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# A cohort longitudinal study identifies morphology and hemodynamics predictors of abdominal aortic aneurysm growth

Florian Joly, Gilles Soulez, Simon Lessard, Claude Kauffmann, Irene Vignon-Clementel

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1 A cohort longitudinal study identifies morphology and  
2 hemodynamics predictors of abdominal aortic aneurysm  
3 growth

4 Florian Joly<sup>1,3</sup>, Gilles Soulez<sup>2</sup>, Simon Lessard<sup>2</sup>, Claude Kauffmann<sup>2</sup>,  
and Irene Vignon-Clementel<sup>1,3</sup>

5 **affiliations:** <sup>1</sup> Inria, Centre de recherche de Paris, 75012 Paris, France <sup>2</sup> Department of  
6 Medical Imaging, University of Montreal Hospital Research Center, H2X0C1 Montreal,  
7 Canada <sup>3</sup> Sorbonne Université, Laboratoire Jacques-Louis Lions, 75005 Paris, France.

8 **abbreviated title:** A cohort longitudinal study identifies AAA risk predictors

9 **corresponding author:** I. Vignon-Clementel,

10 Centre de Recherche Inria de Paris, 2 rue Simone Iff, CS 42112, 75589 Paris Cedex 12  
11 (FRANCE)

12 Phone: +33.1.80.49.42.67

13 e-mail: irene.vignon-clementel@inria.fr

14  
15 **Abstract**

16 Abdominal aortic aneurysms (AAA) are localized, commonly occurring aortic di-  
17 lations. Following rupture only immediate treatment can prevent morbidity and mor-  
18 tality. AAA maximal diameter and growth are the current metrics to evaluate the  
19 associated risk and plan intervention. Although these criteria alone lack patient speci-  
20 ficity, predicting their evolution would improve clinical decision. If the disease is known

21 to be associated with altered morphology and blood flow, intraluminal thrombus de-  
22 posit and clinical symptoms, the growth mechanisms are yet to be fully understood.  
23 In this retrospective longitudinal study of 138 scans, morphological analysis and blood  
24 flow simulations for 32 patients with clinically diagnosed AAAs and several follow-up  
25 CT-scans, are performed and compared to 9 control subjects. Several metrics stratify  
26 patients between healthy, low and high risk groups. Local correlations between hemo-  
27 dynamic metrics and AAA growth are also explored but due to their high inter-patient  
28 variability, do not explain AAA heterogeneous growth. Finally, high-risk predictors  
29 trained with successively clinical, morphological, hemodynamic and all data, and their  
30 link to the AAA evolution are built from supervise learning. Predictive performance  
31 is high for morphological, hemodynamic and all data, in contrast to clinical data. The  
32 morphology-based predictor exhibits an interesting effort-predictability tradeoff to be  
33 validated for clinical translation.

34 **keywords:** abdominal aortic aneurysm; growth; CFD (Computational Fluid Dynam-  
35 ics); haemodynamics; ILT (Intra-Luminal Thrombus); longitudinal study; risk prediction;  
36 supervised learning; wall shear stress

# 1 Introduction

Abdominal aortic aneurysms (AAA) are local dilations of the abdominal aorta which can rupture when blood pressure overcomes artery wall resistance. Following rupture only urgent treatment can prevent morbidity and mortality. It is the 14<sup>th</sup> leading cause of death in the USA<sup>57</sup> with a prevalence of 8.9% for men and 2.2% for women.

AAA are generally asymptomatic and generally detected through unrelated examinations. Risk is assessed using its maximal diameter ( $D_{max}$ )<sup>47</sup>, taken at the outer wall of the aneurysm on a plane perpendicular to the lumen centerline<sup>16</sup>. It includes the lumen, the Intra Luminal Thrombus (ILT) and the arterial wall which diameter cannot be distinguish on CT-scans. If the  $D_{max}$  exceeds a statistically-based threshold of 55 mm for men and 45-50 for women<sup>13</sup> or if AAA  $D_{max}$  growth exceeds  $1\text{cm}\cdot\text{yr}^{-1}$ <sup>17</sup>, patients will undergo open or endovascular aneurysm repair. Otherwise a yearly control is performed.

New guidelines<sup>18</sup> define a more complex follow-up and repair decision process, highlighting the difficulty to predict AAA evolution based on its current diameter.  $D_{max}$  is an imperfect criterion as the estimated annual rupture rate of 4.0 to 4.9 cm AAA, is non-negligible (1.0% per year)<sup>48</sup> and 23% of ruptured AAA are less than 5 cm<sup>20</sup>. In contrast, rupture rate in large aneurysms could be lower than expected with annual rupture rate of 3.5% for 5.5 to 6 cm and 4.1% in 6 to 7 cm AAAs<sup>48</sup>. These data show the maximal diameter/rupture relationship to be nonlinear and inaccurate to predict rupture<sup>28</sup>. Identifying better performing metrics is an active research field<sup>34</sup>. Risk-linked predictors are usually based on geometric shape, mechanical tissue properties and flow topology thanks to the increased availability of patient-specific 3D AAA models from computed tomography angiography (CTA). Several fields can even be combined in multi-physics and multi-scale modelling making it possible to simulate AAA growth<sup>29,67</sup> by coupling the biology and mechanics of the disease. Known metrics of interests are AAA volume, surface, bulge height, tortuosity and local surface curvature<sup>55,56</sup> as well as mechanical stress, intrinsically relying on tissue properties, strongly heterogeneous and nonlinear<sup>49</sup> and also patient specific<sup>50</sup>. From a fluid point of view, blood flow is known to play a crucial role in AAA evolution<sup>54,5</sup>, as well as ILT presence and



65 growth<sup>30,7</sup>.

66 Very few studies focus on local parameters and their variations between two scans. Tzi-  
67 rakis et al.<sup>64</sup> observed on six AAA, a relationship between ILT growth and Time Average  
68 Wall Shear Stress (TAWSS) and Oscillatory Shear Index (OSI) but not with Relative Res-  
69 idence Time (RRT), while Arzani et al.<sup>4</sup> noticed in ten AAAs a significant relationship  
70 between ILT deposition and low OSI but not with low TAWSS. Both studies included small  
71 AAA ( $D_{max} < 53$  and  $< 50$  mm respectively). Zambrano et al.<sup>71</sup> observed a relationship  
72 between low Wall Shear Stress (WSS) and the ILT deposition locations. Furthermore on  
73 their 14 patients, ILT volume accumulation correlated with the AAA growth. The investi-  
74 gation of the hemodynamic mechanisms underlying AAA expansion is a promising approach  
75 to understand, and potentially provide more patient-specific tools to characterize, AAA vul-  
76 nerability. From a solid mechanics point of view, Martufi et al.<sup>41</sup> found that ILT thickness  
77 and wall stress were linked to the local growth rate.

78 In summary, although repair criteria alone lack patient specificity, predicting their evo-  
79 lution would improve clinical decision for follow-up and repair. If the disease is known to  
80 be associated with altered morphology and blood flow, intraluminal thrombus deposit and  
81 clinical symptoms, the growth mechanisms are yet to be fully understood. The goal of this  
82 work is thus to better understand AAA evolution by exploring the potential dependence  
83 between computed hemodynamics factors and morphological metrics of AAA growth on a  
84 larger longitudinal study. In this retrospective longitudinal study of 138 scans, morphologi-  
85 cal analysis and blood flow simulations for 32 patients with clinically diagnosed AAAs and  
86 several follow-up CT-scans, are performed and compared to 9 control subjects. First, the  
87 definition of a healthy group, versus low and high risk groups in terms of AAA evolution  
88 is motivated. The methods also explain the geometrical and blood flow numerical models,  
89 and define their postprocessing into global and local metrics. Global parameters distinguish-  
90 ing the different groups are explored, followed by local correlations between hemodynamics  
91 metrics and AAA growth. Finally, high-risk predictors trained with successively clinical,  
92 morphological, hemodynamic and all data, and their link to the AAA evolution are built

93 from supervise learning. A schematic representation of the article structure is presented in  
94 Figure 1.

95 [Figure 1 about here.]

## 96 **2 Materials and Methods**

97 This section first describes the patient population and associated definitions. Next, the  
98 geometrical model construction and blood flow simulation set-up are explained. Finally,  
99 postprocessing of geometry and CFD results is detailed, defining global and local metrics  
100 associated with each scan, along with the statistical analysis methods used in this study.

### 101 **2.1 Patient population and associated definitions**

102 This study is HIPAA (Health Insurance Portability and Accountability Act) compliant and  
103 approved by the local institutional review board (IRB)<sup>1</sup>. Since all data were anonymized,  
104 the consent form was waived by the IRB for all patients. Forty-one patients are included in  
105 the study, thirty-two with diagnosed AAA and nine healthy. Patients are considered healthy  
106 in the absence of AAA ( $D_{max} < 30$  mm) and significant arterial disease. They necessitated  
107 an abdominal scanner but without peripheral disease, were above 48 year old and were sex-  
108 matched with the AAA patients. AAA patients were selected from a clinical data base of  
109 patients having CT follow-up for AAA in our institution. The inclusion criteria for AAA  
110 patients were: **1.** AAA of more than 30 mm, **2.** At least one baseline CT and 2 following CT  
111 scan examinations, **3.** All selected CT scans were acquired with contrast injections and with  
112 a slice thickness of less than 2.5 mm in order to ensure accurate and efficient segmentation  
113 of the lumen and ILT.

114 This retrospective study does not include ruptured AAA. Usually patients with ruptured  
115 AAA are rarely followed by CT-scan as AAA is usually undiagnosed in such cases. Moreover

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<sup>1</sup>Approval #12.153 from the research ethics committee of the University of Montreal Health Centre (CHUM)

116 the AAA size ( $D_{max}$ ) can be influenced by AAA deflation following rupture and AAA outer  
117 wall is more difficult to evaluate in presence of a periaortic hematoma.  $D_{max}$  value and  
118 growth are therefore combined as a surrogate risk metric. In the text the term *risk* will refer  
119 to this definition and not *rupture risk*.

120 The AAA population is classified in high and low-risk populations based on the recognized  
121 criteria of AAA size and growth over time ( $D_{max}$  and  $D_{max}$  growth). The commonly used  
122 clinical thresholds to indicate an open or endovascular surgery are a  $D_{max}$  of 55 mm for  
123 male and 45-50 mm for women and a growth of more than 5mm in 6 months<sup>17</sup>. New  
124 guidelines<sup>18</sup> temper these thresholds, indicating the need for more personalized approaches.  
125 There is less consensus on the growth threshold. Growth rate has been reported to be  
126 around  $2\text{mm yr}^{-1}$ <sup>11,59</sup>. The 5mm/year growth threshold has previously been recognized as a  
127 fast growth criterion<sup>25</sup> and this growth variation is above the 95% of the confidence interval  
128 of  $D_{max}$  measurement error<sup>58</sup>. To define high risk at scan time  $n$ , we thus choose 'either  
129  $D_{max}^n$  is over 50mm for women and 55mm for men, or  $D_{max}$  variation ( $D_{max}^{n+1} - D_{max}^n$  between  
130 consecutive scans) is above  $5\text{mm yr}^{-1}$ . A patient is considered at low risk if he/she is not at  
131 high risk. Cases are considered as high risk, as soon as one of the high risk criteria is met.  
132 For a patient at low risk, if this occurs, the patient switches to high risk for the rest of the  
133 follow-up scans.

## 134 2.2 Geometrical model construction

135 For all scans, lumens are extracted by an active contour method implemented in *ITK-*  
136 *Snap*<sup>70</sup>. Aortic models include part of the suprarenal aorta including the ostia of coeliac  
137 trunk, mesenteric artery and renal arteries, as well as infrarenal aorta, and internal and  
138 external iliac arteries. ILTs are segmented using *ORS Visual*<sup>37</sup>, which is based on active  
139 snake segmentation.

## 2.3 Blood flow simulation set-up

The incompressible Navier-Stokes equations are solved in each aortic model as detailed in<sup>34</sup>. The flow is considered laminar, homogeneous and non-Newtonian, the viscosity following the Quemada model<sup>40,35</sup>. Model parameters are chosen according to the study of Buchanan et al.<sup>14</sup> based on the rheological data from Kaibara et al.<sup>35</sup>. Peak Reynolds numbers of 1700-2000 at the proximal inlet in the simulations are within the physiological range<sup>28</sup> as well as the Womersley numbers, ranging from 10 to 15<sup>44</sup>. A generic flow rate is imposed at the inlet<sup>43</sup> (see Figure I) with Womersley profile<sup>66</sup>. The lumen is defined as the space inside the aorta, either bounded by the ILT or the arterial wall. Both are considered rigid and a no-slip condition for the blood is imposed on the boundary they form. The ILT is thus excluded from the computational domain. Complex re-circulation patterns oftentimes exists stretching up to the outlet planes. Additionally, reverse flow during diastole<sup>27</sup> is likely to create numerical instability. Gradient stabilization to control complex backflow in the domain similarly to Bertoglio et al.<sup>6</sup> is implemented. At outlets, an RCR Windkessel model is applied (see Table I in Supplementary materials for parameter value). The domain is discretized using a polyhedral mesh with refined boundary layers around 0.8-1 million elements (edge length  $\approx 0.35mm$ ), and the Navier-Stokes equations are discretized with finite volume methods (FVM) implemented in the OpenFOAM toolbox. The convective and diffusive term are discretized using a second order Gauss scheme and the time scheme is Crank-Nicholson, also second order<sup>31,32</sup>. The solver is a large time-step transient solver for an incompressible fluid for solving pressurevelocity coupling, the PIMPLE (merged PISO-SIMPLE) algorithm. The solution is considered converged if:

- each time step is fully converged under chosen residuals criteria, i.e.  $10^{-6}$  for pressure and  $10^{-8}$  for velocity; an adaptive time-step was used with the  $CFL < 1$  criteria.
- the periodic convergence is achieved, typically after 5-7 cardiac cycles.
- the solution (velocity, WSS) is independent of further mesh refinement, computed using the Grid Convergence Index (GCI)<sup>52</sup>

## 2.4 Definition of global and local metrics

*Clinical metrics.* The clinical metrics are listed in Table 1. Their availability among the patient population is reported in the same table.

*Lumen centerline and patch description.* Most morphological metrics rely on the computation of the centerline of the lumen. The centerline is extracted with *VMTK*<sup>2</sup>, which is based on the Voronoï diagram decomposition of the lumen. The subdomain of interest, i.e. the lumen between the lower renal artery and the iliac bifurcation, is automatically extracted by splitting the surface using the centerline bifurcation information<sup>1</sup>. It allows a reproducible domain split necessary for surface and volume comparison. Once extracted, the lumen is split along its rotational (24 divisions or 15°) and longitudinal axis, with respect to the centerline curvature (25 divisions), resulting in 600 patches<sup>3</sup> (see Figure 2 for the method and Figure II in Electronic Supplementary Material for an example). All fields defined on the lumen are averaged on each subdivision. Assuming spatial deformation is spatially homogeneous between acquisitions, each averaged field is compared to its value at the next time step at the estimated same location. Local change is thus computed on a grid-like array : it is the patch-wise variation.

The statistical analysis is thus divided in the following manner:

- Unique value for each AAA, (e.g. ILT volume) and its annual variation ; see Table 2 and Table 3
- Spatially distributed metrics, such as *TAWSS*. First, the distribution information is reported (extrema, average and standard deviations, see Table 4), and then the patch-wise annual variation, also reported as extrema, average and standard deviation. For example, the local change of  $OSI_{max}$  refers the maximal change of OSI value from one patch at time  $t$  to the same patch at time  $t + 1$ . See Table 5 and Table 6.

[Figure 2 about here.]

192 *Morphological metrics.* To characterize the AAA morphology, we consider (see Table II for  
193 definition and references): 1) the maximal lumen diameter  $D_{max}^{lumen}$ , computed as the maximal  
194 diameter of the AAA luminal sections, defined perpendicular to the lumen centerline, 2)  
195 the maximal diameter  $D_{max}$  measured at the outer wall, computed normal to the outer  
196 wall centerline, 3) the ILT thickness (local and global metric), computed as the Euclidean  
197 distance between the lumen and the outer AAA wall, 4) the lumen centerline curvature, 5)  
198 the lumen centerline tortuosity, 6) the Normalized Shape Index (NSI) which characterizes  
199 the deviation from a sphere (NSI = 1). As the arterial wall is not discernible from the ILT,  
200 it is considered of constant thickness and subtracted from the measured distance. The wall  
201 thickness covered by ILT is chosen of a constant value of 1mm<sup>33</sup>. A few other metrics are  
202 also considered. The lumen surface and volume are defined by the surface area and the  
203 volume of the portion of the aortic lumen comprised between the lowest renal and the iliac  
204 bifurcation. The ILT volume is also computed for the same region of interest, and the total  
205 aortic volume is the sum of lumen and ILT volumes. The ILT coverage is defined as the  
206 percentage of the lumen covered with ILT, computed from the number of surface patches  
207 on which the average ILT thickness was over one millimetre. The local growth criteria, as  
208 defined in the patch-description paragraph, is the ILT thickness change<sup>60</sup>.

209 *Hemodynamics metrics.* Finally, to evaluate the flow alteration at the wall, the TAWSS,  
210 OSI, RRT and Endothelial Cell Activation Potential (ECAP) are computed from the WSS  
211 at the lumen wall (see Table II), leading to local and global metrics as defined in the patch-  
212 description paragraph.

## 213 **2.5 Statistical analysis**

214 *Global descriptive statistics.* First, descriptive statistics are performed to report population  
215 characteristics with a univariate analysis to compare patient populations Figure 1. The  
216 population is divided into three groups, as defined in section 2.1: control cases without AAAs,  
217 cases with AAA but considered at low-risk, and cases with AAA at high-risk. Potential

218 correlation between groups for each variable is computed by a Welch’s t-test. Similar to  
 219 the Student’s t-test, it accounts for the unequal variance between the samples. Samples are  
 220 normally distributed as required by the test. In the results, the tables report the lists of  
 221 variables or global metrics used to describe the AAA and the distribution of their values  
 222 among the healthy (H), low-risk (LR) and high-risk (HR) patients. For each variable, a  
 223 Welch’s t-test is performed between the healthy and low-risk groups (H-LR), the healthy and  
 224 low-risk groups (H-HR) and the low-risk and high-risk groups (LR-HR). When significant  
 225 difference is observed ( $p < 0.05$ ) between two groups, it is reported in the 4<sup>th</sup> column.  
 226 Annual variation of hemodynamic parameters and thrombus thickness are computed locally;  
 227 i.e. patch to patch.

228 *Local descriptive statistics* Descriptive statistics are also performed locally (patch-wise) to  
 229 evaluate the relationships between flow and local morphological metrics Figure 1, in terms  
 230 of local Euclidean lumen border distance to the centerline (thereafter called ‘distance to  
 231 the centerline’), ILT thickness and patch surface area. Unsupervised outlier detection is  
 232 performed on each dataset with the Local Outlier Factor (LOF) method<sup>12</sup>. As described  
 233 in Rowland et al. in particular for WSS<sup>51</sup>, local correlation between a phenomena and a  
 234 bio-mechanical metric is hindered by spatial auto-correlation. One reported alternative is  
 235 bootstrapping<sup>26</sup> and performing the statistical test on the new dataset. Here, repeating  
 236 10000 times the non-parametric Spearman test yields reproducible results. Considering the  
 237 large amount of data, distribution of Spearman’s  $\rho$  is reported. Indeed, with a large enough  
 238 sample size, a very weak correlation can be significant, when the observed effect is likely not  
 239 real and due to chance in a statistical sense.

240 *Risk predictor methods.* Next, we try to anticipate the behaviour of AAA, i.e. to predict the  
 241 risk based on current information Figure 1. The (predicted) risk criteria is therefore chosen  
 242 to account for the state after the time evaluated  $t^n$ : the  $D_{max}$  variation was conserved  
 243  $((D_{max}^{n+1} - D_{max}^n)/(t^{n+1} - t^n))$  but the  $D_{max}$  considered is  $D_{max}^{n+1}$ . The thresholds defining low  
 244 versus high risks are the same as in section 2.1.

245 To better understand the contribution of the different groups of metrics on risk assess-  
246 ment, the predictor is first built using each set separately, i.e.  $D_{max}$  only, clinical, morpholog-  
247 ical and hemodynamic metrics and then all mixed. The features (input layer) are combined  
248 using a neural network to classify whether the next time step is at high-risk or not (output  
249 layer). Back-propagation is used to determine weights. Here, a multi-layer perceptron net-  
250 work, implemented in *Theano*<sup>63</sup> is used. The ten features explaining the most the dataset  
251 variance are chosen based on a Principal Components Analysis (PCA). This prevents having  
252 too many features compared to the number of samples and the associated risk of overfitting.  
253 Hyperparameters are automatically tuned<sup>61</sup> to maximize the Area Under the Curve (AUC)  
254 of the Receiver Operating Characteristic (ROC) curve and f1-score.

255 To evaluate the five estimators performance and avoid overfitting, we run repeated k-  
256 fold cross correlation with  $k = 3$  and 10 repetitions. Features finally selected for each set  
257 are reported in Figure 8. For clinical interpretation of the results, the ROC curves with  
258 AUC value, and the relative rank of features with respect to the predictability of the target  
259 variable evaluated by a multi-class *AdaBoost*<sup>15</sup>, are reported. AUCs medians are compared  
260 with the DeLong et al.<sup>21</sup> method.

## 261 3 Results

### 262 3.1 Population description

263 Healthy population mean age is estimated at  $60.4 \pm 12.4$  years while AAA patient mean age  
264 is  $73.5 \pm 7.4$  ( $p < 0.05$ ). Among the AAA patients, 5 are women (15.6%, mean age  $73.6 \pm 9.4$   
265 years) and 27 men (84.4%, mean age  $73.5 \pm 7.0$  years, ( $p = 0.98$ )) while in the healthy  
266 group, one is a woman (11.2%, 78 years) and 8 are men (88.8%, mean age  $58.4 \pm 11.6$  years).  
267 At least three follow-up CT-scans are available and suitable for domain reconstruction for  
268 AAA patients (mean  $4 \pm 1.47$ , range 3-9). Mean time between follow-up CT is  $12.74 \pm 12.41$   
269 months (range : 0.16 to 79.63 months and one case where two CTs were performed on the  
270 same day) and the mean follow-up duration is  $38.62 \pm 22.53$  months (range : 6.35 to 111.42



271 months). Clinical data is available for most patients (see Table 1).

272 [Table 1 about here.]

273 Regarding the healthy group,  $D_{max}$  is  $18.2 \pm 3.71\text{mm}$  (range:  $14.5 - 27.45\text{mm}$ ) whereas  
274 in AAA patients  $D_{max}$  is estimated  $42.68 \pm 8.39\text{mm}$  (range:  $22.65 - 67.49\text{mm}$ ). At baseline,  
275 7 (21.9%) AAA  $D_{max}$  are over the high-risk threshold and 4 (12.5%) have a growth over  
276  $5\text{mm}/\text{year}$  ; 2 (6.25%) achieve both. At the last exam, and 16 (50%) are over the high-risk  
277  $D_{max}$  threshold and 9 (28.1%) have reached the high-risk growth threshold at the previous  
278 follow-up (defined as  $D_{max}^{n+1} - D_{max}^n$ ) ; 7 (21.9%) achieve both. The lumen of the healthy  
279 aortas are shown in Figure 3. Most of them present various degrees of tortuosity, their  
280 length increasing with age<sup>69</sup>.

## 281 **3.2 Distribution of clinical, morphological and hemodynamic pa-** 282 **rameters in the studied population**

283 [Figure 3 about here.]

284 This section first studies how metrics associated with the different scans vary among the  
285 population and which ones distinguish the different patient groups (see Figure 1). The distri-  
286 bution of the clinical, morphological and hemodynamic variables among the three groups is  
287 presented in tables ( Table 2, Table 3, Table 4, Table 5 and Table 6) as well as the correlations  
288 between groups for each variable.

289 139 CT-scans and simulations, from 41 patients, are split into three study groups (healthy  
290 (H), low (LR) and high-risk (HR)) as defined in the Methods section. The LR and HR groups  
291 include 59 and 70 cases respectively. Univariate analysis reveals that the  $D_{max}$  as well as 10  
292 other variables significantly separate all three groups, some of those being highly correlated,  
293 such as volumes and diameters. 18 variables could significantly separate the healthy from the  
294 low-risk group, 18 the healthy from the high-risk group, and 27 the low-risk from the high-risk  
295 group. For the clinical metrics, all but BMI, separate the groups: pressure for low vs high

296 risks, age, dyslipidemia and statins for healthy vs the other groups. Regarding morphology,  
297 all metrics defined for healthy and AAAs can separate the three groups, except for the lumen  
298 shape factor (NSI) which separates healthy from AAA but not low-risk from high-risk AAA.  
299 Among AAAs, ILT metrics separate low from high risk groups, except ILT coverage and  
300 minimum ILT thickness. Regarding annual variations,  $D_{max}$  as expected distinguishes the  
301 two groups but among all other metrics, only local change of minimum and maximum ILT  
302 thickness make that difference, hinting on a particular role of ILT in the local growth process  
303 that we will explore in the next section. For all these morphological metrics, significant  
304 difference is achieved mostly from mean values but not from their standard deviation (all  
305 but the  $D_{max}$ ). In contrast, for the fluid-based metrics, Table 4 and Table 6, both average  
306 values and standard deviations can discern groups (e.g. the  $ECAP_{max}$  and local  $ECAP_{max}$   
307 variation). Almost all hemodynamics variables have several metrics that separate healthy  
308 from AAAs. TAWSSmin, RRTmean, ECAPmax,mean,stdev further separate low from high-  
309 risk groups. Regarding local changes, minimum metrics always separate the two groups,  
310 as well as RRTmax and ECAPmax. These results suggest that both instantaneous metric  
311 values and their changes are important to understand growth.

312 [Figure 4 about here.]

313 In Figure 4, the segmented lumen and ILT of two patients during their follow-up are  
314 shown. The one on the left shows no major shape change or growth with time, with a  
315 fusiform shape and a thin ILT. For the right one, ILT becomes more saccular with time and  
316 lumen thinner. This major difference in behaviour is plotted in Figure 5 for all patients  
317 during their follow-up.  $D_{max}$ ,  $D_{max}^{lumen}$ , lumen tortuosity and shape index plots illustrate the  
318 important diversity of the population. The difference between groups is detailed in Table 3  
319 and Table 5.

320 [Table 2 about here.]

321 [Table 3 about here.]

322 [Table 4 about here.]

323 [Table 5 about here.]

324 [Table 6 about here.]

325 [Figure 5 about here.]

326 [Figure 6 about here.]

327 [Figure 7 about here.]

328 Next, we present results to understand if there is a local correlation between morpholog-  
329 ical and hemodynamic metrics that could explain local growth Figure 1. Figure 7 describes  
330 the correlation coefficients between the wall metrics and two morphological metrics, com-  
331 puted on all patches of each scan : the distance from the lumen wall to the centerline,  
332 normalized by the proximal i.e. near the renal arteries distance, and the ILT thickness.  
333 There is a large dispersion between patients and scans (see Figure III for the individual  
334 data). As a consequence, some exhibit nice correlations (Figure 6a), while others do not  
335 (Figure 6c). The large dispersion of Spearman's  $\rho$  distribution is illustrated in Figure 6 for  
336 one metric. Despite a very large dispersion of data for both the distance to the centerline  
337 and the ILT thickness, visible trends stand out (Figure 7). TAWSS and WSSG strongly  
338 negatively and OSI positively correlate with the centerline distance. Coherently, RRT and  
339 ECAP also present strong positive correlation with the distance to the centerline. RRT and  
340 TAWSS distributions do not include  $\rho = 0$ . Regarding ILT thickness, no strong correlation  
341 emerges. TAWSS negatively correlates with ILT thickness. This finding is coherent with the  
342 common knowledge of low WSS being linked to thrombogenesis. WSSG and OSI also show  
343 slightly negative correlation with ILT thickness while no conclusion can be drawn from the  
344 RRT and ECAP  $\rho$  distributions. In fact, all five hemodynamic metrics  $\rho$  distributions are  
345 divided between positive and negative values, sign of a great heterogeneity between scans.  
346 When the statistics are computed on each patient instead of each scan separately, trends are  
347 conserved with however lower dispersions (Figure 7, bottom).

### 3.3 Global classification as a risk predictor

Finally, we study if the AAA evolution can be predicted (Figure 1). The ability of the classifier to discern future high-risks from low-risks cases is presented in Table 2. Recall that this prediction is based on features of the current time. The features are initially divided into 5 sets:  $D_{max}$  only, clinical, morphological and hemodynamic separately and then all features merged. The relative influence of the individual features on the dataset is also plotted for a better understanding of their role.

For reference, the classification is evaluated with  $D_{max}$  only and the corresponding AUC is  $0.75 \pm 0.08$ . No feature ranking is present as the entire classification information comes from  $D_{max}$ . For clinical features alone, the AUC is  $0.73 \pm 0.09$  and the most separating features are age,  $p_{sys}$  and  $p_{dias}$ . With only morphological features ( $D_{max}$  excluded), the AUC is  $0.93 \pm 0.09$ . The information mostly comes from the lumen centerline curvature, the ILT volume and thickness, and the lumen NSI. Concerning hemodynamic features, the AUC is  $0.96 \pm 0.10$  with information mostly gained from  $OSI_{mean}$ ,  $ECAP_{stdev}$ ,  $RRT_{max}$  and  $ECAP_{max}$ . Finally, with all features combined, the AUC reaches  $0.98 \pm 0.06$ : information is mostly gained from ILT volume,  $OSI_{max}$ ,  $OSI_{mean}$  and  $WSSG_{stdev}$ . To evaluate the statistical difference between features sets, p-values between AUCs are computed and reported in Table 7. Significant differences are observed when all the features are compared to a single feature class, and also when the flow features are compared to the  $D_{max}$ .

[Figure 8 about here.]

[Table 7 about here.]

## 4 Discussion

Quantifying AAA rupture risk has been an active field of research for at least the last decade without dethroning the  $D_{max}$  criteria. However, parameters accompanying the disease progression have been observed and discussed, including clinical observation, morphology, struc-

373 tural or fluid analysis and a mix of those. High risk AAA are essentially either undiagnosed  
374 or repaired, hence the scarcity of longitudinal studies with very fast growing aneurysms. If  
375 metrics such as WSS or arterial wall solid stress alone cannot specifically single out high-risk  
376 aneurysms, their influence on the temporal evolution of AAA may be more relevant<sup>58</sup>.

377 In this work we have attempted to find potential underlying relationships between clini-  
378 cally available variables or computed metrics that quantitatively characterize AAA and their  
379 hazardous growth. An AAA is considered at risk after reaching a threshold  $D_{max}$  or exceeded  
380 a  $D_{max}$  monthly variation threshold. If such relationship exists, one can envision a new com-  
381 bination of parameters to be a reliable predictor of an AAA evolution from a single scan, and  
382 thereby enhancing the patient-specific decision-making process about increased surveillance  
383 or type of treatment.

#### 384 4.1 Descriptive statistics

385 A total of 129 AAA from 32 patients and 9 healthy aortas were considered. The non-  
386 newtonian flow was simulated with FVM including backflow stabilization, and all WSS-based  
387 fields and geometrical metrics were discretized on the patch-parameterized AAA lumen. All  
388 data were mapped onto the same patch space to be able to compute local time variation of  
389 metrics. When exploring the local relationships, i.e. patch-wise, both WSSG and TAWSS  
390 negatively strongly and OSI positively correlate with the local distance from the lumen wall  
391 to the centerline. This distance is normalized for each scan by the distance at the proximal  
392 neck of the AAA. This local distance thus contains information on the local dilation of the  
393 AAA, likely creating low TAWSS and high OSI zones. RRT and ECAP, by construction, have  
394 an opposite behavior from the OSI and TAWSS. By contrast, it is difficult to conclude for  
395 the local relationships with the ILT thickness given the variation among scans. Correlations  
396 with the annual variation of the lumen wall distance to the centerline and ILT thickness  
397 were not reported, presenting no visible trend. Considering all local variables may not be  
398 the appropriate measure to understand local growth. However, the risk prediction based on  
399 hemodynamic features works well (see section 3.3): mean, extrema or standard deviation of

400 the local metrics seem to be the overall drivers for AAA growth. Nonetheless, previous work,  
401 especially Tzirakis et al.<sup>64</sup> found weak relationship between ILT growth and TAWSS (see  
402 Figure 7). However, data from their study do not reveal correlation with low OSI as weakly  
403 shown in Figure 7 and Arzani et al.<sup>4</sup> did. TAWSS seemed relevant in both studies as well as  
404 in Zambrano et al.<sup>71</sup>. These studies considered few patients. To our understanding and as  
405 Figure 7 illustrates, correlations with local morphological growth are highly heterogeneous  
406 among patients, even if for a given patient strong relations can emerge. This behavior  
407 prevents emanation of general correlations. Finding a relevant normalization space between  
408 all patients may lead to a better understanding of the local growth causes.

409 Figure 5 and Figure III illustrate the variety of situations encountered by clinicians when  
410 following an AAA over a given period of time. When all patient data is overlaid, no group  
411 separation visibly arises from the curves. However, from Table 2 to Table 6 one can observe  
412 that many parameters can separate patients; especially 27 of them can discern the high from  
413 the low-risk group. As expected, the classical  $D_{max}$  was one of the parameters sensitive  
414 enough to discern healthy aortas from low-risk AAAs, and also low from high-risk AAAs.  
415 ILT and total volume present the same capacity, as all three are directly linked. Despite the  
416 tendency of ILT to fill the AAA cavity, tending to reshape the lumen into a more tubular  
417 fashion, Figure 5 shows that lumens of AAA at higher risk tend to be more tortuous with  
418 a larger  $D_{max}^{lumen}$ . At the same time, while for low-risk AAA the  $D_{max}^{lumen}$  shows little to no  
419 growth, the  $D_{max}$  is continuously increasing. A major hypothesis to explain AAA growth  
420 is acceleration of the loss of mechanical properties of the aortic wall due to ILT deposition.  
421 ILT leads to local wall hypoxia and inflammation<sup>62</sup>, smooth muscle cells apoptosis, elastin  
422 degradation and MMP-2 (matrix metalloproteinase-2) concentration. Shifting the pressure  
423 load normally mostly borne by elastin cells to collagen fibers contributes to the wall stretching  
424 and diameter increase. The shape modification can lead to an increase of the lumen surface  
425 prone to ILT deposition, thus maintaining the vicious cycle. Figure 5 could indicate that  
426 some AAA could remain at low-risk provided that their lumen keeps its shape and size  
427 relatively constant, and the  $D_{max}$  growth remains below the repair threshold. This could

428 lead to a better understanding of the difficulty to assess AAA risk, given the presence of  
429 patients with large AAAs who will have a lower proportion of rupture than expected<sup>48</sup> and  
430 relatively small aneurysms that rupture<sup>20</sup>.

431 Currently, sex-adjusted  $D_{max}$ , absolute value and progression, is obviously significantly  
432 associated with the high risk population. Surprisingly volume and surface progression, de-  
433 spite a theoretically higher sensitivity, were not associated with patient risk. Similarly, no  
434 other morphological metrics annual variation could, despite higher theoretical sensitivity  
435 such as volume and surface versus diameters. One hypothesis is that the cumulative seg-  
436 mentation error induces a higher variability than the observed growth, especially for slow  
437 growing AAAs.

438 Low TAWSS and high OSI are linked to atheroprone regions of AAAs and predominate at  
439 site of rupture<sup>10</sup>. Di Achille et al.<sup>24</sup> combined both to form the ECAP. This metric does not  
440 offer a mechanistic explanation on ILT deposition but more an imprint on the wall of the near  
441 wall flow features that are related to thrombus deposition. Additionally, AAA wall is mostly  
442 covered by ILT, and if not, is highly atherosclerotic; therefore seeking metrics related to the  
443 wall mechano-adaptation resulting from endothelial cell triggering may not be successful.  
444 However, low wall shear can inform about two different phenomena : it is the imprint on the  
445 wall of the local flow alteration, and it also favors activated platelets adhesion. As expected,  
446  $ECAP_{max}$  and  $ECAP_{mean}$  can separate the population but, interestingly, also  $ECAP_{stdev}$ .  
447 Standard deviations were added for all metrics, motivated by the highly patient specific  
448 data distribution (see Figure III to Figure VI) and can be considered as an indicator of the  
449 wall roughness. CT-scan resolution cannot report wall roughness due to atherosclerosis and  
450 smoothing prior to meshing removes any small scale perturbation. Nonetheless, larger scale  
451 perturbation persists that cannot be explained. Hypotheses include poor segmentation of  
452 calcifications, often overestimated on CT-scans, contrast inhomogeneity, recurrent in large  
453 blood filled cavities such as AAAs or real morphological alteration. Numerically the WSS is  
454 computed using the vector normal to the wall, at each cell, and is therefore highly dependent  
455 on surface quality. However, because WSS derived metrics allow to statistically separate

456 groups and being visually consistent (e.g. see the ECAP distribution plot in Figure VI), we  
457 believe the geometrical perturbation is likely of biological origin.

458 Looking at the local change, i.e. patch-wise, is more challenging. Significant variations  
459 of  $OSI_{min}$ ,  $TAWSS_{min}$ ,  $WSSG_{min}$ ,  $RRT_{min}$  and  $ECAP_{min}$  are negative and average values  
460 are lower for high-risk than for low-risk patients. Whereas for ECAP, mean values increase  
461 faster for high-risk AAA while  $ECAP_{max}$  is increasing faster but  $ECAP_{min}$  is decreasing  
462 faster too. This indicates a larger dispersion of the values with time for high-risk AAA than  
463 for low-risk AAA, explaining the added value of the standard deviation of variables.

## 464 4.2 Risk prediction

465 The classification process aimed at building a risk predictor based on information acquired  
466 at a given time to anticipate if the patient will evolve to a high-risk state or stay at low-risk  
467 in the foreseeable future. Knowing that many of the evaluated metrics of interest contain  
468 powerful information to separate the low from the high-risk population, but does not give  
469 better results than the  $D_{max}$  if taken alone, a combination of metrics was sought.

470 For reference, we started with the  $D_{max}$  alone as feature to predict the future risk, pro-  
471 viding a mediocre yet above the average predictor. Clinical information did not perform  
472 well either but the missing clinical features for some patient may have a large impact on the  
473 predictor and results shall be taken cautiously. However, age, systolic and diastolic pres-  
474 sure and BMI are known factors associated with AAA risk. When the morphological and  
475 hemodynamic features are considered separately, the predictor performs well, even with the  
476 repetition of the 3-folds splits on a small cohort of patients. Once all features are merged,  
477 the AUC reaches 0.95. However, despite high values of AUCs for flow and morphological  
478 features, Table 7 shows that taking either flow metrics or all features leads to a significant  
479 difference with using the  $D_{max}$  alone. We believe that the very conservative results of the  
480 p-values (in Table 7) comes from the variability of the AUCs during the k-fold repetition  
481 (visible in Figure 8). A larger patient database with a prospective follow-up should confirm  
482 the clinical relevance of the AUC obtained here. However, morphological features can now



483 be easily obtained by lumen and thrombus segmentation<sup>37</sup> for a significant increase in clas-  
484 sification power. Even if the relation between flow alteration and AAA growth is still poorly  
485 understood, the combination of flow pattern with morphological analyses clearly improves  
486 patient risk stratification and should be integrated in future clinical algorithms.

### 487 **4.3 Limitation**

488 This study presents limitations discussed below:

- 489 • Simulation did not include wall deformation due to the pressure variation during the  
490 cardiac cycle. While FSI models for the aorta exist, the aortic wall was considered  
491 rigid, in accordance both with previous measurements<sup>34</sup> and literature<sup>49</sup>. Also, in  
492 the context of diseased aortas, the wall is highly heterogeneous and no non-invasive  
493 measurement can currently capture such heterogeneous mechanical properties.
- 494 • Boundary conditions are literature-based as this was a retrospective study. Thus,  
495 no patient-specific measurement was available, as often in such cases. However, flow  
496 patterns were favorably compared with PC-MRI data on a few patients with AAA<sup>34</sup>.
- 497 • For some patients the  $D_{max}$  profiles are not monotonically increasing. However, it seems  
498 to be unlikely that small diameter reduction ( $\Delta D_{max} < 2\text{mm}$ ) is in fact outer wall  
499 shrinkage. Several possible explanations include: segmentation fluctuation localized  
500 on artifacts or calcifications; AAA shape change due to the patient positioning in the  
501 scanner, altering the observed geometry, thus the maximal diameter; the limitation of  
502 the measurement approach using planes normal to the centerlines in complex shaped  
503 AAAs. Considering the inter-observer agreement of  $<3\text{mm}$  on the  $D_{max}$ <sup>37</sup>, the same  
504 error tolerance is expected by using the same segmentation tool.
- 505 • While flow in healthy aortas remains essentially laminar, complex flow<sup>46</sup> and transition  
506 to turbulence<sup>38,65</sup> may occur in AAAs due to the brutal enlargement and could impact  
507 the studied wall fields.

- 508 • To characterize AAA growth, metrics were compared patch to patch which does not  
509 reflect the non-homogeneous and anisotropic growth of AAA. In the absence of local  
510 wall displacement tracking method, this approach still gives insights on AAA growth.
- 511 • Considering the number of follow-up scans available, the learning approach did not  
512 considered AAAs as time-series. An approach similar to Lipton et al.<sup>39</sup> could eventually  
513 be implemented on a database with more follow-up scans per patient.
- 514 • The healthy population was 13 years younger than the AAA population on average  
515 (but with aortas already showing signs of aging, see Figure 3) and clinical data was  
516 not available for all patients, see Table 1.
- 517 • The database did not include ruptured aneurysms for the reasons described in the  
518 Methods section. When such data become available for AAA, the link between 'high  
519 risk' as defined here by clinicians and rupture prediction should be studied. A very  
520 recent study in cerebral aneurysms showed adverse morphology and hemodynamics  
521 to be related to aneurysm rupture<sup>22</sup>. The corresponding statistical model of rupture  
522 probability was then successfully validated<sup>23</sup>. These results combined with our findings  
523 give hope that such approach should be successful for AAAs as well.

## 524 4.4 Conclusion

525 We have presented a retrospective population study on the metrics quantifying the growth  
526 of AAA, and have built a model to anticipate their further evolution towards rupture. This  
527 longitudinal study included clinical and imaging data available at different time points for  
528 a total number of 138 scans from 42 patients. The analysis considered clinical, morpho-  
529 logical and simulation-based hemodynamic metrics, separately or combined to incorporate  
530 a diversity of potential growth markers. Different global and local metrics or their time  
531 evolution were found to separate the healthy, low-risk and high-risk groups. Local hemo-  
532 dynamics metrics presented in fact a large intra- and interpatient variability: even if for  
533 some patients a clear relationship could be established between hemodynamics variables

534 and growth, their extrapolation to the whole population is yet to be found. Nevertheless,  
535 a risk predictor could be built with supervised learning from the clinical, morphological  
536 and simulation-based hemodynamic metrics. From a clinical point of view, we have shown  
537 that, compared to the current clinical criteria, morphological metrics describing the lumen  
538 and ILT shape could already greatly improve risk prediction, and thus potentially patient  
539 follow-up or treatment decision, at a moderate analysis cost. Blood flow simulations provide  
540 valuable additional information for the predictor, as well as for understanding the underlying  
541 relationship between flow alteration and AAA growth. Finally, risk prediction works best by  
542 combining all metrics. Although the results show the high predictive value of this approach,  
543 validation of the risk predictors on another set of data is needed before clinical translation.

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## 551 **References**

- 552 1. Antiga, L., B. Ene-Iordache, and A. Remuzzi. Computational geometry for patient-  
553 specific reconstruction and meshing of blood vessels from MR and CT angiography. *IEEE*  
554 *Transactions on Medical Imaging* 22:674–684, 2003.
- 555 2. Antiga, L. Patient-specific modeling of geometry and blood flow in large arteries. *Politecnico di Milano*, 2002.

- 557 3. Antiga, L. and D. A. Steinman. Robust and objective decomposition and mapping of  
558 bifurcating vessels. *IEEE Transactions on Medical Imaging* 23:704–713, 2004.
- 559 4. Arzani, A., G.-Y. Suh, R. L. Dalman, and S. C. Shadden. A longitudinal comparison of  
560 hemodynamics and intraluminal thrombus deposition in abdominal aortic aneurysms.  
561 *American Journal of Physiology-Heart and Circulatory Physiology* 307:H1786–H1795,  
562 2014.
- 563 5. Basciano, C., C. Kleinstreuer, S. Hyun, and E. A. Finol. A relation between near-wall  
564 particle-hemodynamics and onset of thrombus formation in abdominal aortic aneurysms.  
565 *Annals of Biomedical Engineering* 39:2010–2026, 2011.
- 566 6. Bertoglio, C., A. Caiazzo, Y. Bazilevs, M. Braack, M. Esmaily, V. Gravemeier, A. L. Mars-  
567 den, O. Pironneau, I. E. Vignon-Clementel, and W. A. Wall. Benchmark problems for  
568 numerical treatment of backflow at open boundaries. *International Journal for Numerical*  
569 *Methods in Biomedical Engineering* , 2018.
- 570 7. Bhagavan, D., P. D. Achille, and J. D. Humphrey. Strongly Coupled Morphological  
571 Features of Aortic Aneurysms Drive Intraluminal Thrombus. *Scientific Reports* pp. 1–18,  
572 2018.
- 573 8. Björck, M. and A. Wanhainen. Pathophysiology of AAA: Heredity vs Environment.  
574 *Progress in Cardiovascular Diseases* 56:2–6, 2013.
- 575 9. Bluestein, D., L. Niu, R. T. Schoepfoerster, and M. K. Dewanjee. Steady Flow in an  
576 Aneurysm Model: Correlation Between Fluid Dynamics and Blood Platelet Deposition.  
577 *Journal of Biomechanical Engineering* 118:280, 1996.
- 578 10. Boyd, A. J., D. C. Kuhn, R. J. Lozowy, and G. P. Kulbisky. Low wall shear stress  
579 predominates at sites of abdominal aortic aneurysm rupture. *Journal of Vascular Surgery*  
580 63:1613–1619, 2016.

- 581 11. Brady, A. R., Thompson, S. G., Fowkes, F. G. R., Greenhalgh, R. M., and Powell, J. T.  
582 Abdominal aortic aneurysm expansion: risk factors and time intervals for surveillance.  
583 *Circulation*, 110(1), 16-21, 2004.
- 584 12. Breunig, M. M., H.-P. Kriegel, R. T. Ng, and J. Sander. LOF: Identifying Density-  
585 Based Local Outliers. *Proceedings of the 2000 Acm Sigmod International Conference on*  
586 *Management of Data* , 2000.
- 587 13. Brewster, D. C., J. L. Cronenwett, J. W. Hallett, K. W. Johnston, W. C. Krupski, and  
588 J. S. Matsumura. Guidelines for the treatment of abdominal aortic aneurysms: Report  
589 of a subcommittee of the Joint Council of the American Association for Vascular Surgery  
590 and Society for Vascular Surgery. *Journal of Vascular Surgery* 37:1106–1117, 2003.
- 591 14. Buchanan, J. R., C. Kleinstreuer, and J. K. Comer. Rheological effects on pulsatile  
592 hemodynamics in a stenosed tube. *Computers and Fluids* 29:695–724, 2000.
- 593 15. Busa-Fekete, R., B. Kégl, G. Szarvas, O. Chapelle, Y. Chang, and T.-Y. Liu. Ranking  
594 by calibrated AdaBoost. In: *Learning to Rank Challenge*, volume 14, pp. 37–48. 2011.
- 595 16. Chaikof, E. L., J. D. Blankensteijn, P. L. Harris, G. H. White, C. K. Zarins, V. M.  
596 Bernhard, J. S. Matsumura, J. May, F. J. Veith, M. F. Fillinger, R. B. Rutherford, and  
597 K. Craig Kent. Reporting standards for endovascular aortic aneurysm repair. *Journal of*  
598 *Vascular Surgery* , 2002.
- 599 17. Chaikof, E. L., D. C. Brewster, R. L. Dalman, M. S. Makaroun, K. A. Illig, G. A.  
600 Sicard, C. H. Timaran, G. R. Upchurch, and F. J. Veith. The care of patients with an  
601 abdominal aortic aneurysm: The Society for Vascular Surgery practice guidelines. *Journal*  
602 *of Vascular Surgery* 50:49, 2009.
- 603 18. Chaikof, E. L., R. L. Dalman, M. K. Eskandari, B. M. Jackson, W. A. Lee, M. A.  
604 Mansour, T. M. Mastracci, M. Mell, M. H. Murad, L. L. Nguyen, G. S. Oderich, M. S.  
605 Patel, M. L. Schermerhorn, and B. W. Starnes. The Society for Vascular Surgery practice

- 606 guidelines on the care of patients with an abdominal aortic aneurysm. *Journal of Vascular*  
607 *Surgery* , 2018.
- 608 19. Chisci, E., N. Alamanni, F. Iacoponi, S. Michelagnoli, T. Procacci, G. Colombo, and  
609 C. Setacci. Grading abdominal aortic aneurysm rupture risk. *The Journal of cardiovas-*  
610 *cular surgery* 59:87–94, 2018.
- 611 20. Darling, R. C., C. R. Messina, D. C. Brewster, and L. W. Ottinger. Autopsy study  
612 of unoperated abdominal aortic aneurysms. The case for early resection. *Circulation*  
613 56:161–4, 1977.
- 614 21. DeLong, E. R., D. M. DeLong, and D. L. Clarke-Pearson. Comparing the areas under two  
615 or more correlated receiver operating characteristic curves: a nonparametric approach.  
616 *Biometrics* 44:837–45, 1988.
- 617 22. Detmer, F. J., Chung, B. J., Jimenez, C., Hamzei-Sichani, F., Kallmes, D., Putman, C.,  
618 and Cebal, J. R.. Associations of hemodynamics, morphology, and patient characteristics  
619 with aneurysm rupture stratified by aneurysm location. *Neuroradiology*, 61(3), 275-284,  
620 2019.
- 621 23. Detmer, F. J., Fajardo-Jimnez, D., Mut, F., Juchler, N., Hirsch, S., Pereira, V. M.,  
622 and Cebal, J. R.. External validation of cerebral aneurysm rupture probability model  
623 with data from two patient cohorts. *Acta neurochirurgica. Acta neurochirurgica*, 160(12),  
624 2425-2434., 2018.
- 625 24. Di Achille, P., G. Tellides, C. A. Figueroa, and J. D. Humphrey. A haemodynamic  
626 predictor of intraluminal thrombus formation in abdominal aortic aneurysms. *Proceedings*  
627 *of the Royal Society A: Mathematical, Physical and Engineering Sciences* 470:20140163–  
628 20140163, 2014.
- 629 25. Duellman, T., C. L. Warren, J. Matsumura, and J. Yang. Analysis of multiple ge-  
630 netic polymorphisms in aggressive-growing and slow-growing abdominal aortic aneurysms.  
631 *Journal of Vascular Surgery* 60:613–621, 2014.

- 632 26. Efron, B. and R. Tibshirani. Bootstrap Methods for Standard Errors, Confidence Inter-  
633 vals, and Other Measures of Statistical Accuracy. *Statistical Science* 1:54–75, 1986.
- 634 27. Esmaily Moghadam, M., Y. Bazilevs, T. Y. Hsia, I. E. Vignon-Clementel, and A. L.  
635 Marsden. A comparison of outlet boundary treatments for prevention of backflow diver-  
636 gence with relevance to blood flow simulations. *Computational Mechanics* 48:277–291,  
637 2011.
- 638 28. Finol, E. A. and C. H. Amon. Blood Flow in Abdominal Aortic Aneurysms: Pulsatile  
639 Flow Hemodynamics. *Journal of Biomechanical Engineering* 123:474, 2001.
- 640 29. Grytsan, A., P. N. Watton, and G. A. Holzapfel. A Thick-Walled FluidSolid-Growth  
641 Model of Abdominal Aortic Aneurysm Evolution: Application to a Patient-Specific Ge-  
642 ometry. *Journal of Biomechanical Engineering* 137:031008, 2015.
- 643 30. Haller, S. J., J. D. Crawford, K. M. Courchaine, C. J. Bohannon, G. J. Landry, G. L.  
644 Moneta, A. F. Azarbal, and S. Rugonyi. Intraluminal thrombus is associated with early  
645 rupture of abdominal aortic aneurysm. *Journal of Vascular Surgery* 67:1051–1058, 2018.
- 646 31. Jasak, H. Error Analysis and Estimation for the Finite Volume Method with Applications  
647 to Fluid Flows. Ph.D. thesis, Imperial College, University of London, 1996.
- 648 32. Jasak, H. and H. G. Weller. Application of the finite volume method and unstructured  
649 meshes to linear elasticity. *International Journal for Numerical Methods in Engineering*  
650 48:267–287, 2000.
- 651 33. Kazi, M., Thyberg, J., Religa, P., Roy, J., Eriksson, P., Hedin, U., and Swedenborg, J.  
652 Influence of intraluminal thrombus on structural and cellular composition of abdominal  
653 aortic aneurysm wall . *Journal of vascular surgery*, 38(6), 1283-1292, 2003.
- 654 34. Joly, F., G. Soulez, D. Garcia, S. Lessard, and C. Kauffmann. Flow stagnation volume  
655 and abdominal aortic aneurysm growth: Insights from patient-specific computational flow

- 656 dynamics of Lagrangian-coherent structures. *Computers in Biology and Medicine* 92:98–  
657 109, 2018.
- 658 35. Kaibara, M. Rheology of blood coagulation. *Biorheology* 33:101–117, 1996.
- 659 36. Himburg, H. A., D. M. Grzybowski, A. L. Hazel, J. A. LaMack, X. M. Li, and  
660 M. H. Friedman. Spatial comparison between wall shear stress measures and porcine  
661 arterial endothelial permeability. *American Journal of Physiology-Heart and Circulatory*  
662 *Physiology*, 286(5), H1916-H1922, 2004.
- 663 37. Kauffmann, C., A. Tang, A. Dugas, E. Therasse, V. Oliva, and G. Soulez. Clinical  
664 validation of a software for quantitative follow-up of abdominal aortic aneurysm maximal  
665 diameter and growth by CT angiography. *European Journal of Radiology* 77:502–508,  
666 2011.
- 667 38. Les, A. S., S. C. Shadden, C. A. Figueroa, J. M. Park, M. M. Tedesco, R. J. Herfkens  
668 and C. A. Taylor. Quantification of hemodynamics in abdominal aortic aneurysms during  
669 rest and exercise using magnetic resonance imaging and computational fluid dynamics.  
670 *Annals of biomedical engineering*, 38(4), 1288-1313, 2010
- 671 39. Lipton, Z. C., D. C. Kale, C. Elkan, and R. Wetzell. Learning to Diagnose with LSTM  
672 Recurrent Neural Networks. arXiv preprint 1511.03677, 2015.
- 673 40. Marcinkowska-Gapińska, A., J. Gapinski, W. Elikowski, F. Jaroszyk, and L. Kubisz.  
674 Comparison of three rheological models of shear flow behavior studied on blood samples  
675 from post-infarction patients. *Medical and Biological Engineering and Computing* 45:837–  
676 844, 2007.
- 677 41. Martufi, G., M. Lindquist Liljeqvist, N. Sakalihasan, G. Panuccio, R. Hultgren, J. Roy,  
678 and T. C. Gasser. Local Diameter, Wall Stress, and Thrombus Thickness Influence the  
679 Local Growth of Abdominal Aortic Aneurysms. *Journal of Endovascular Therapy* 23,  
680 2016.



- 681 42. McGloughlin, T. M. Biomechanics and Mechanobiology of Aneurysms, volume 7 of *Stud-*  
682 *ies in Mechanobiology, Tissue Engineering and Biomaterials*, Berlin, Heidelberg: Springer  
683 Berlin Heidelberg 2011, 1–33 pp.
- 684 43. Mills, C. J., I. T. Gabe, J. H. Gault, D. T. Mason, J. Ross, E. Braunwald, and J. P.  
685 Shillingford. Pressure-flow relationships and vascular impedance in man. *Cardiovascular*  
686 *Research* 4:405–417, 1970.
- 687 44. Moore, J., S. Maier, D. Ku, and P. Boesiger. Hemodynamics in the abdominal aorta: A  
688 comparison of in vitro and in vivo measurements. *Journal of Applied Physiology* 76:1520–  
689 1527, 1994.
- 690 45. Nagel, T., N. Resnick, C. F. Dewey, and M. A. Gimbrone. Vascular Endothelial Cells Re-  
691 spond to Spatial Gradients in Fluid Shear Stress by Enhanced Activation of Transcription  
692 Factors. *Arteriosclerosis, Thrombosis, and Vascular Biology* , 1999.
- 693 46. ORourke, M. J., J. P., McCullough, and S. Kelly. An investigation of the relationship  
694 between hemodynamics and thrombus deposition within patient-specific models of ab-  
695 dominal aortic aneurysm. *Proceedings of the Institution of Mechanical Engineers, Part*  
696 *H: Journal of Engineering in Medicine*, 226(7), 548-564, 2012.
- 697 47. Ouriel, K., R. M. Green, C. Donayre, C. K. Shortell, J. Elliott, and J. A. DeWeese. An  
698 evaluation of new methods of expressing aortic aneurysm size: Relationship to rupture.  
699 *Journal of Vascular Surgery* 15:12–20, 1992.
- 700 48. Parkinson, F., S. Ferguson, P. Lewis, I. M. Williams, C. P. Twine, and South East  
701 Wales Vascular Network. Rupture rates of untreated large abdominal aortic aneurysms  
702 in patients unfit for elective repair. *Journal of Vascular Surgery* 61:1606–1612, 2015.
- 703 49. Raghavan, M. L., J. Kratzberg, E. M. Castro de Tolosa, M. M. Hanaoka, P. Walker, and  
704 E. S. da Silva. Regional distribution of wall thickness and failure properties of human  
705 abdominal aortic aneurysm. *Journal of Biomechanics* 39:3010–3016, 2006.

- 706 50. Reeps, C., A. Maier, J. Pelisek, F. Härtl, V. Grabher-Meier, W. A. Wall, M. Essler,  
707 H. H. Eckstein, and M. W. Gee. Measuring and modeling patient-specific distributions  
708 of material properties in abdominal aortic aneurysm wall. *Biomechanics and Modeling in*  
709 *Mechanobiology* 12:717–733, 2013.
- 710 51. Rowland, E. M., Y. Mohamied, K. Yean Chooi, E. L. Bailey, and P. D. Weinberg.  
711 Comparison of Statistical Methods for Assessing Spatial Correlations Between Maps of  
712 Different Arterial Properties. *Journal of Biomechanical Engineering* 137:101003, 2015.
- 713 52. P. J. Roache Perspective: A Method for Uniform Reporting of Grid Refinement Studies  
714 *Journal of Fluids Engineering* 116(3), 405-413, 1994)
- 715 53. Shadden, S. C. and S. Hendabadi. Potential fluid mechanic pathways of platelet activa-  
716 tion. *Biomechanics and Modeling in Mechanobiology* 12:467–474, 2013.
- 717 54. Hansen, K. B., A. Arzani, and S. C. Shadden. Mechanical platelet activation potential  
718 in abdominal aortic aneurysms. *Journal of biomechanical engineering*, 137(4), 041005,  
719 2015.
- 720 55. Shum, J., G. Martufi, E. Di Martino, C. B. Washington, J. Grisafi, S. C. Muluk, and  
721 E. A. Finol. Quantitative assessment of abdominal aortic aneurysm geometry. *Annals of*  
722 *Biomedical Engineering* 39:277–286, 2011.
- 723 56. Shum, J., A. Xu, I. Chatnuntawech, and E. A. Finol. A framework for the automatic gen-  
724 eration of surface topologies for abdominal aortic aneurysm models. *Annals of Biomedical*  
725 *Engineering* 39:249–259, 2011.
- 726 57. Silverberg, E., C. C. Boring, and T. S. Squires. *Cancer statistics, 1990*. CA: A Cancer  
727 *Journal for Clinicians* 40:9–26, 1990.
- 728 58. Stenbaek, J., B. Kalin, and J. Swedenborg. Growth of thrombus may be a better pre-  
729 dictor of rupture than diameter in patients with abdominal aortic aneurysms. *European*  
730 *Journal of Vascular and Endovascular Surgery* 20:466–469, 2000.

- 731 59. Solberg, S., Singh, K., Wilsgaard, T., and Jacobsen, B. K. Increased growth rate of  
732 abdominal aortic aneurysms in women. The Troms study.. *European journal of vascular*  
733 *and endovascular surgery*, 29(2), 145-149,2005
- 734 60. Stevens, R. R., A. Grytsan, J. Biasetti, J. Roy, M. L. Liljeqvist, and T. Chris-  
735 tian Gasser. Biomechanical changes during abdominal aortic aneurysm growth. *PLoS*  
736 *ONE* 12:e0187421, 2017.
- 737 61. Strub, F., H. De Vries, J. Mary, B. Piot, A. Courvile, and O. Pietquin. End-to-end  
738 optimization of goal-driven and visually grounded dialogue systems. *IJCAI International*  
739 *Joint Conference on Artificial Intelligence* 13:2765–2771, 2017.
- 740 62. Tanios, F., M. W. Gee, J. Pelisek, S. Kehl, J. Biehler, V. Grabher-Meier, W. A. Wall,  
741 H. H. Eckstein, and C. Reeps. Interaction of Biomechanics with Extracellular Matrix  
742 Components in Abdominal Aortic Aneurysm Wall. *European Journal of Vascular and*  
743 *Endovascular Surgery* 50:167–174, 2015.
- 744 63. The Theano Development Team, R. Al-Rfou, G. Alain, A. Almahairi, C. Angermueller,  
745 D. Bahdanau, N. Ballas, F. Bastien, J. Bayer, A. Belikov, A. Belopolsky, Y. Ben-  
746 gio, A. Bergeron, J. Bergstra, V. Bisson, J. B. Snyder, N. Bouchard, N. Boulanger-  
747 Lewandowski, X. Bouthillier, A. de Brébisson, O. Breuleux, P.-L. Carrier, K. Cho,  
748 J. Chorowski, P. Christiano, T. Cooijmans, M.-A. Côté, M. Côté, A. Courville, Y. N.  
749 Dauphin, O. Delalleau, J. Demouth, G. Desjardins, S. Dieleman, L. Dinh, M. Ducoffe,  
750 V. Dumoulin, S. E. Kahou, D. Erhan, Z. Fan, O. Firat, M. Germain, X. Glorot, I. Goodfel-  
751 low, M. Graham, C. Gulcehre, P. Hamel, I. Harlouchet, J.-P. Heng, B. Hidasi, S. Honari,  
752 A. Jain, S. Jean, K. Jia, M. Korobov, V. Kulkarni, A. Lamb, P. Lamblin, E. Larsen,  
753 C. Laurent, S. Lee, S. Lefrancois, S. Lemieux, N. Léonard, Z. Lin, J. A. Livezey, C. Lorenz,  
754 J. Lowin, Q. Ma, P.-A. Manzagol, O. Mastropietro, R. T. McGibbon, R. Memisevic, B. van  
755 Merriënboer, V. Michalski, M. Mirza, A. Orlandi, C. Pal, R. Pascanu, M. Pezeshki, C. Raf-  
756 fel, D. Renshaw, M. Rocklin, A. Romero, M. Roth, P. Sadowski, J. Salvatier, F. Savard,  
757 J. Schlüter, J. Schulman, G. Schwartz, I. V. Serban, D. Serdyuk, S. Shabaniyan, C. Simon,

- 758 S. Spieckermann, S. R. Subramanyam, J. Sygnowski, J. Tanguay, G. van Tulder, J. Turian,  
759 S. Urban, P. Vincent, F. Visin, H. de Vries, D. Warde-Farley, D. J. Webb, M. Willson,  
760 K. Xu, L. Xue, L. Yao, S. Zhang, and Y. Zhang. Theano: A Python framework for fast  
761 computation of mathematical expressions. arXiv e-prints p. 19, 2016.
- 762 64. Tzirakis, K., Y. Kamarianakis, E. Metaxa, N. Kontopodis, C. V. Ioannou, and Y. Papa-  
763 harilaou. A robust approach for exploring hemodynamics and thrombus growth associa-  
764 tions in abdominal aortic aneurysms. *Medical and Biological Engineering and Computing*  
765 55:1493–1506, 2017.
- 766 65. Vergara, C., D. Le Van, M. Quadrio, L. Formaggia, and M. Domanin. Large eddy  
767 simulations of blood dynamics in abdominal aortic aneurysms. *Medical engineering &*  
768 *physics*, 47, 38-46, 2017
- 769 66. Womersley, J. R. Method for the calculation of velocity, rate of flow and viscous drag  
770 in arteries when the pressure gradient is known. *The Journal of Physiology* 127:553–563,  
771 1955.
- 772 67. Wu, J. and S. C. Shadden. Coupled Simulation of Hemodynamics and Vascular Growth  
773 and Remodeling in a Subject-Specific Geometry. *Annals of biomedical engineering*, 43(7),  
774 1543-1554.
- 775 68. Xiao, N., J. D. Humphrey, and C. A. Figueroa. Multi-scale computational model of  
776 three-dimensional hemodynamics within a deformable full-body arterial network. *Journal*  
777 *of Computational Physics* 244:22–40, 2013.
- 778 69. Xu, X., B. Wang, C. Ren, J. Hu, D. A. Greenberg, T. Chen, L. Xie, and K. Jin. Age-  
779 related Impairment of Vascular Structure and Functions. *Aging and disease* 8:590–610,  
780 2017.
- 781 70. Yushkevich, P. A., J. Piven, H. C. Hazlett, R. G. Smith, S. Ho, J. C. Gee, and G. Gerig.  
782 User-guided 3D active contour segmentation of anatomical structures: Significantly im-  
783 proved efficiency and reliability. *NeuroImage* 31:1116–1128, 2006.

784 71. Zambrano, B. A., H. Gharahi, C. Y. Lim, F. A. Jaber, J. Choi, W. Lee, and S. Baek.  
785 Association of Intraluminal Thrombus, Hemodynamic Forces, and Abdominal Aortic  
786 Aneurysm Expansion Using Longitudinal CT Images. *Annals of Biomedical Engineer-*  
787 *ing* 44:1502–1514, 2016.

## 788 **6 Electronic Supplementary Material**

### 789 **6.1 Boundary conditions**

790 [Figure 9 about here.]

791 [Table 8 about here.]

### 792 **6.2 Metrics description**

793 [Table 9 about here.]

### 794 **6.3 Local distribution**

795 [Figure 10 about here.]

796 [Figure 11 about here.]

797 [Figure 12 about here.]

798 [Figure 13 about here.]

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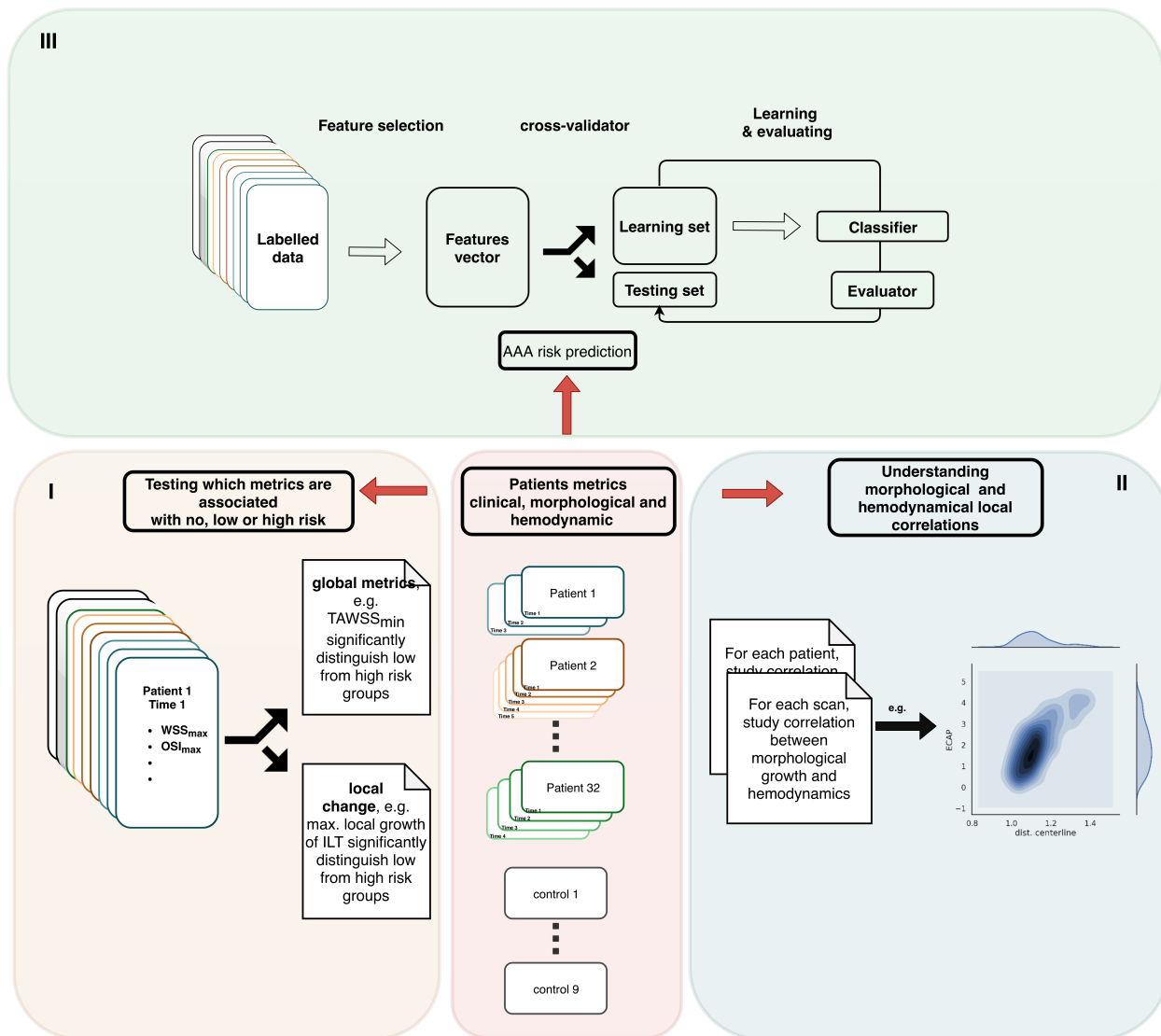


Figure 1: Overview of the study.



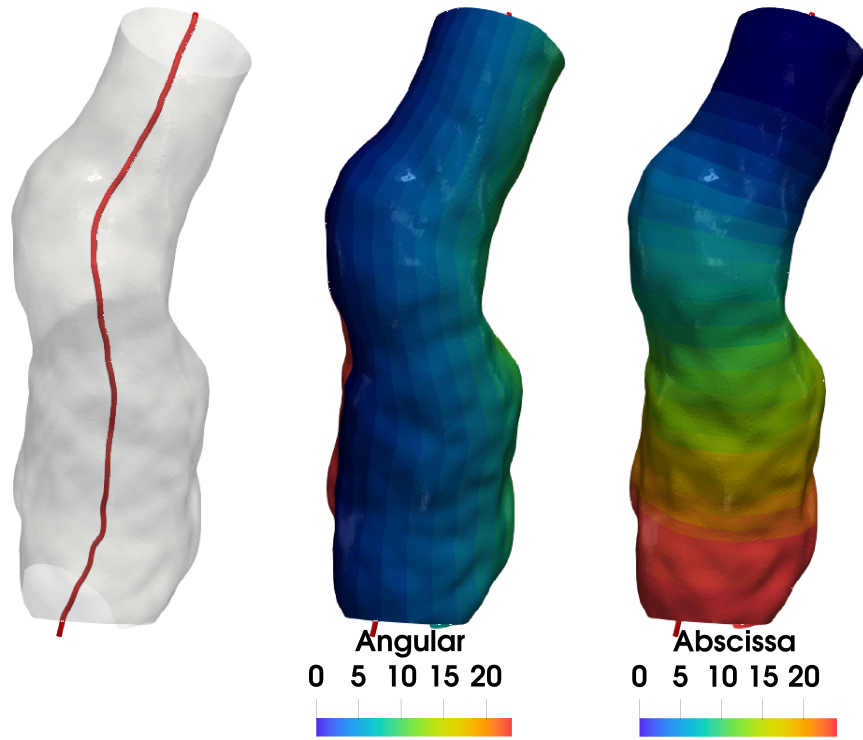


Figure 2: Patching process of the lumen surface. Left: centerline of the vessel lumen, Center: circumferential discretization, colored by the angular index. Right: centerline-based longitudinal discretization colored by the abscissa along the centerline.

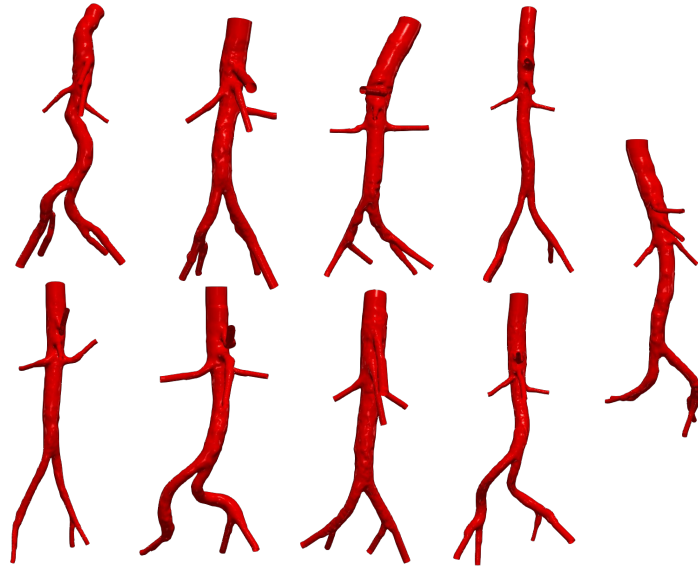
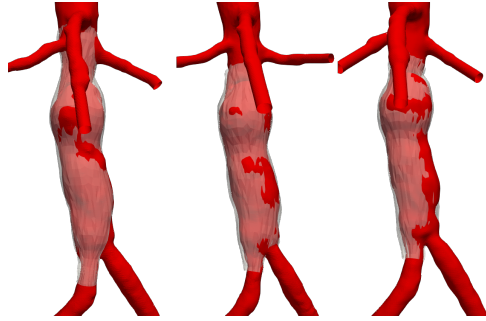
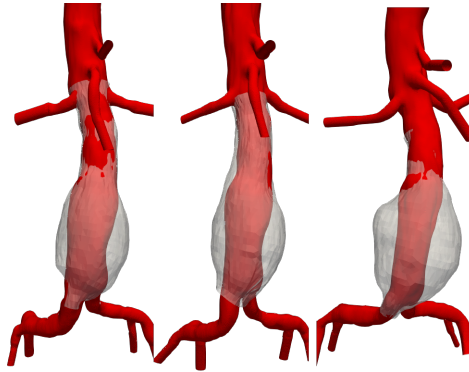


Figure 3: Aorta of the 9 healthy patients included in the study as control subjects. Most present various degrees of tortuosity, due to arteries aging.

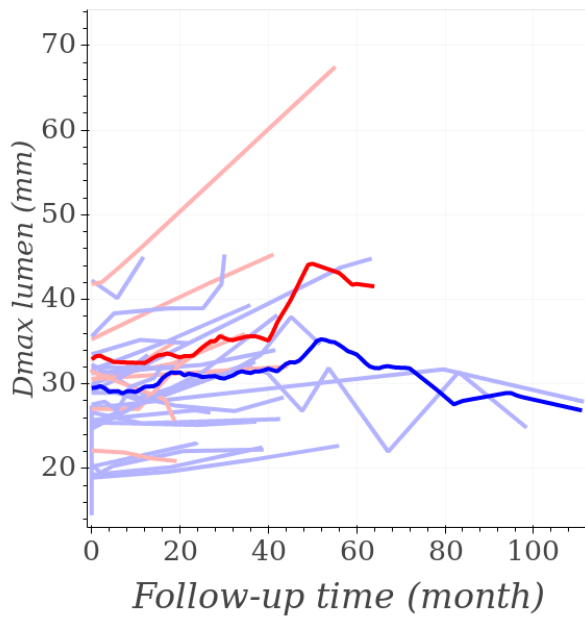


(a)

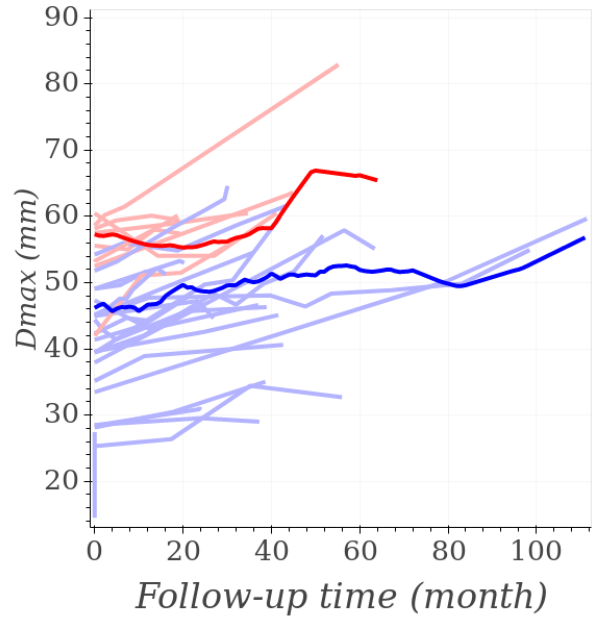


(b)

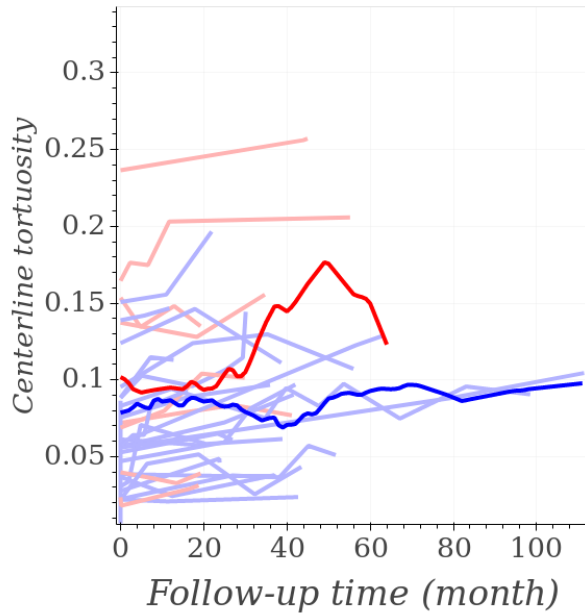
Figure 4: Example of different growth dynamics on two patients. The segmented lumen is in red, while ILT is transparent.



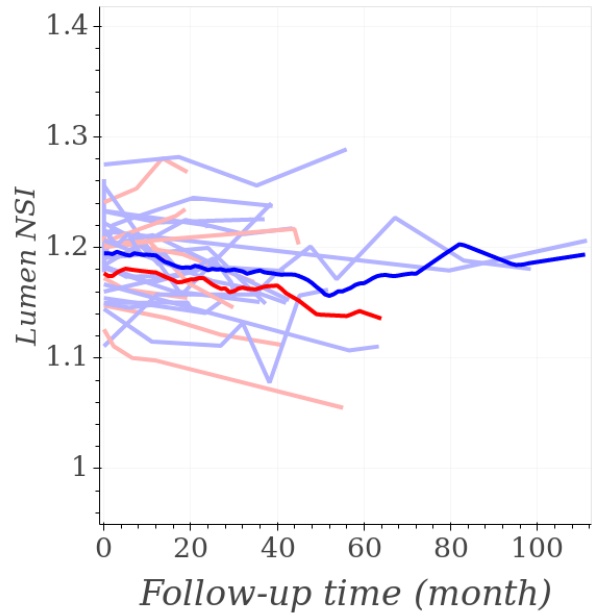
(a)  $D_{max}^{lumen}$



(b)  $D_{max}$

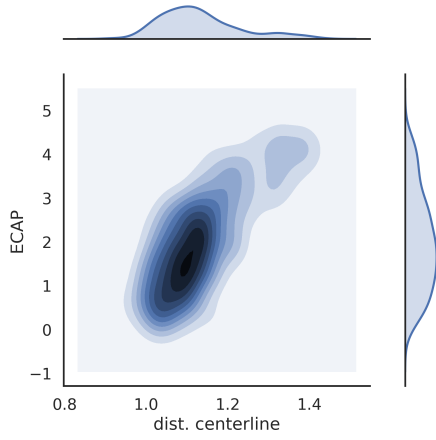


(c) Lumen centerline tortuosity

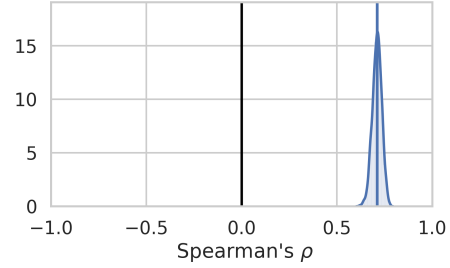


(d) Lumen NSI

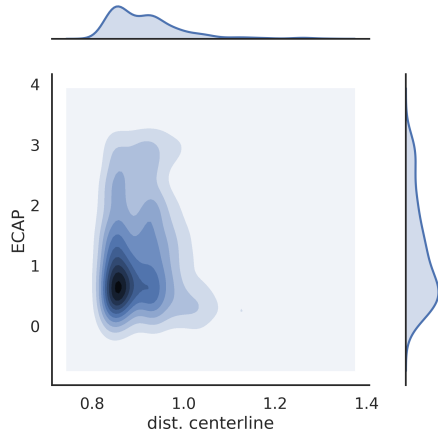
Figure 5: Evolution with time of selected parameters among patients. AAA ending up as high-risk are represented by red lines while low-risk AAA are in blue. Averaged behaviours of the two groups are in bold color.



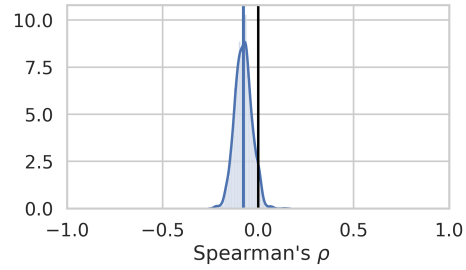
(a)



(b)

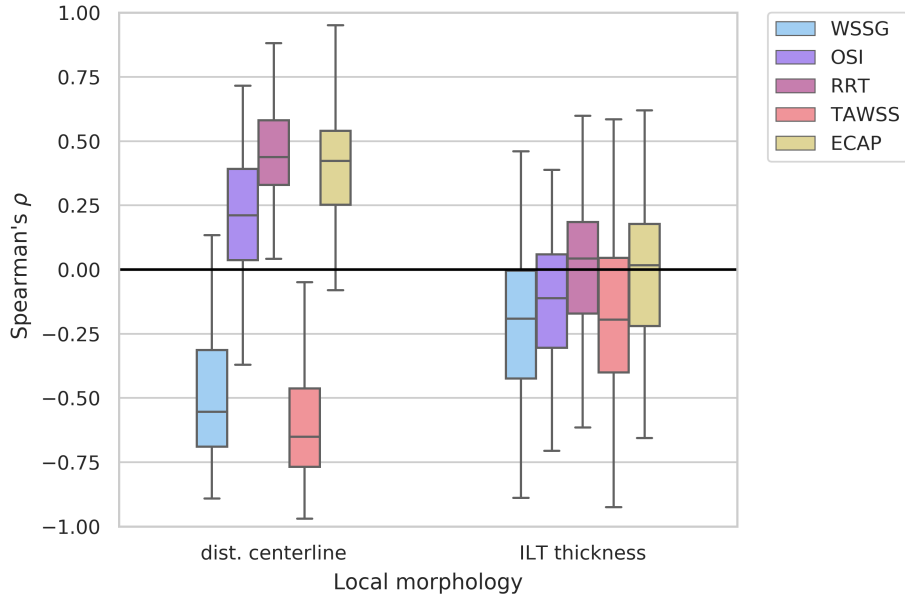


(c)

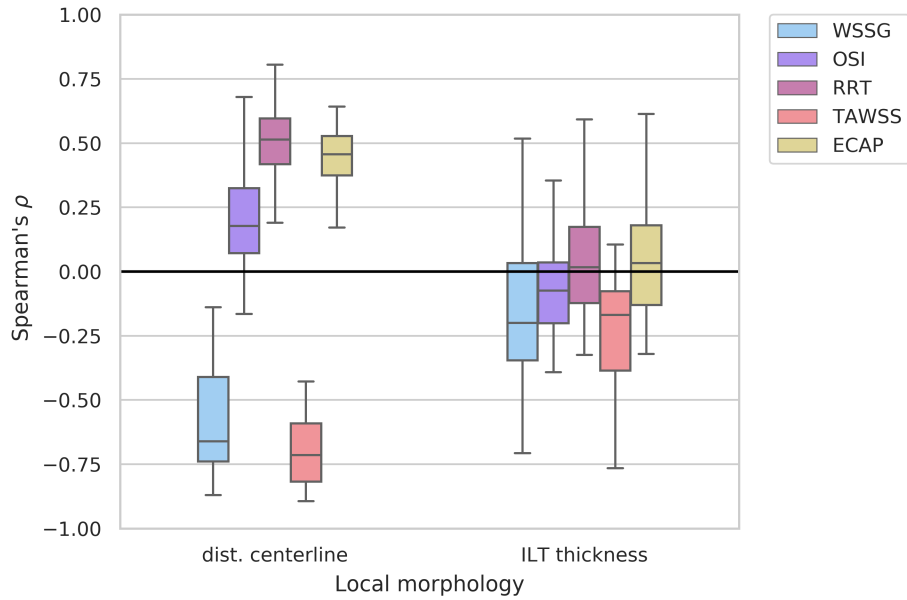


(d)

Figure 6: a and c: Bivariate distributions and kernel density plot of ECAP ( $Pa^{-1}$ ) versus the normalized distance from the lumen wall to the centerline of two simulations from two different patients. b and c: Distribution plots of the Spearman's  $\rho$  from the bootstrap evaluations. The top and bottom cases illustrate the variety of the bivariate distributions and correlations encountered in the study.



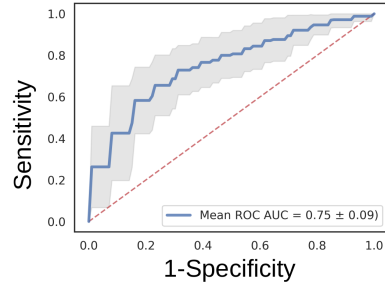
(a) All CTs evaluated independently.



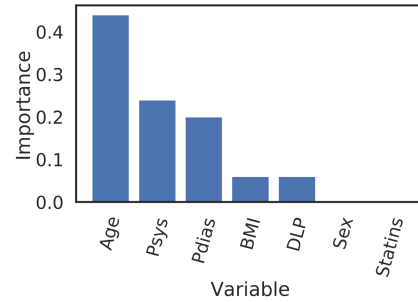
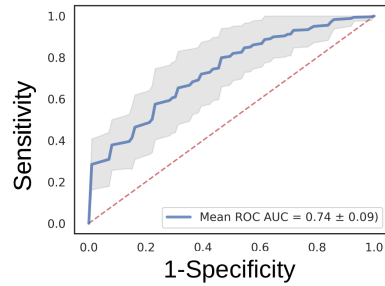
(b) Statistics performed on each patient, (one correlation for all scans of that patient).

Figure 7: Boxplot of the distribution of Spearman's  $\rho$  between local flow and morphological evaluation metrics. On the left, all scans are evaluated separately and on the right statistics are patient-wise. The boxes represent the inter-quartile range (IQR) i.e. data between the 25 (Q1) and 75% (Q3) percentile. Bottom whisker is  $Q1 - 1.5IQR$  and top whisker is  $Q3 + 1.5IQR$ . Outliers are not represented for readability. Correlations are computed on patch-wise data for each scan. The large dispersion of Spearman's  $\rho$  distribution is illustrated in Figure 6 for one metric.

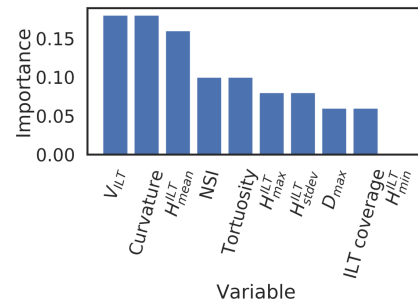
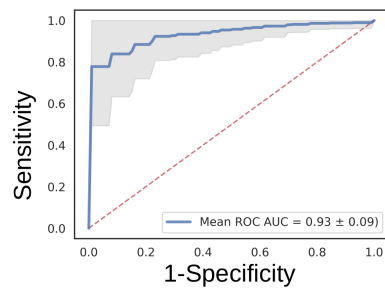
$D_{max}$



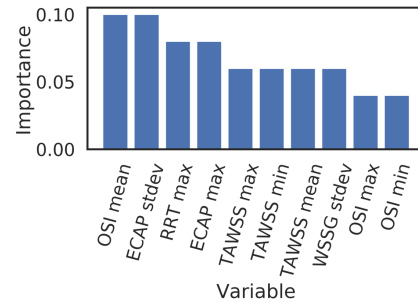
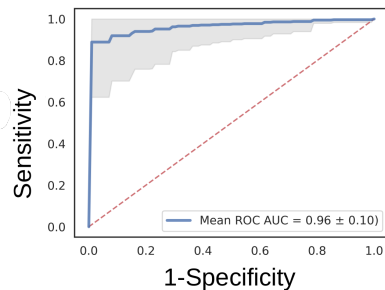
Clinical features



Morphological features



Hemodynamic features



Combined features

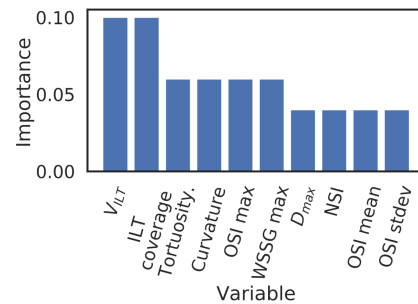
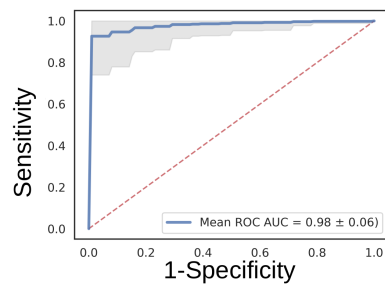


Figure 8: Left: ROC curves for the classification of high risk (i.e. risk predictor). Right: Top 10 features ranked with respect to predictability of the target variable. The gray area represents the standard deviation ( $\pm 1$  st. dev.) of all ROC generated during the repeated cross-validation process.

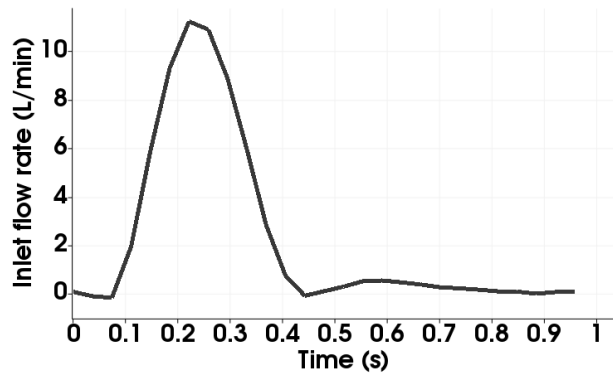


Figure I: Volumetric flow rate imposed at the inlet of the AAA.



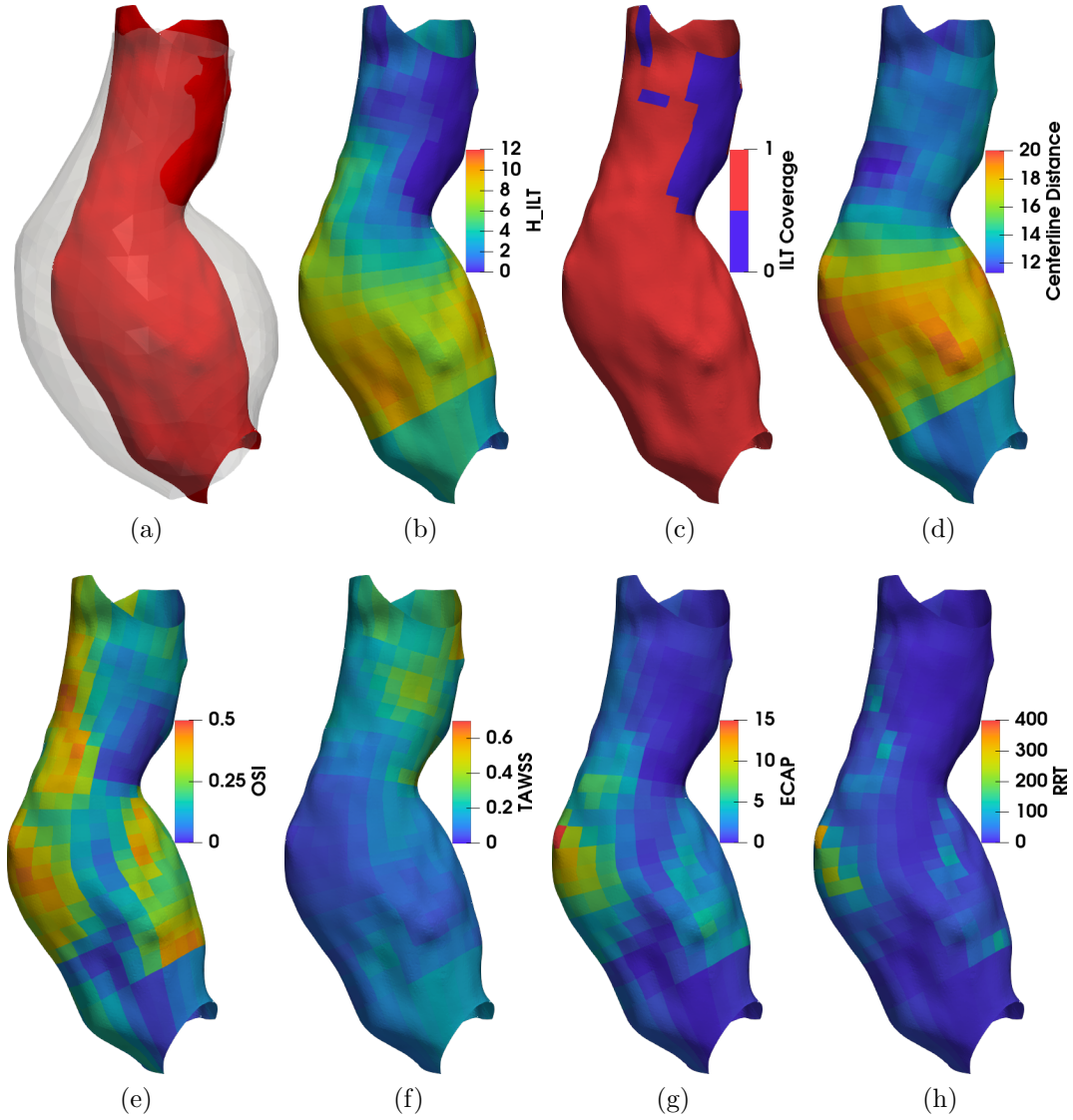
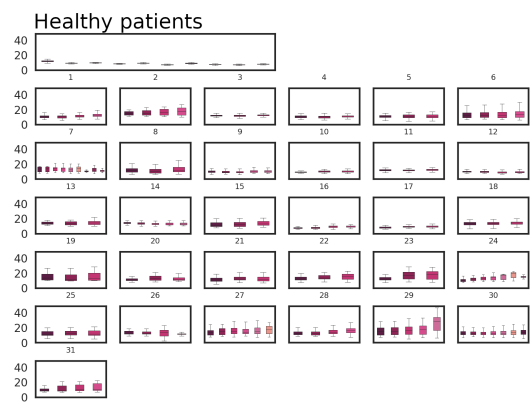
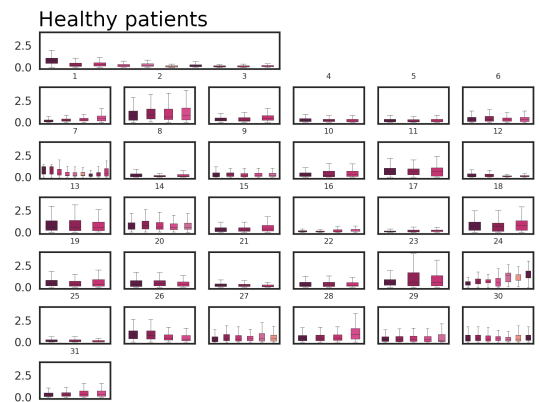


Figure II: View of patched metrics on an aneurysm. From left to right and top to bottom: lumen with ILT overlaid,  $H^{ILT}$  [mm], ILT coverage [·], local distance to the centerline [mm], OSI [·], TAWSS [Pa], ECAP [Pa<sup>-1</sup>] and RRT [Pa<sup>-1</sup>]. The displayed AAA is also visible in Figure V and Figure VI



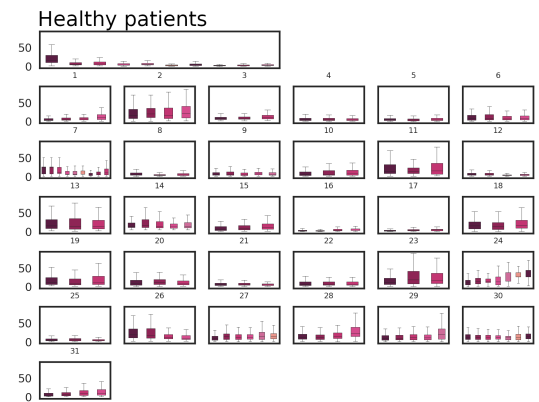
a) lumen - centerline distance



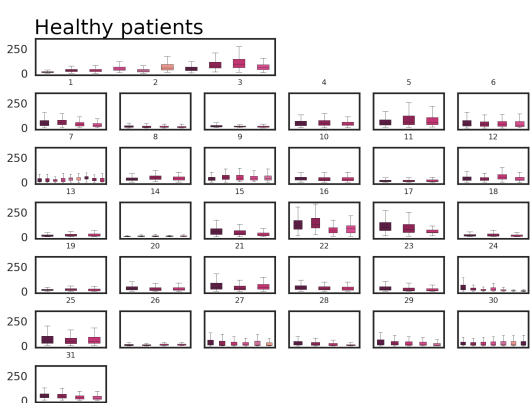
b) RRT



c)  $H_{max}^{ILT}$



d) ECAP



e) WSSG

Figure III: Boxplot of local distribution of various metrics, for all patient, along their follow-up. Statistical distribution is built from data from all 600 patches. The box represents the inter-quartile range (IQR) or data between the 25% (Q1) and 75% (Q3) percentile. Bottom whisker is  $Q1 - 1.5IQR$  and top whisker is  $Q3 + 1.5IQR$ . Outliers are not represented for the sake of readability.

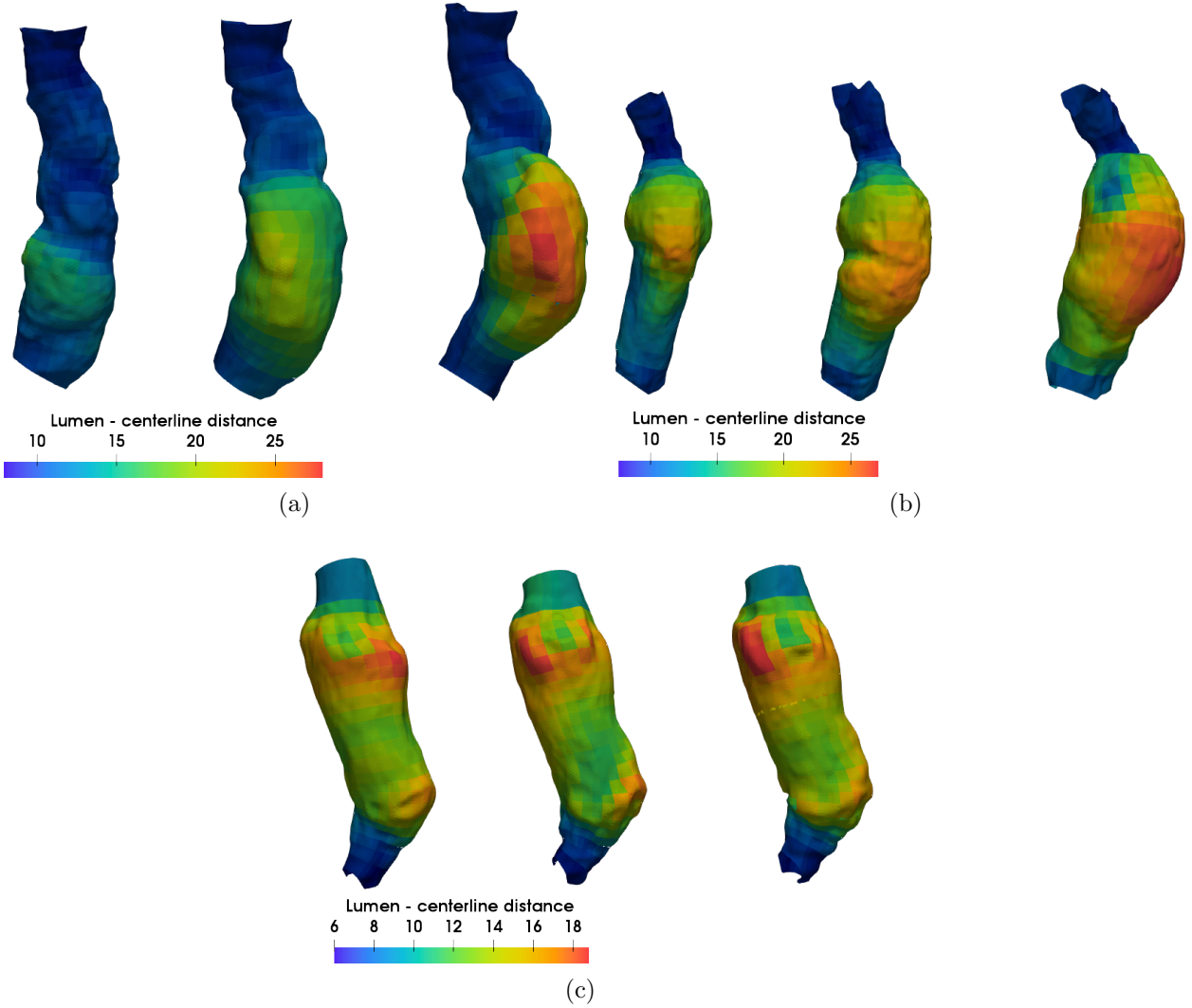


Figure IV: View of local distance ( $mm$ ) from the lumen to the centerline mapped on the lumen and averaged on patches for patient 6 (a), 22 (b) and 21 (c). Patient 6 exhibits a strong and localized growth of the lumen. Patient 21s lumen is pretty tubular with a constant diameter while patient 22's diameter is healthy at the proximal neck and over 50 mm at the  $D_{max}$  location, hence the large dispersion of values seen on the boxplot.

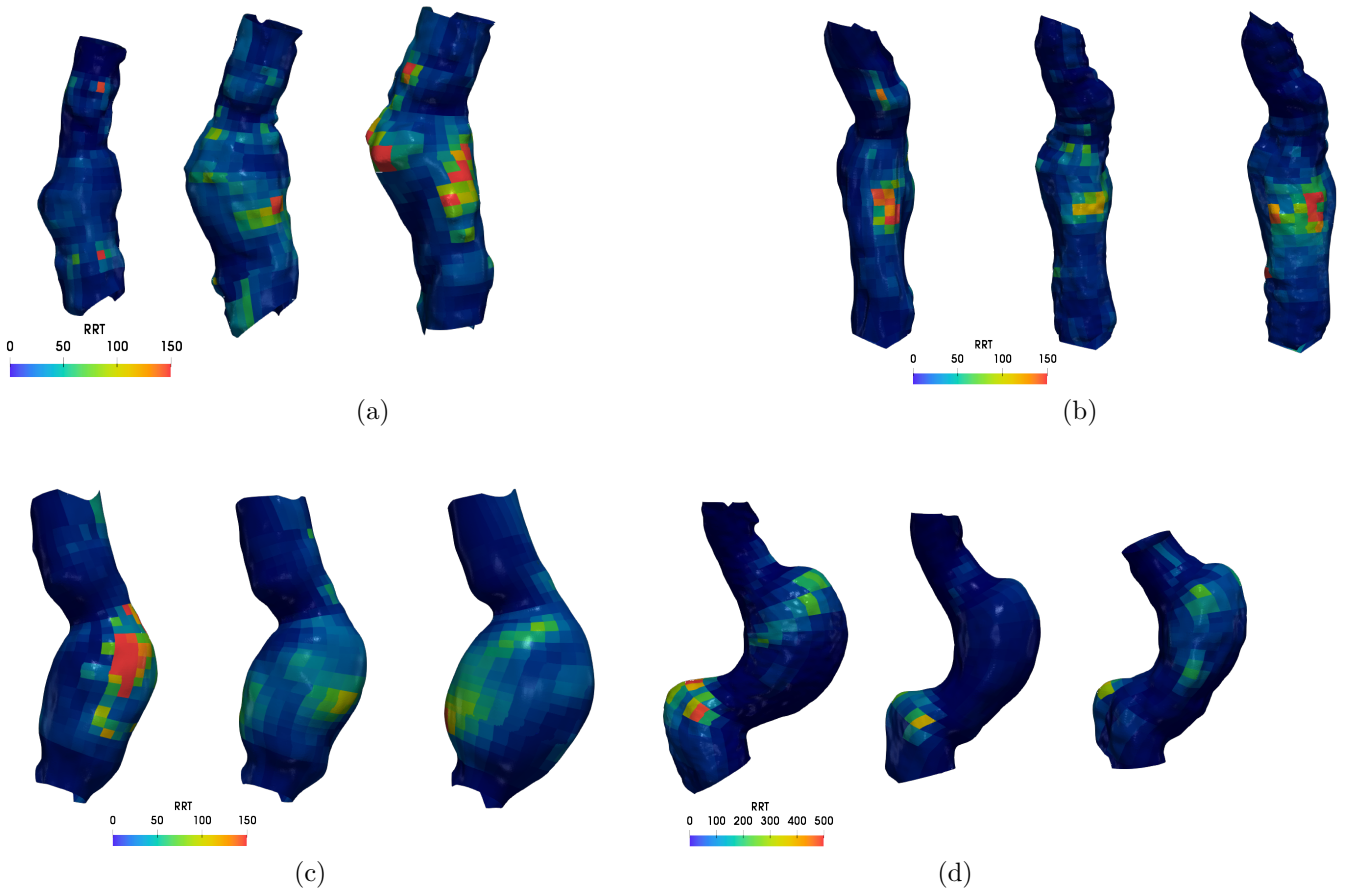


Figure V: For 4 patients, RRT averaged on patches. Patient 10 (a), exhibits a steady growth with time. Patient 28 (b): RRT standard deviation is relatively small compared to patient 29 (c). For patient 15 (d), RRT decreases before increasing.

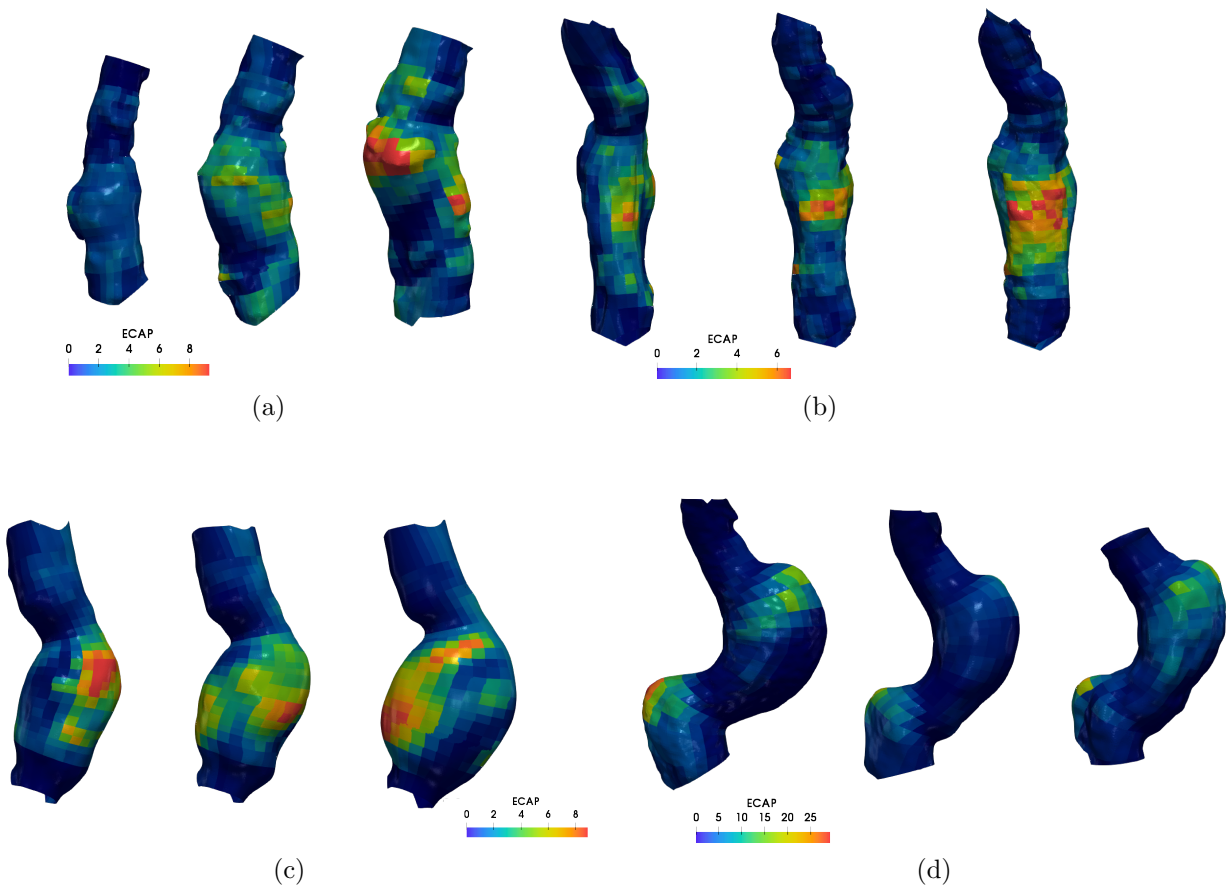


Figure VI: ECAP averaged on patches, for 4 patients. ECAP, similarly to the RRT contains information from OSI and TAWSS. Patient 10 (a), monotonic growth, patient 28 (b) with a small standard deviation compared to patient 29 (c). Patient 15 (d) ECAP average, decreases and then increases.

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Clinical metric	Availability among patients (%)
Age	71.4
Sex	100
BMI	40.5
$p_{sys}$	61.9
$p_{dias}$	61.9
Dyslipidemia	69.1
Statins	69.1

Table 1: Percentage of the 42 patients for which clinical data are available, per variable. *Age*, *BMI* (body mass index),  $p_{sys}$  (systolic pressure) and  $p_{dias}$  (diastolic pressure) are continuous variable and *Sex*, *Dyslipidemia* (DLP) and *statins* are discrete.

Clinical variables	Healthy	Low-risk	High-risk	Statistical significance
Age (yr)	60.40 (12.44)	73.66 (7.03)	73.88 (7.85)	H-LR, H-HR
Systolic pressure (mmHg)	129.25 (16.89)	119.80 (11.54)	130.73 (17.24)	LR-HR
Diastolic pressure (mmHg)	74.88 (8.67)	68.91 (8.65)	77.21 (13.85)	LR-HR
Dyslipidemia (DLP) (%)	0.33 (0.47)	0.84 (0.37)	0.82 (0.38)	H-LR, H-HR
BMI	25.92 (4.91)	31.20 (5.73)	28.65 (5.95)	
Statins (%)	0.33 (0.47)	0.82 (0.38)	0.80 (0.40)	H-LR, H-HR

Table 2: Statistical distribution of the clinical variables among the three groups. When a significant difference was observed ( $p < 0.05$ ) between two groups, it was reported in the 4<sup>th</sup> column. H-LR means a statistical difference between the High and Low-Risk groups, H-HR between the Healthy and High-Risk groups and LR-HR between the Low and High-Risk groups. Standard deviations are given in parentheses.



Morphological variables	Healthy	Low-risk	High-risk	Statistical significance
Lumen surface area (cm <sup>2</sup> )	60.32 (16.93)	98.74 (23.03)	120.90 (27.10)	H-LR, H-HR, LR-HR
Lumen surface area, annual (cm <sup>2</sup> yr <sup>-1</sup> )	-	6.51 (13.99)	-2.14 (81.85)	
Lumen volume (cm)	24.95 (11.58)	57.17 (20.75)	79.62 (34.28)	H-LR, H-HR, LR-HR
Lumen volume, annual (cm <sup>3</sup> yr <sup>-1</sup> )	-	6.34 (16.24)	7.43 (80.96)	
ILT volume (cm)	0.00 (0.00)	38.99 (30.80)	65.90 (44.25)	H-LR, H-HR, LR-HR
ILT volume, annual (cm <sup>3</sup> yr <sup>-1</sup> )	-	3.28 (22.55)	33.95 (154.98)	
Total volume (cm)	24.95 (11.58)	96.17 (41.25)	145.52 (53.53)	H-LR, H-HR, LR-HR
Total volume, annual (cm <sup>3</sup> yr <sup>-1</sup> )	-	9.38 (14.77)	29.43 (85.82)	
$D_{max}^{lumen}$ (mm)	18.18 (3.52)	28.89 (5.74)	32.94 (8.04)	H-LR, H-HR, LR-HR
$D_{max}^{lumen}$ , annual (mm yr <sup>-1</sup> )	-	1.07 (3.85)	2.81 (10.72)	
$D_{max}$ (mm)	18.18 (3.52)	43.72 (7.37)	54.40 (8.77)	H-LR, H-HR, LR-HR
$D_{max}$ , annual (mm yr <sup>-1</sup> )	-	1.14 (3.31)	3.61 (4.55)	LR-HR
Lumen NSI (-)	1.22 (0.02)	1.18 (0.04)	1.18 (0.05)	H-LR, H-HR
ILT coverage (%)	-	64.63 (24.92)	67.89 (19.09)	
ILT coverage, annual (yr <sup>-1</sup> )	-	-2.07 (13.06)	33.92 (237.39)	
$H_{max}^{ILT}$ (mm)	-	7.89 (4.12)	11.65 (5.31)	LR-HR
$H_{min}^{ILT}$ (mm)	-	0.31 (0.65)	0.17 (0.46)	
$H_{mean}^{ILT}$ (mm)	-	3.09 (1.80)	4.05 (2.34)	LR-HR
$H_{stdev}^{ILT}$ (mm)	-	2.55 (1.36)	3.71 (1.64)	LR-HR

Table 3: Statistical distribution of the morphological variables among the three groups. When a significant difference was observed ( $p < 0.05$ ) between two groups, it was reported in the 4<sup>th</sup> column. H-LR means a statistical difference between the High and Low-Risk groups, H-HR between the Healthy and High-Risk groups and LR-HR between the Low and High-Risk groups. Standard deviations are given in parentheses.

hemodynamic variables	Healthy	Low-risk	High-risk	Statistical significance
$OSI_{max}$ (-)	0.36 (0.04)	0.38 (0.04)	0.37 (0.05)	
$OSI_{min}$ (-)	0.02 (0.02)	0.02 (0.02)	0.02 (0.03)	
$OSI_{mean}$ (-)	0.16 (0.04)	0.18 (0.04)	0.17 (0.04)	
$OSI_{stdev}$ (-)	0.11 (0.01)	0.11 (0.01)	0.11 (0.02)	
$TAWSS_{max}$ (Pa)	0.66 (0.31)	0.58 (0.28)	0.54 (0.22)	
$TAWSS_{min}$ (Pa)	0.23 (0.08)	0.11 (0.06)	0.09 (0.05)	H-LR, H-HR, LR-HR
$TAWSS_{mean}$ (Pa)	0.40 (0.17)	0.27 (0.11)	0.23 (0.10)	H-LR, H-HR
$TAWSS_{stdev}$ (Pa)	0.16 (0.09)	0.16 (0.09)	0.16 (0.07)	
$WSSG_{max}$ (Pa m <sup>-1</sup> )	135.60 (71.51)	124.55 (70.32)	116.32 (61.23)	
$WSSG_{min}$ (Pa m <sup>-1</sup> )	17.42 (9.48)	9.30 (7.30)	6.79 (7.10)	H-LR, H-HR
$WSSG_{mean}$ (Pa m <sup>-1</sup> )	61.03 (32.52)	44.74 (25.82)	38.89 (23.32)	
$WSSG_{stdev}$ (Pa m <sup>-1</sup> )	61.04 (44.25)	41.97 (24.82)	45.17 (25.02)	
$RRT_{max}$ (Pa <sup>-1</sup> )	22.64 (17.25)	48.26 (30.80)	58.15 (34.73)	H-LR, H-HR
$RRT_{min}$ (Pa <sup>-1</sup> )	2.34 (1.33)	2.63 (1.32)	3.12 (1.84)	
$RRT_{mean}$ (Pa <sup>-1</sup> )	8.20 (6.17)	15.68 (8.01)	19.00 (10.00)	H-LR, H-HR, LR-HR
$RRT_{stdev}$ (Pa <sup>-1</sup> )	8.20 (6.51)	21.68 (16.56)	24.22 (15.69)	H-LR, H-HR
$ECAP_{max}$ (Pa <sup>-1</sup> )	0.66 (0.39)	1.42 (0.76)	1.77 (0.92)	H-LR, H-HR, LR-HR
$ECAP_{min}$ (Pa <sup>-1</sup> )	0.03 (0.03)	0.02 (0.03)	0.04 (0.06)	
$ECAP_{mean}$ (Pa <sup>-1</sup> )	0.26 (0.19)	0.48 (0.22)	0.59 (0.32)	H-LR, H-HR, LR-HR
$ECAP_{stdev}$ (Pa <sup>-1</sup> )	0.20 (0.11)	0.48 (0.27)	0.59 (0.31)	H-LR, H-HR, LR-HR

Table 4: Statistical distribution of the hemodynamic variables among the three groups. When a significant difference was observed ( $p < 0.05$ ) between two groups, it was reported in the 4<sup>th</sup> column. H-LR means a statistical difference between the High and Low-Risk groups, H-HR between the Healthy and High-Risk groups and LR-HR between the Low and High-Risk groups. Standard deviations are given in parentheses.

Local morphological variables	Low-risk	High-risk	Statistical significance
local change of $H_{max}^{ILT}$ (mm yr <sup>-1</sup> )	4.55 (4.27)	7.31 (4.58)	LR-HR
local change of $H_{min}^{ILT}$ (mm yr <sup>-1</sup> )	-4.96 (6.47)	-16.78 (33.77)	LR-HR
local change of $H_{mean}^{ILT}$ (mm yr <sup>-1</sup> )	-0.11 (1.60)	-1.18 (5.38)	

Table 5: Statistical distribution of the local annual variation of ILT thickness among the low and high-risk groups. When a significant difference was observed ( $p < 0.05$ ) between two groups, it was reported in the 4<sup>th</sup> column. H-LR means a statistical difference between the High and Low-Risk groups, H-HR between the Healthy and High-Risk groups and LR-HR between the Low and High-Risk groups. Standard deviations are given in parentheses.

Local hemodynamic variables	Low-risk	High-risk	Statistical significance
local change of $OSI_{max}$ ( $\text{yr}^{-1}$ )	0.29 (0.41)	1.26 (3.70)	
local change of $OSI_{min}$ ( $\text{yr}^{-1}$ )	-0.29 (0.38)	-1.14 (2.67)	LR-HR
local change of $OSI_{mean}$ ( $\text{yr}^{-1}$ )	0.00 (0.06)	0.05 (0.47)	
local change of $TAWSS_{max}$ ( $\text{Pa yr}^{-1}$ )	0.27 (0.36)	1.08 (3.50)	
local change of $TAWSS_{min}$ ( $\text{Pa yr}^{-1}$ )	-0.42 (0.70)	-1.47 (3.86)	LR-HR
local change of $TAWSS_{mean}$ ( $\text{Pa yr}^{-1}$ )	-0.02 (0.10)	-0.04 (0.25)	
local change of $WSSG_{max}$ ( $\text{Pa m}^{-1} \text{yr}^{-1}$ )	81.56 (108.31)	287.46 (963.86)	
local change of $WSSG_{min}$ ( $\text{Pa m}^{-1} \text{yr}^{-1}$ )	-111.53 (176.19)	-350.49 (829.66)	LR-HR
local change of $WSSG_{mean}$ ( $\text{Pa m}^{-1} \text{yr}^{-1}$ )	-3.86 (24.29)	4.27 (109.43)	
local change of $RRT_{max}$ ( $\text{Pa}^{-1} \text{yr}^{-1}$ )	44.64 (73.56)	245.22 (658.03)	LR-HR
local change of $RRT_{min}$ ( $\text{Pa}^{-1} \text{yr}^{-1}$ )	-44.47 (90.49)	-225.57 (538.46)	LR-HR
local change of $RRT_{mean}$ ( $\text{Pa}^{-1} \text{yr}^{-1}$ )	0.64 (6.76)	8.16 (55.48)	
local change of $ECAP_{max}$ ( $\text{Pa}^{-1} \text{yr}^{-1}$ )	4.61 (7.11)	23.63 (58.92)	LR-HR
local change of $ECAP_{min}$ ( $\text{Pa}^{-1} \text{yr}^{-1}$ )	-0.44 (0.56)	-1.85 (3.48)	LR-HR
local change of $ECAP_{mean}$ ( $\text{Pa}^{-1} \text{yr}^{-1}$ )	1.31 (2.35)	7.39 (21.40)	

Table 6: Statistical distribution of the local hemodynamic variables among the low and high-risk groups. When a significant difference was observed ( $p < 0.05$ ) between two groups, it was reported in the 4<sup>th</sup> column. LR-HR means a statistical difference between the Low and High-Risk groups. Standard deviations are given in parentheses.

	Dmax	Clinical	Morpho.	Flow	All
Dmax		0.393	0.008	0.006	0.006
Clinical			0.004	0.004	0.004
Morpho.				0.561	0.207
Hemo.					0.281
All					

Table 7: p-values between AUCs from Figure 8 according to Delong et al.<sup>21</sup> method. Significant values ( $\leq 0.05$ ) are in orange cells.

<b>Outlets</b>	<b>Rp</b>	<b>C</b>	<b>Rd</b>
<b>Mes. Sup.</b>	$6.7 * 10^3$	$8.11 * 10^6$	$1.13 * 10^5$
<b>Celiac</b>	$6.7 * 10^3$	$8.11 * 10^6$	$1.13 * 10^5$
<b>Renal</b>	$1.2 * 10^4$	$1.8 * 10^{-5}$	$4.8 * 10^4$
<b>Int. Iliac</b>	$4.55 * 10^3$	$1.582 * 10^{-5}$	$7.7 * 10^4$
<b>Ext. Iliac</b>	$4.8 * 10^3$	$1.75 * 10^{-5}$	$8.2 * 10^4$

Table I: Proximal resistance, compliance and distal resistance for the 0D-RCR model, from Xiao et al.<sup>68</sup> (in [CGS] units).

	Metric notation	Extraction	Remarks & litt.
Morphological parameters	$D_{max}^{lumen}$	maximal diameter of the lumen in a plane orthogonal to the luminal centerline	-
	$D_{max}$	maximal diameter of the AAA (inc. ILT) in a plane orthogonal to the luminal centerline	Current clinical criteria.
	$H^{ILT}$	thrombus thickness, computed as the Euclidean distance between the lumen and ILT	-
	Lumen centerline curvature	inverse of the radius of the local oscillating circle	Shum et al. <sup>55</sup>
	Lumen centerline tortuosity	ratio between the centerline length and the endpoints distance.	Shum et al. <sup>55</sup>
	Lumen NSI	$\frac{1}{2.199} \frac{\sqrt{Area}}{\sqrt[3]{Volume}}$	Raghavan et al. <sup>49</sup>
	Lumen (ILT) volume	volume of the lumen (ILT) between the renal and the iliac bifurcation.	-
	Lumen (ILT) surface area	surface of the lumen (ILT) between the renal and the iliac bifurcation.	-
	ILT coverage	percentage of the lumen covered with thrombus. The observed quantity is the ratio of lumen outer wall area exposed to ILT to the total area, not the aortic wall covered in ILT	-
hemodynamic param.	TAWSS	$\frac{1}{T} \int_0^T  \tau_W  dt$	Bluestein et al. <sup>9</sup> and Arzani et al. <sup>4</sup>
	OSI	$\frac{1}{2} \left( 1 - \frac{ \int_0^T \tau_W dt }{\int_0^T  \tau_W  dt} \right)$	Arzani et al. <sup>4</sup>
	RRT	$\frac{1}{(1-2OSI) TAWSS}$	Himburg et al. <sup>36</sup>
	ECAP	$\frac{OSI}{TAWSS}$	Di Achille et al. <sup>24</sup>
	WSSG	$ \nabla WSS $	Nagel et al. <sup>45</sup>

Table II: Description of the various metrics used in the article.