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

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

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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 14th leading cause of death in the USA⁵⁷ 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})⁴⁷, taken at the outer wall of the aneurysm on a plane perpendicular to the lumen centerline¹⁶. 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 women¹³ or if AAA D_{max} growth exceeds $1\text{cm}\cdot\text{yr}^{-1}$ ¹⁷, patients will undergo open or endovascular aneurysm repair. Otherwise a yearly control is performed.

New guidelines¹⁸ 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)⁴⁸ and 23% of ruptured AAA are less than 5 cm²⁰. 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 AAAs⁴⁸. These data show the maximal diameter/rupture relationship to be nonlinear and inaccurate to predict rupture²⁸. Identifying better performing metrics is an active research field³⁴. 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^{29,67} by coupling the biology and mechanics of the disease. Known metrics of interests are AAA volume, surface, bulge height, tortuosity and local surface curvature^{55,56} as well as mechanical stress, intrinsically relying on tissue properties, strongly heterogeneous and nonlinear⁴⁹ and also patient specific⁵⁰. From a fluid point of view, blood flow is known to play a crucial role in AAA evolution^{54,5}, as well as ILT presence and

65 growth^{30,7}.

66 Very few studies focus on local parameters and their variations between two scans. Tzi-
67 rakis et al.⁶⁴ 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.⁴ 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.⁷¹ 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.⁴¹ 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)¹. 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

¹Approval #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 months¹⁷. New
124 guidelines¹⁸ 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 2mm yr^{-1} ^{11,59}. The 5mm/year growth threshold has previously been recognized as a
127 fast growth criterion²⁵ and this growth variation is above the 95% of the confidence interval
128 of D_{max} measurement error⁵⁸. 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 5mm 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*⁷⁰. 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*³⁷, 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 in³⁴. The flow is considered laminar, homogeneous and non-Newtonian, the viscosity following the Quemada model^{40,35}. Model parameters are chosen according to the study of Buchanan et al.¹⁴ based on the rheological data from Kaibara et al.³⁵. Peak Reynolds numbers of 1700-2000 at the proximal inlet in the simulations are within the physiological range²⁸ as well as the Womersley numbers, ranging from 10 to 15⁴⁴. A generic flow rate is imposed at the inlet⁴³ (see Figure I) with Womersley profile⁶⁶. 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 diastole²⁷ is likely to create numerical instability. Gradient stabilization to control complex backflow in the domain similarly to Bertoglio et al.⁶ 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^{31,32}. 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)⁵²

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*², 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 information¹. 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 patches³ (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 1mm³³. 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 change⁶⁰.

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 4th 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) method¹². As described
 233 in Rowland et al. in particular for WSS⁵¹, local correlation between a phenomena and a
 234 bio-mechanical metric is hindered by spatial auto-correlation. One reported alternative is
 235 bootstrapping²⁶ 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 ρ 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*⁶³ 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 tuned⁶¹ 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*¹⁵, are reported. AUCs medians are compared
260 with the DeLong et al.²¹ method.

261 3 Results

262 3.1 Population description

263 Healthy population mean age is estimated at 60.4 ± 12.4 years while AAA patient mean age
264 is 73.5 ± 7.4 ($p < 0.05$). Among the AAA patients, 5 are women (15.6%, mean age 73.6 ± 9.4
265 years) and 27 men (84.4%, mean age 73.5 ± 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 ± 11.6 years).
267 At least three follow-up CT-scans are available and suitable for domain reconstruction for
268 AAA patients (mean 4 ± 1.47 , range 3-9). Mean time between follow-up CT is 12.74 ± 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 ± 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 age⁶⁹.

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 ρ 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 ρ distributions. In fact, all five hemodynamic metrics ρ 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 ± 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 ± 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 ± 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 ± 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 ± 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 relevant⁵⁸.

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.⁶⁴ 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.⁴ did. TAWSS seemed relevant in both studies as well as
404 in Zambrano et al.⁷¹. 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 inflammation⁶², 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 expected⁴⁸ and
430 relatively small aneurysms that rupture²⁰.

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 rupture¹⁰. Di Achille et al.²⁴ 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 segmentation³⁷ 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 measurements³⁴ and literature⁴⁹. 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 AAA³⁴.
- 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} ³⁷, the same
504 error tolerance is expected by using the same segmentation tool.
- 505 • While flow in healthy aortas remains essentially laminar, complex flow⁴⁶ and transition
506 to turbulence^{38,65} 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.³⁹ 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 rupture²². The corresponding statistical model of rupture
522 probability was then successfully validated²³. 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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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**

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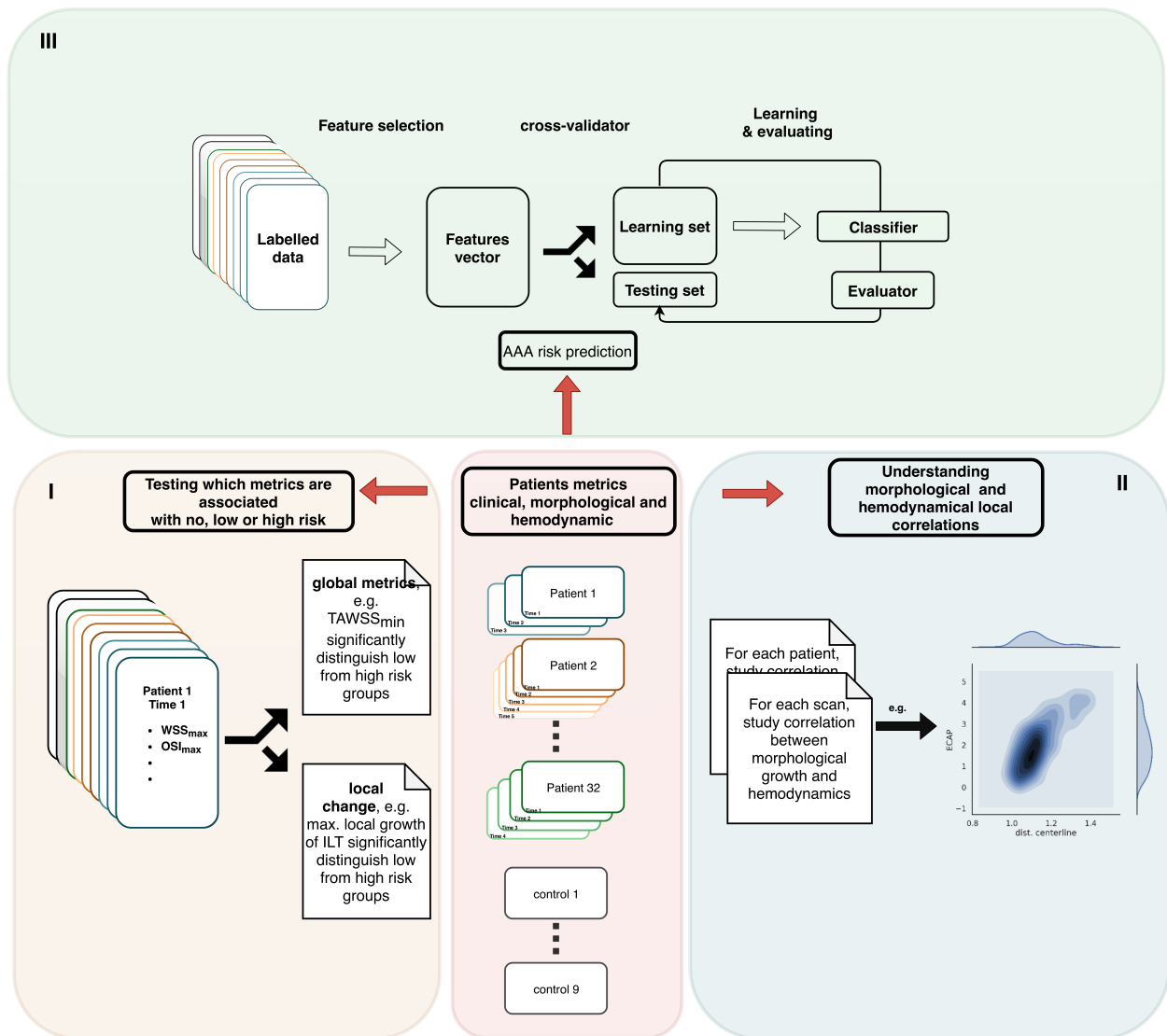


Figure 1: Overview of the study.

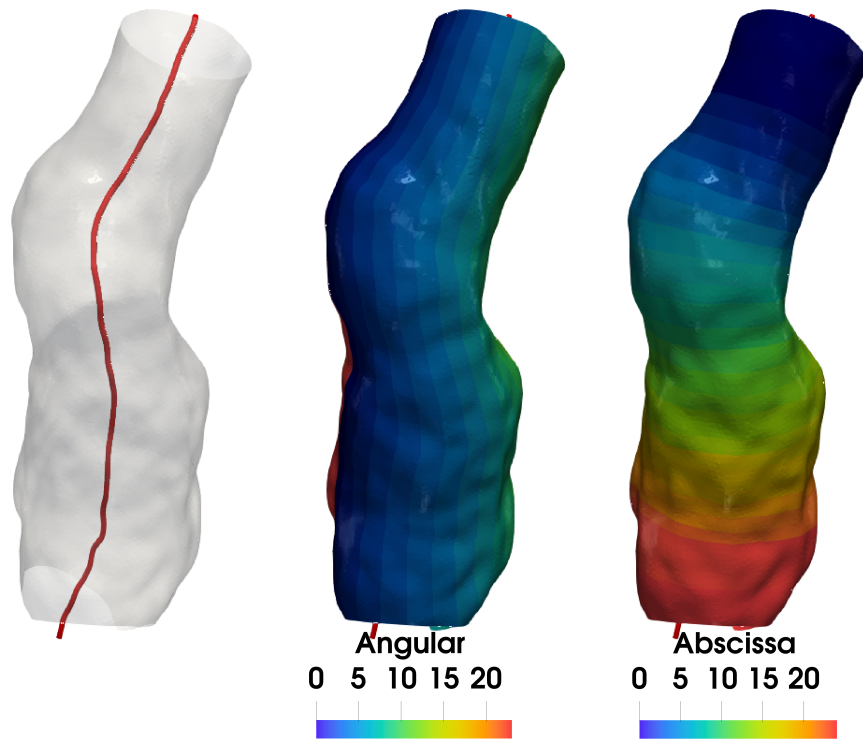


Figure 2: Patching process of the lumen surface. Left: centerline of the vessel lumen, Center: circumferential discretization, colored by the angular index. Right: centerline-based longitudinal discretization colored by the abscissa along the centerline.

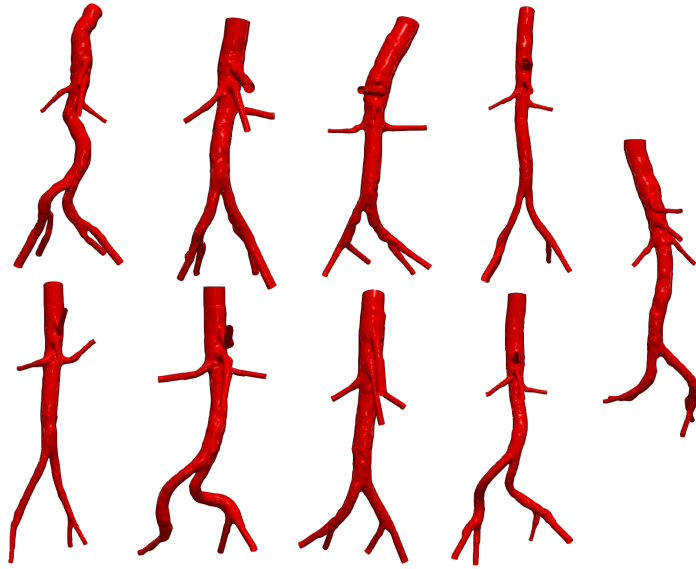
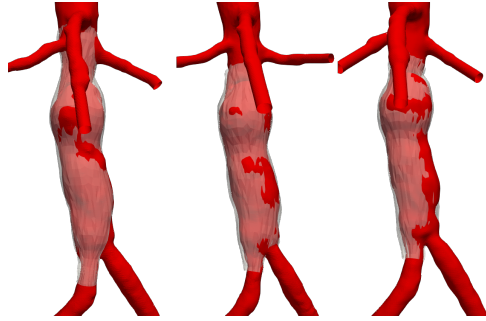
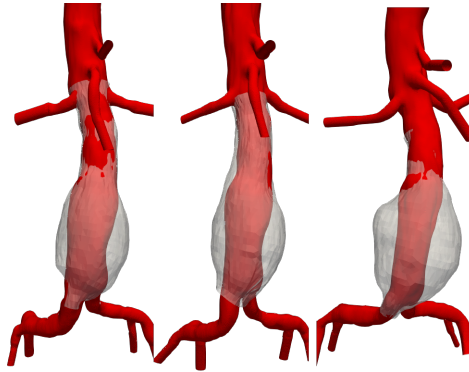


Figure 3: Aorta of the 9 healthy patients included in the study as control subjects. Most present various degrees of tortuosity, due to arteries aging.

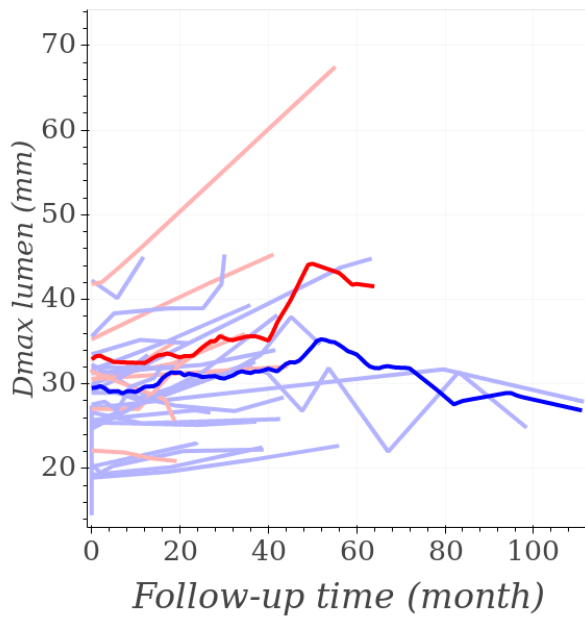


(a)

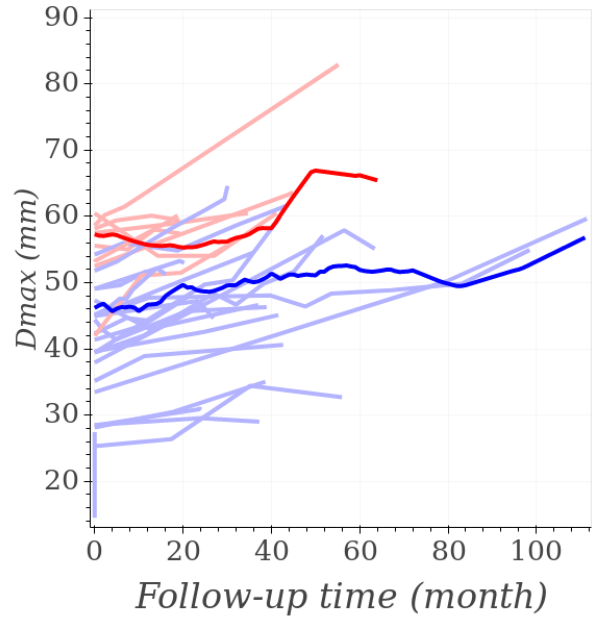


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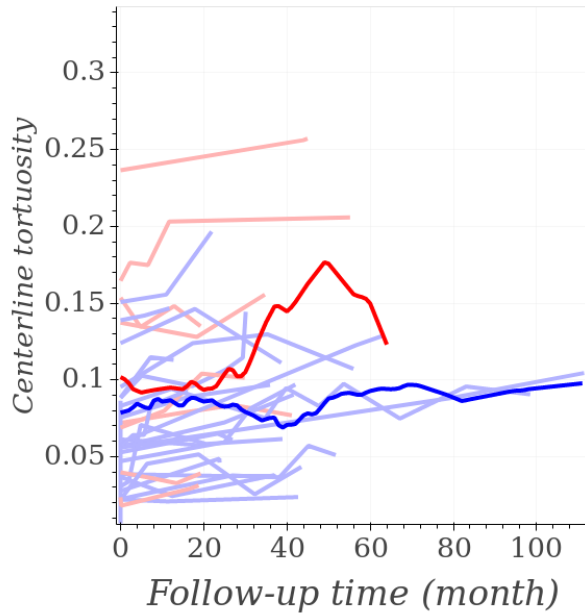
Figure 4: Example of different growth dynamics on two patients. The segmented lumen is in red, while ILT is transparent.



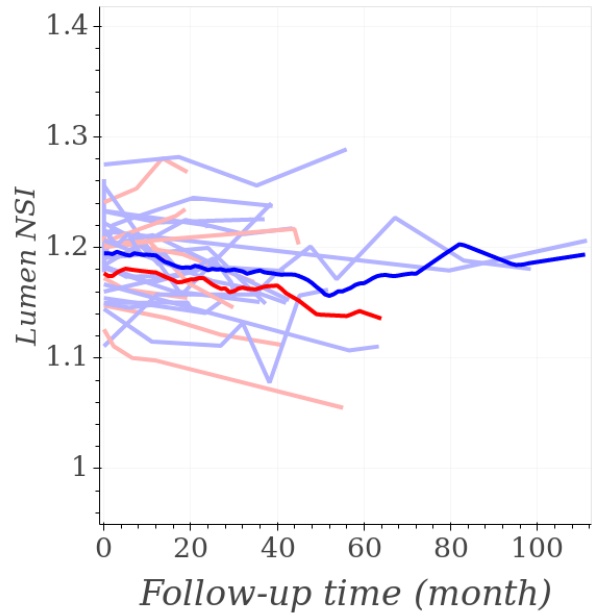
(a) D_{max}^{lumen}



(b) D_{max}

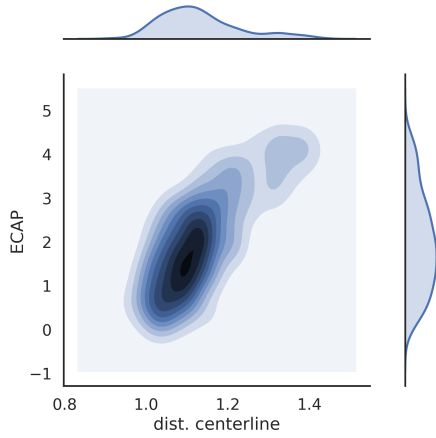


(c) Lumen centerline tortuosity

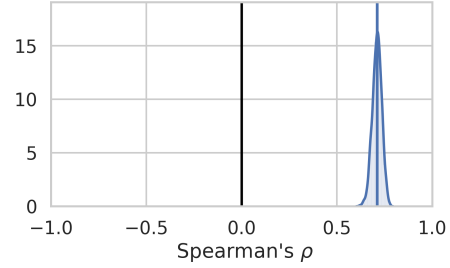


(d) Lumen NSI

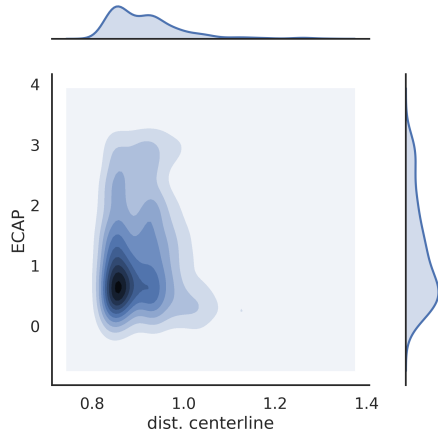
Figure 5: Evolution with time of selected parameters among patients. AAA ending up as high-risk are represented by red lines while low-risk AAA are in blue. Averaged behaviours of the two groups are in bold color.



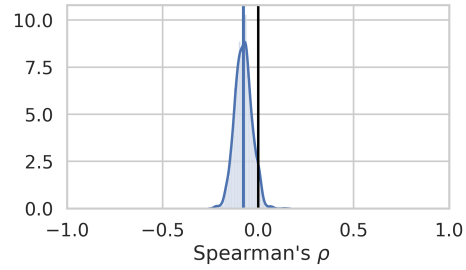
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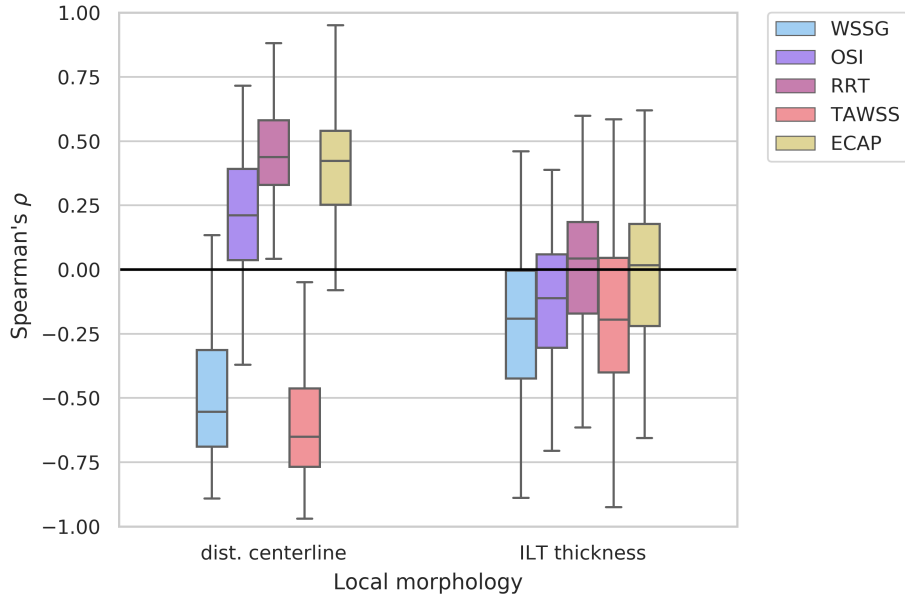


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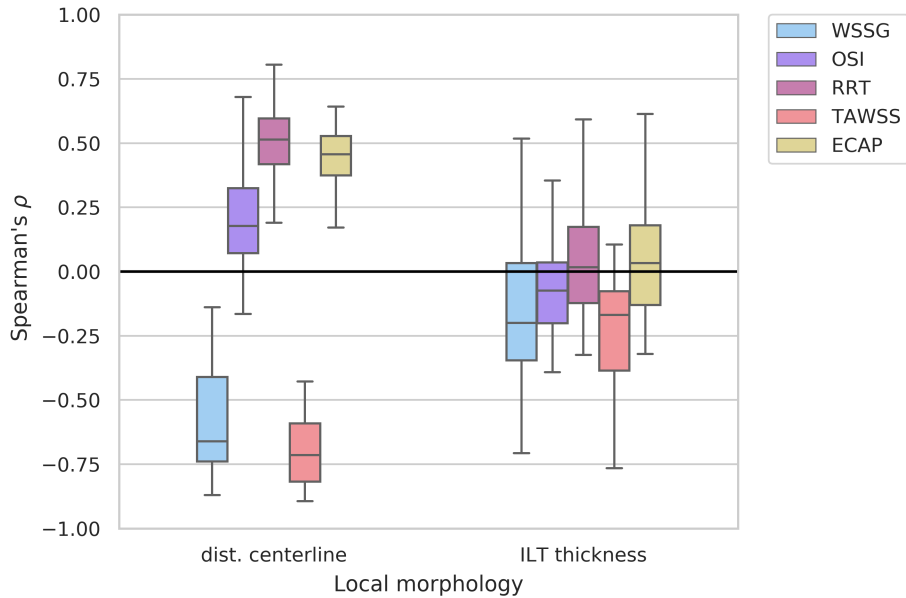


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Figure 6: a and c: Bivariate distributions and kernel density plot of ECAP (Pa^{-1}) versus the normalized distance from the lumen wall to the centerline of two simulations from two different patients. b and c: Distribution plots of the Spearman's ρ 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 ρ 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 ρ distribution is illustrated in Figure 6 for one metric.

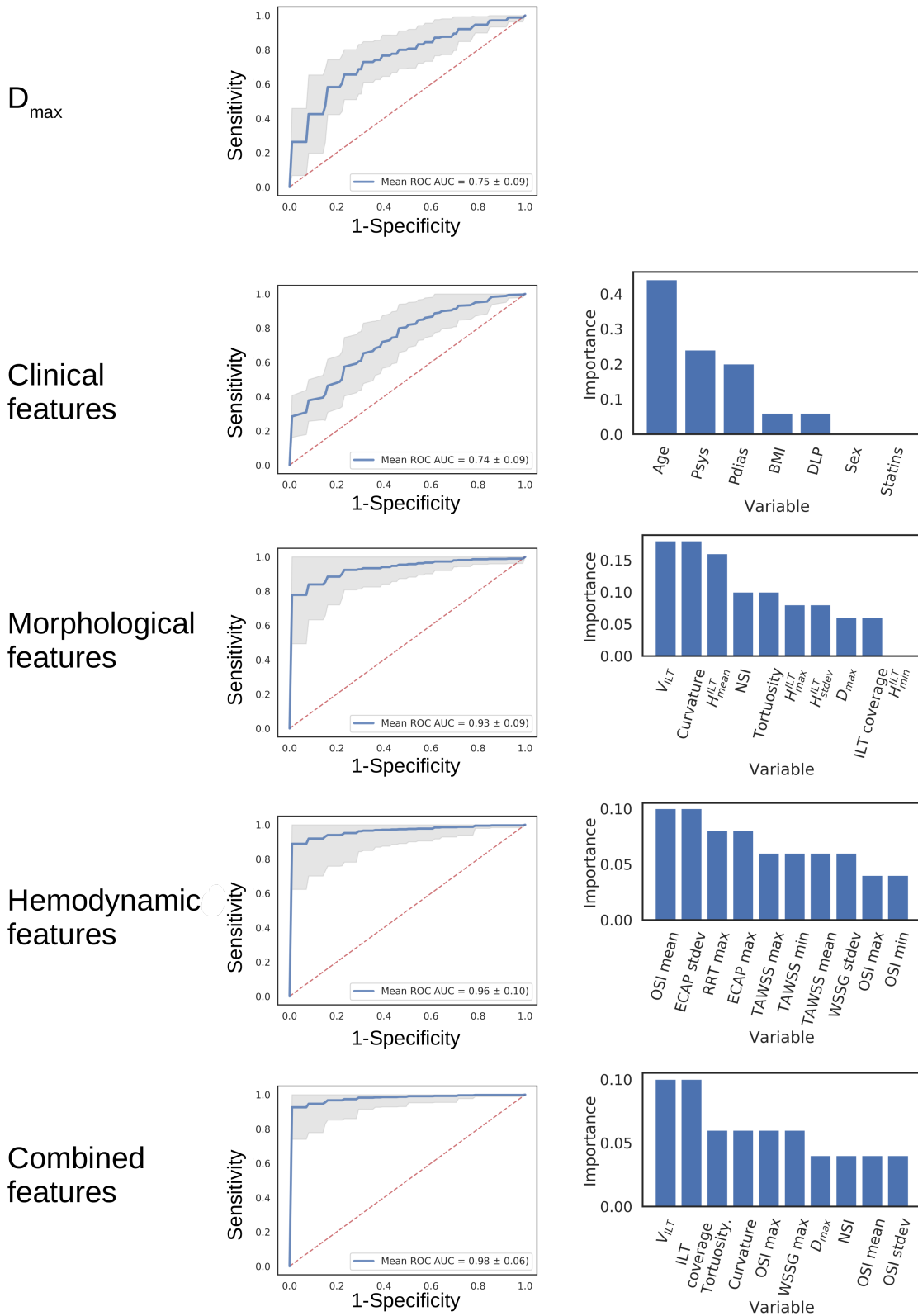


Figure 8: Left: ROC curves for the classification of high risk (i.e. risk predictor). Right: Top 10 features ranked with respect to predictability of the target variable. The gray area represents the standard deviation (± 1 st. dev.) of all ROC generated during the repeated cross-validation process.

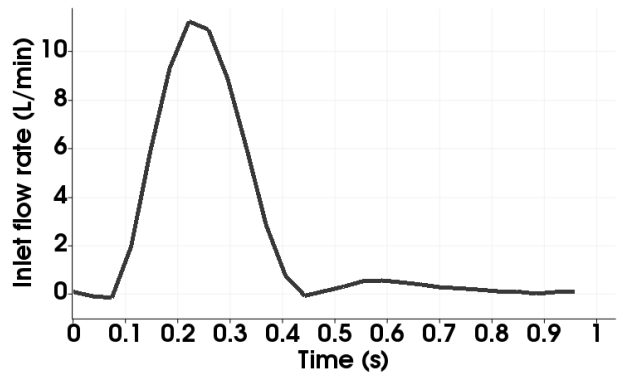


Figure I: Volumetric flow rate imposed at the inlet of the AAA.

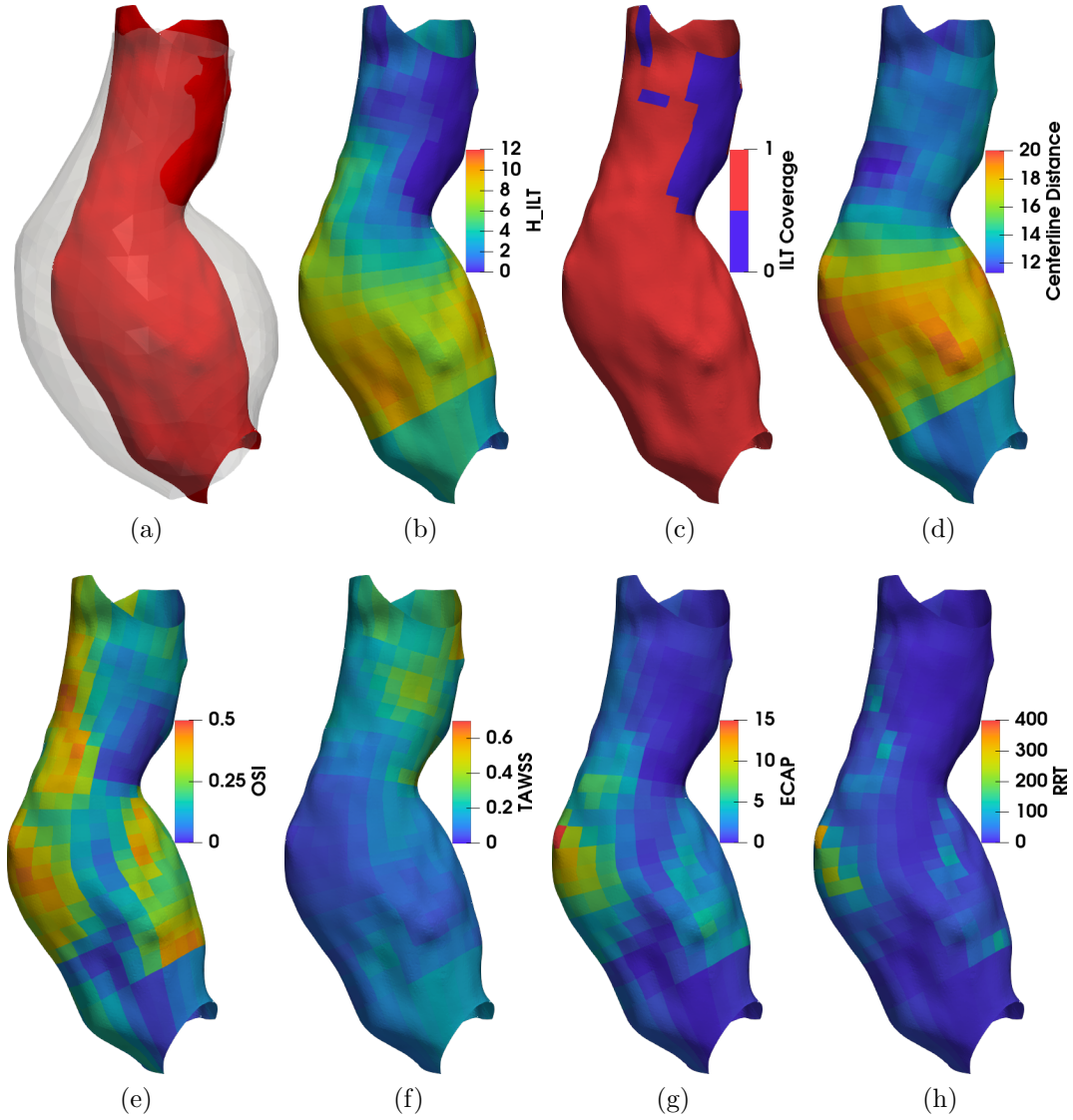
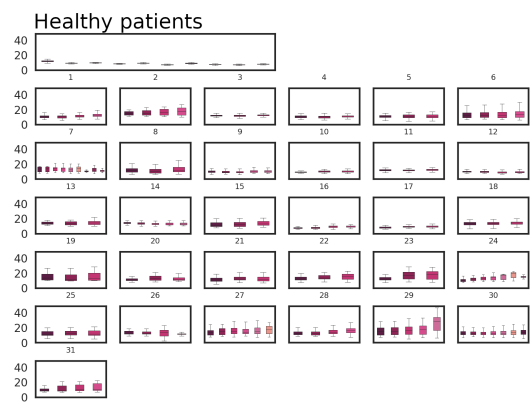
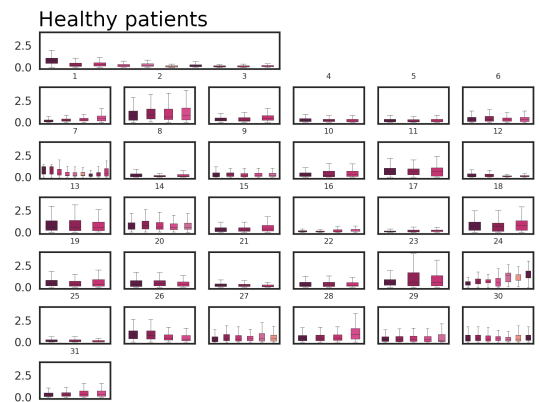


Figure II: View of patched metrics on an aneurysm. From left to right and top to bottom: lumen with ILT overlaid, H^{ILT} [mm], ILT coverage [·], local distance to the centerline [mm], OSI [·], TAWSS [Pa], ECAP [Pa⁻¹] and RRT [Pa⁻¹]. The displayed AAA is also visible in Figure V and Figure VI



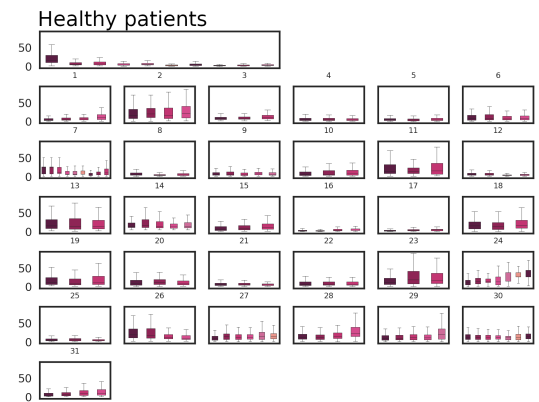
a) lumen - centerline distance



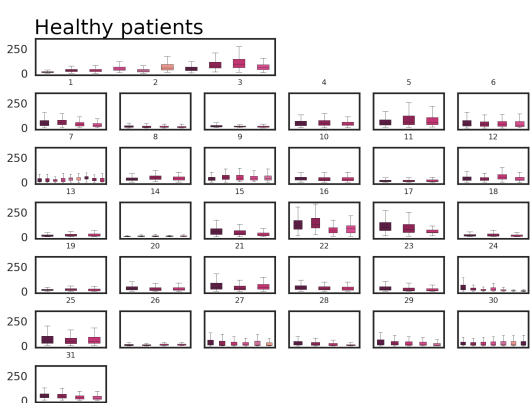
b) RRT



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.

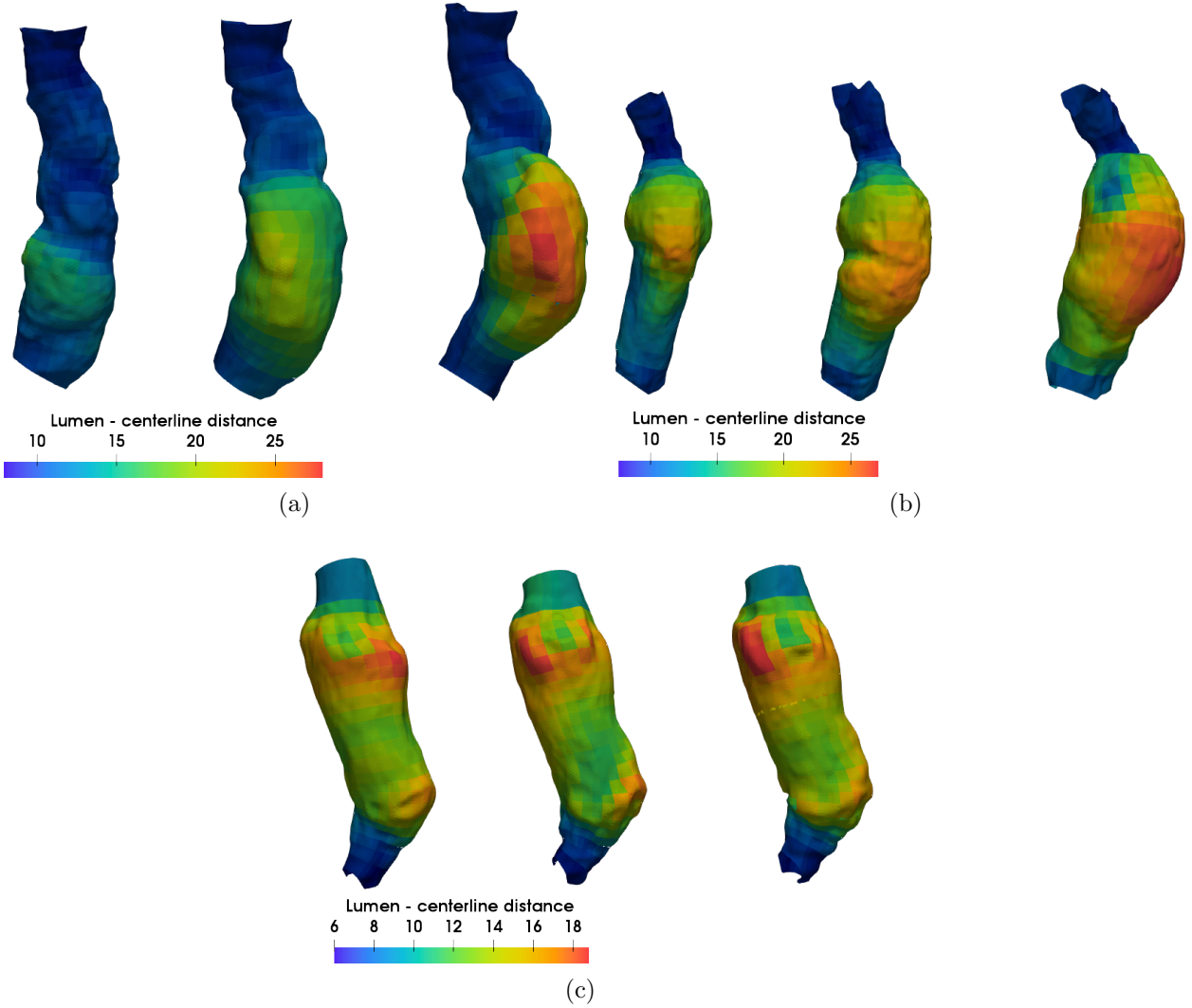


Figure IV: View of local distance (mm) from the lumen to the centerline mapped on the lumen and averaged on patches for patient 6 (a), 22 (b) and 21 (c). Patient 6 exhibits a strong and localized growth of the lumen. Patient 21s lumen is pretty tubular with a constant diameter while patient 22's diameter 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.

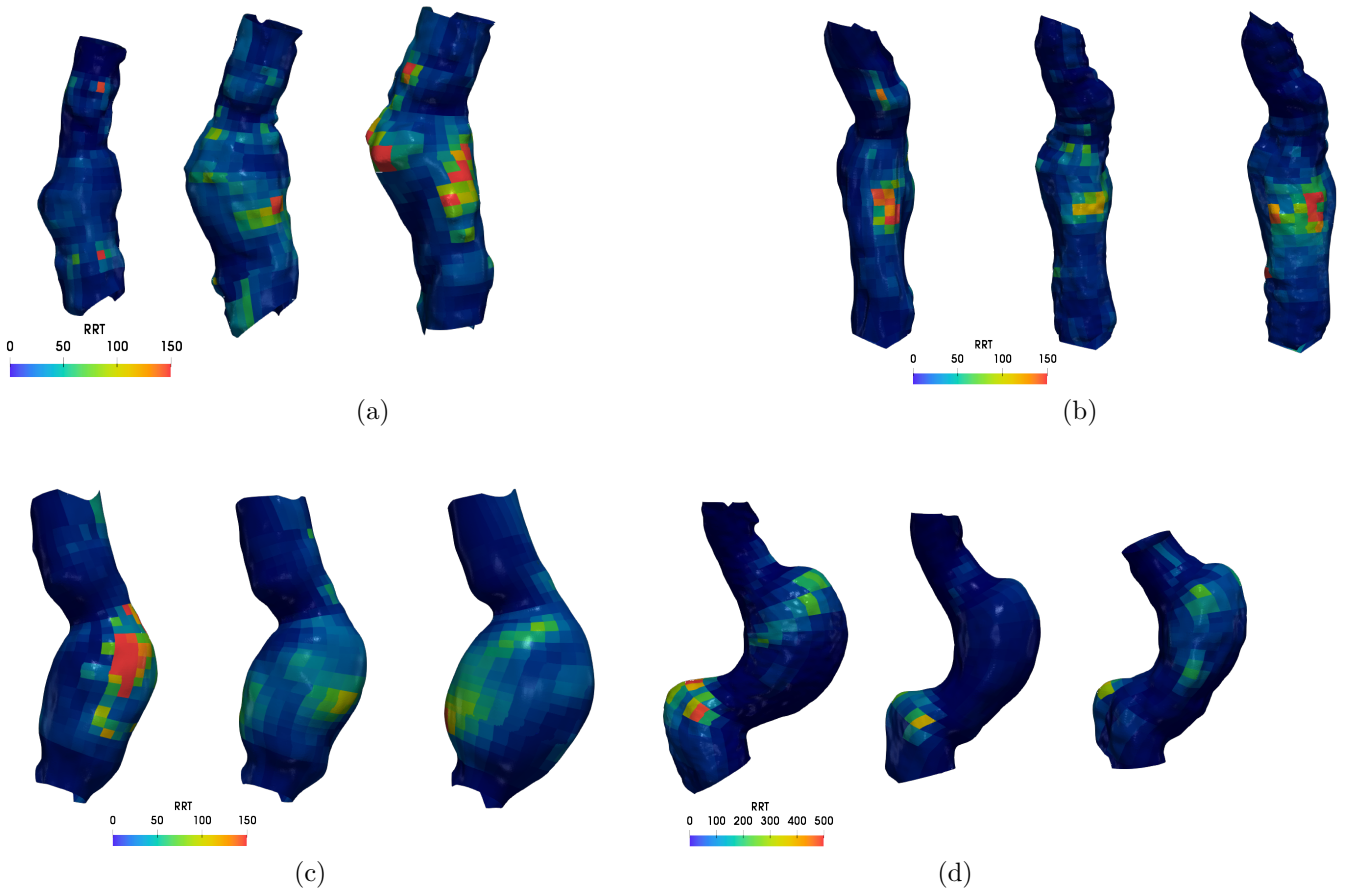


Figure V: For 4 patients, RRT averaged on patches. Patient 10 (a), exhibits a steady growth with time. Patient 28 (b): RRT standard deviation is relatively small compared to patient 29 (c). For patient 15 (d), RRT decreases before increasing.

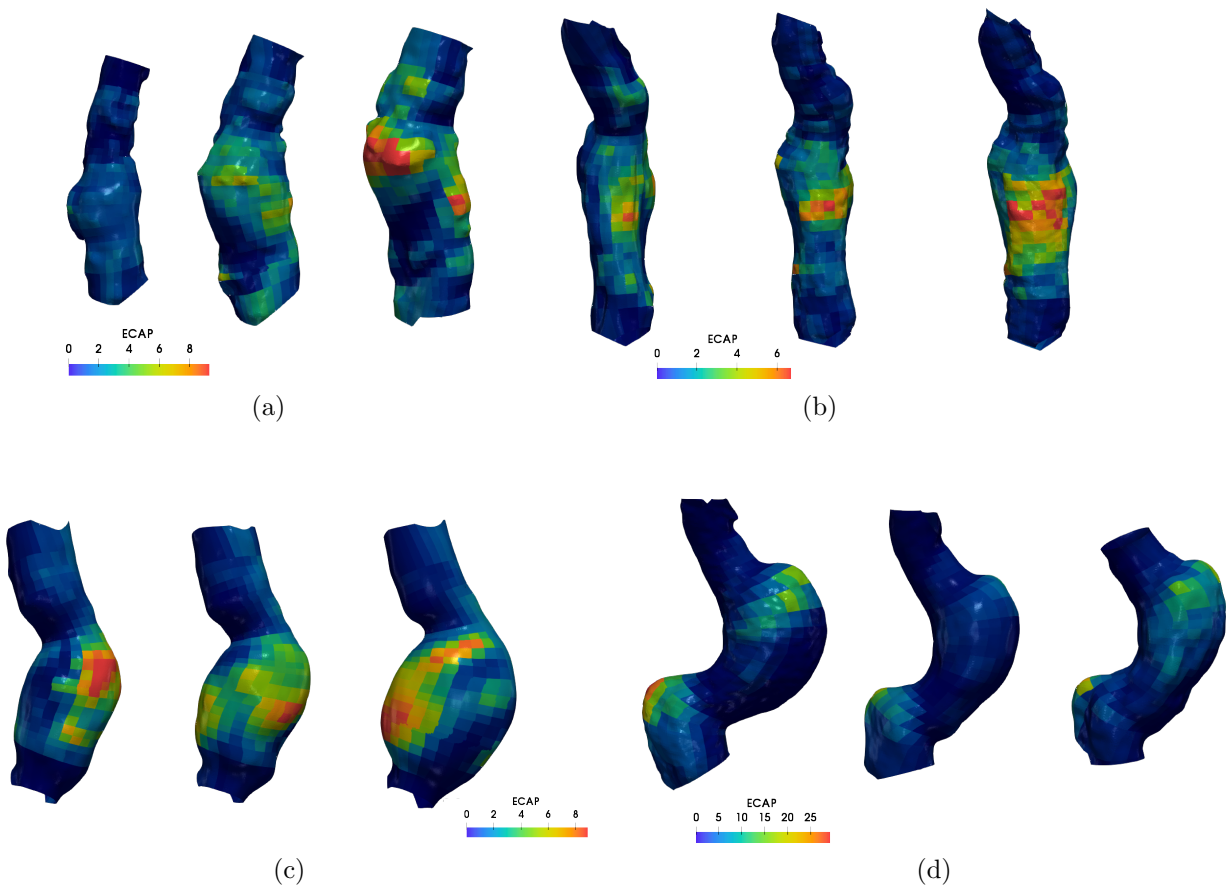


Figure VI: ECAP averaged on patches, for 4 patients. ECAP, similarly to the RRT contains information from OSI and TAWSS. Patient 10 (a), monotonic growth, patient 28 (b) with a small standard deviation compared to patient 29 (c). Patient 15 (d) ECAP average, decreases and then increases.

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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 4th 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 ²)	60.32 (16.93)	98.74 (23.03)	120.90 (27.10)	H-LR, H-HR, LR-HR
Lumen surface area, annual (cm ² yr ⁻¹)	-	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 ³ yr ⁻¹)	-	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 ³ yr ⁻¹)	-	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 ³ yr ⁻¹)	-	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 ⁻¹)	-	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 ⁻¹)	-	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 ⁻¹)	-	-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 4th 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 ⁻¹)	135.60 (71.51)	124.55 (70.32)	116.32 (61.23)	
$WSSG_{min}$ (Pa m ⁻¹)	17.42 (9.48)	9.30 (7.30)	6.79 (7.10)	H-LR, H-HR
$WSSG_{mean}$ (Pa m ⁻¹)	61.03 (32.52)	44.74 (25.82)	38.89 (23.32)	
$WSSG_{stdev}$ (Pa m ⁻¹)	61.04 (44.25)	41.97 (24.82)	45.17 (25.02)	
RRT_{max} (Pa ⁻¹)	22.64 (17.25)	48.26 (30.80)	58.15 (34.73)	H-LR, H-HR
RRT_{min} (Pa ⁻¹)	2.34 (1.33)	2.63 (1.32)	3.12 (1.84)	
RRT_{mean} (Pa ⁻¹)	8.20 (6.17)	15.68 (8.01)	19.00 (10.00)	H-LR, H-HR, LR-HR
RRT_{stdev} (Pa ⁻¹)	8.20 (6.51)	21.68 (16.56)	24.22 (15.69)	H-LR, H-HR
$ECAP_{max}$ (Pa ⁻¹)	0.66 (0.39)	1.42 (0.76)	1.77 (0.92)	H-LR, H-HR, LR-HR
$ECAP_{min}$ (Pa ⁻¹)	0.03 (0.03)	0.02 (0.03)	0.04 (0.06)	
$ECAP_{mean}$ (Pa ⁻¹)	0.26 (0.19)	0.48 (0.22)	0.59 (0.32)	H-LR, H-HR, LR-HR
$ECAP_{stdev}$ (Pa ⁻¹)	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 4th 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 ⁻¹)	4.55 (4.27)	7.31 (4.58)	LR-HR
local change of H_{min}^{ILT} (mm yr ⁻¹)	-4.96 (6.47)	-16.78 (33.77)	LR-HR
local change of H_{mean}^{ILT} (mm yr ⁻¹)	-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 4th 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} (yr^{-1})	0.29 (0.41)	1.26 (3.70)	
local change of OSI_{min} (yr^{-1})	-0.29 (0.38)	-1.14 (2.67)	LR-HR
local change of OSI_{mean} (yr^{-1})	0.00 (0.06)	0.05 (0.47)	
local change of $TAWSS_{max}$ (Pa yr^{-1})	0.27 (0.36)	1.08 (3.50)	
local change of $TAWSS_{min}$ (Pa yr^{-1})	-0.42 (0.70)	-1.47 (3.86)	LR-HR
local change of $TAWSS_{mean}$ (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 4th 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.²¹ method. Significant values (≤ 0.05) are in orange cells.

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

Table I: Proximal resistance, compliance and distal resistance for the 0D-RCR model, from Xiao et al.⁶⁸ (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. ⁵⁵
	Lumen centerline tortuosity	ratio between the centerline length and the endpoints distance.	Shum et al. ⁵⁵
	Lumen NSI	$\frac{1}{2.199} \frac{\sqrt{Area}}{\sqrt[3]{Volume}}$	Raghavan et al. ⁴⁹
	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. ⁹ and Arzani et al. ⁴
	OSI	$\frac{1}{2} \left(1 - \frac{ \int_0^T \tau_W dt }{\int_0^T \tau_W dt} \right)$	Arzani et al. ⁴
	RRT	$\frac{1}{(1-2OSI) TAWSS}$	Himburg et al. ³⁶
	ECAP	$\frac{OSI}{TAWSS}$	Di Achille et al. ²⁴
	WSSG	$ \nabla WSS $	Nagel et al. ⁴⁵

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