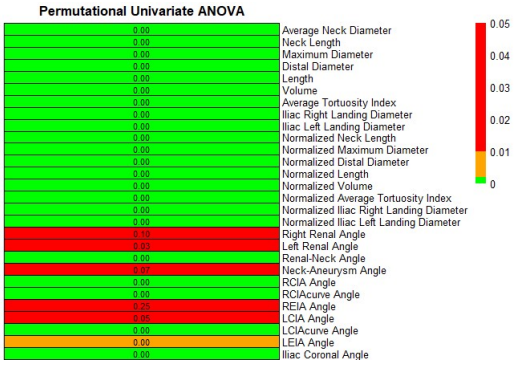


Figure 3: The results of the Permutational ANOVA performed on each variable. Red values are associated with discarded features while green ones are associated with a p-value lower than 0.001.

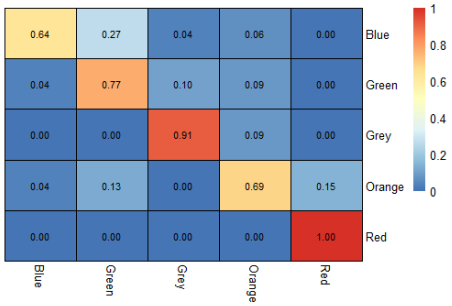


Figure 4: A confusion matrix containing the cardinality of each combination of original (rows) and reduced (columns) groups, standardized by rows to highlight their similarity.

Redoing the cluster analysis, the new clusters were found to be consistent with the previous ones, meaning that the groups found by the algorithm are not only clinically interesting but also robust to a change of distance and to a variable reduction, as can be seen in Figure 4.

These results provide an initial evidence that patients' stratification, based on AAA's morphological features, is possible. They also provide an overview of the different deformations that can affect the aorta when AAA develops.
Despite that, this initial dataset has been put aside, as well as the initial aim, given the lack of other features to better describe the aortic morphology. It was then chosen to opt for another type of data: instead of exploit global descriptors, a new dataset has been built combining data derived from Computed Tomography Angiography (CTA) scans, the most frequent imaging source for the diagnosis of arterial diseases, and Persistent Homology, a widely used method in Topological Data Analysis (TDA) to study objects' topological features.

4. Models and Methods

CTA scans consist of a detailed 3D imaging of a part of interest in the human body in the form of a volume composed by voxels of different shades of grey. Each shade of color is associated to a different biological tissue making possible to differentiate between not only fat, bones and muscle but also artery, veins and thrombus or calcification inside them (See Figure 5).

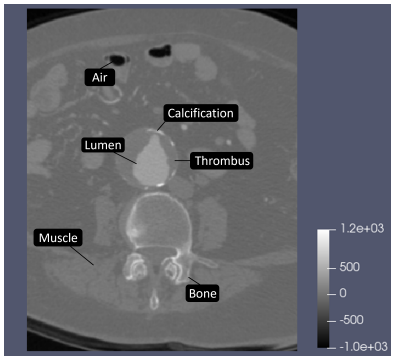


Figure 5: Coronal slice of a CTA scan of the abdomen. The lumen of the aorta is visible, surrounded by thrombus and calcifications.

In this work, the main utility of CTA scans is not visualization purposes, as could be for the clinicians, but the fact that they allow to create a segmentation of the aortic lumen, the region where the blood flows.
In the medical field, arterial segmentation refers to the process that leads to obtain a 3-dimensional reconstruction of the object of interest via a finite number of points.

The product of the segmentation is called mesh, a set of vertices, edges and cells, as can be seen in Figure 6.
Another object obtained by the segmentation is the centerline. The idea of centerline of a vessel is to find a continuous curve in space that represents the center of the analysed vessel, creating a powerful descriptor of its shape.
Segmentation is made possible thanks to a complex pipeline provided by *Moxoff*, that makes use of the *Python* library *vmtk* [7].

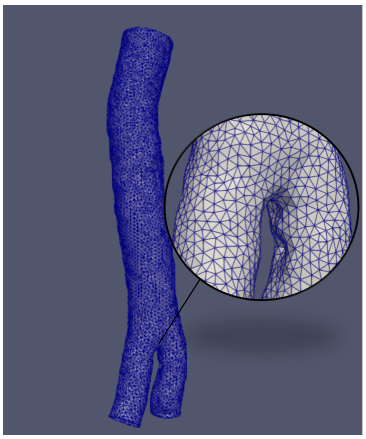


Figure 6: The mesh of a healthy aorta. Edges and cells composing it are highlighted in the zoomed detail.

The tract of the abdominal aorta considered in this study ranges between the distal renal artery and the common iliac arteries, including the area eventually affected by the AAA, when present.

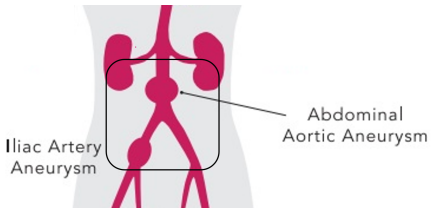


Figure 7: A schematic view of the area of interest segmented by the pipeline.

This leads to the creation of a dataset consisting of 22 meshes (10 healthy aorta and 12 aneurysmatic ones) provided by *Policlinico di Milano*. Segmentation, making it possible to obtain digital models of the aorta, allows the use of Persistent Homology. Roughly speaking, Persistent Homology describes the differences that occur in the homology of a shape detecting the presence of k-cycles in the object, also called *holes*, when a parameter changes. Holes in dimension 0 are path-connected components while in dimension 1 are closed paths surrounding a hole [8].
The function used to record the "time" of change in the object's homology, in terms of *birth* and *death* of its k-cycles, is called filtration. In this work, each point of the mesh was assigned, as a filtration value, the least Euclidean distance from the points of the centerline.
In fact, the distance from the centerline seems to be the most natural way in order to study the irregularities in the lumen's surface, in the sense of indentations and bumps, made by stretches of the aortic wall, keeping track at the same time of the AAA's radius.
Finally, all distances have been normalized dividing them with the average neck's radius. This is necessary in order to make possible the comparison between different patients whose arteries can be quite variable and to keep into account the relative growth of the AAA, similar to how done in the exploratory analysis.
This process leads to the final data, the Persistence Diagrams. Persistence Diagram is a visualization and representation method of the "times" of birth and death of holes, also called persistence pairs.

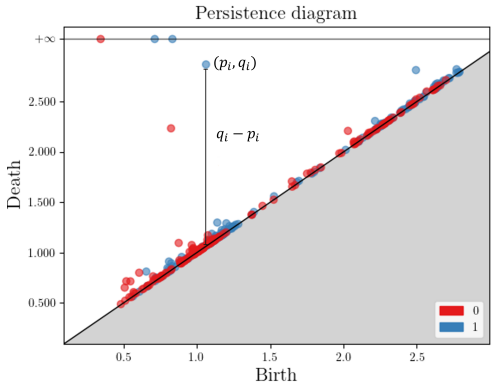


Figure 8: An example of persistence diagram, the points in red are 0-holes while the blue ones are 1-holes.

A Persistence Diagram is a collection of persistence pairs drawn as points in the Cartesian plane. Each point has 3 variables: type of cycle (0 or 1-dimensional), birth (p) and death (q). The difference between the latters is the persistence, the more a pair persists, the more relevant is the topological features associated to it.
Another important aspect of persistence dia-

gram is that it is possible to add a notion of distance with proved stability results [9], making quantification of the dissimilarity between diagrams possible and allowing to perform statistical analysis.
The whole procedure has been conducted on *python 3.8*. After this process, all 22 meshes have been turned into Persistence Diagrams, ready to be visualized and studied.

5. Results

To understand the power of the obtained representation, a comparison between the original mesh and the associated diagram has been made for every patient, searching for a possible link between the most important aortic wall features such as calcification and thrombus to the diagram's points.

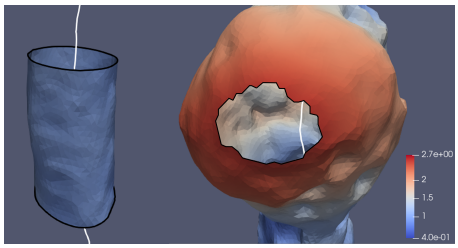


Figure 9: An example of the two types of 1-cycle, with the centerline and the meshes' contours highlighted respectively in white and black.

The first discovery is the meaning of 0 and 1 dimensional holes in application. In fact, 0-holes are recesses in the lumen's surface. On the contrary, 1-holes are associated with two phenomena. Being closed path around an hole a persistence pair associated to a 1-hole can represent both the natural tubular structure of the aorta or an hole created by points more distant from the surface an thus, an outgrowth in the lumen surface (See Figure 9).

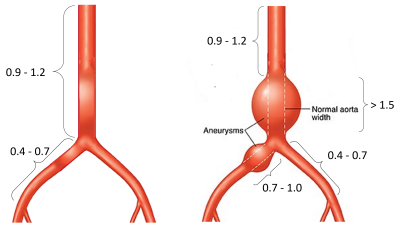
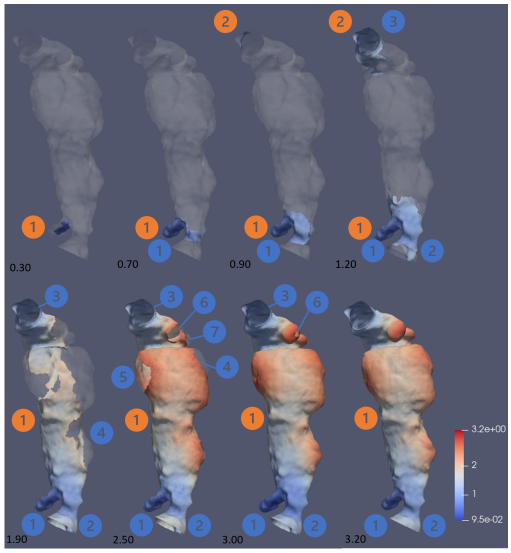


Figure 10: A schematic view of the aorta, with the filtration values explicited.

In particular, it is also possible to specifically link 0-cycles with the presence calcification, while 1-cycles are connected with aneurysm and thrombus.
Another important aspect regarding the filtration chosen is that it is a mean to understand in which portion of the aorta the change in homology occurs: when a pair is born (or dies) at value 1 ± 0.2 (mean neck's radius), a change in homology is located on the healthy portion of the aorta. If this value is lower, then the change affects the iliac arteries (anatomically smaller than the main aorta) while if it is much greater an AAA affects the artery (See Figure 10).



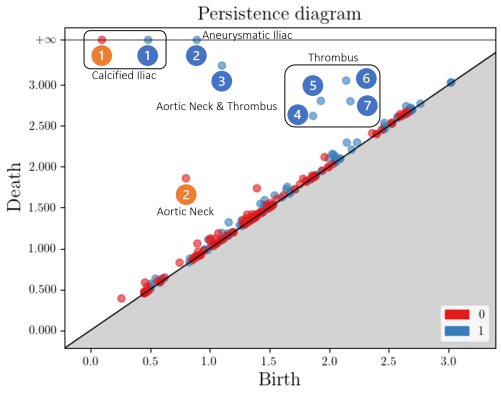
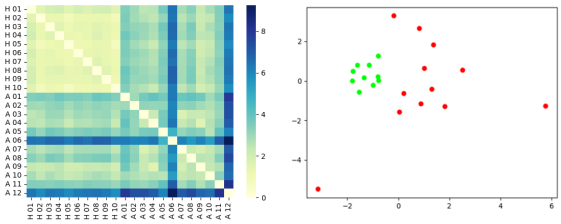


Figure 11: An example of the completeness of representation of persistence diagram on qualitative side along with the associated diagram.

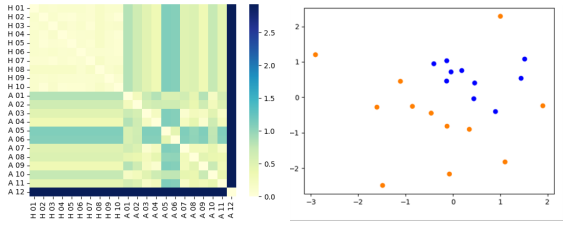
A final significant feature is that there are notable pairs in the diagram. For example, any aorta has one 0-cycle and two 1-cycle with infinite persistence, associated to the aorta itself

and one of the two iliacs. To recap, each pair's variable (type, birth and death) gives to the reader of the diagram insight not only on the aortic shape but also on the pathologies that affect it (See Figure 11 for a detailed example).
Finally, the capacity to enclose and summarize the topological information has been tested using Bottleneck and Wasserstein distances performing a Multidimensional Scaling (MDS) (See Figure 12 and 13).



(a) (b)

Figure 12: On the left, an heatmap based on the Wasserstein distances comparing 1-pair diagrams, with healthy aortas labelled with "H" while the rest is marked with "A". On the right, the result of MDS with green and red points respectively the patients with healthy and aneurysmatic aortas.



(a) (b)

Figure 13: Here, instead the heatmap based on the Wasserstein distances comparing 0-pair diagrams. On the right, the result of MDS with blue and orange points respectively patients without and with presence of calcification.

If the previous results (Figure 11) were an evidence of the potential of this representation, this result show it on the quantitative extent: not only aneurysmatic aortas are in a separate region respect the healthy one, that are also less scattered (in fact healthy aortas have little variability regarding the morphology), but it is also possible to recognize advanced aortic wall's features such as calcifications (Figure 13). Thus demonstrating the advanced ability for discrimination offered by persistence diagrams.

6. Limitations and Future Developments

Many are the possible future developments and can be aimed both at enhancing the analysis, by solving the major limitations encountered, or further expand this work.
The most important limitation of this study is the length of the process that leads to the extraction of the Persistence Diagram from the CTA scan. This brings to a second limit: future improvements should focus on the replication of the previous findings in larger cohorts, considering also epidemiological and clinical risk factors related to AAA's development and aim to add thrombus segmentation to obtain the full aortic wall.
Further developments could also regard a sensitivity study. In fact, given the strong connection between segmentation and final diagram, it is worth to perform an analysis on the high number of parameters used, such as the thickness of the mesh's resolution.
Focusing on the statistical core of the work, the use of different models to classify or cluster patients based on their persistence diagram or make regression by adding clinical features as covariates could be another interesting exploration. These changes, if combined with hemodynamical studies, could open the way to define new models for the quantification of AAA's rupture risk.

7. Conclusion

TDA allows to expand the use of statistics to CTA analysis in a mathematically rigorous way, retrieving a low-dimensional representation of the aorta that could be effective for clinical research.
This brings to an accurate summary of the aortic morphology, making Persistent Homology a promising mathematical tool that could be adopted in future studies on AAA's growth. It could also be used by clinicians in the always growing awareness and knowledge of AAA and other vascular pathologies.

Acronyms

AAA Abdominal Aortic Aneurysm. 1–6
ANOVA Analysis of Variance. 3

CTA Computed Tomography Angiography. 3, 6

MDS Multidimensional Scaling. 6

OSI Oscillatory Shear Index. 1

TDA Topological Data Analysis. 3, 6

WSS Wall Shear Stress. 1

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