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AAA RISK ASSESSMENT-INTEGRATING MORPHOLOGIC, BIOMECHANIC, MOLECULAR AND CLINICAL RISK FACTORS TO IMPROVE DECISION MAKING IN THE MANAGEMENT OF ABDOMINAL AORTIC ANEURYSM DISEASE

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INTRODUCTION

In an effort to improve abdominal aortic aneurysm (AAA) rupture risk assessment several studies have identified demographic, morphometric, thrombus-related, biomechanic, and biological characteristics that associate with rupture risk. However, it is unlikely that parameters from either the biomechanics or the biology aspect of AAA rupture alone can capture the multifactorial pathology of AAA rupture, accurately predict the rupture risk and thus be trusted by surgeons for rupture risk assessment. Therefore, a paradigm shift to our approach is needed that will better capture the multifactorial pathology of AAA.

The structure of a decision tree is one that is appealing intuitively and congruent with methods of decision-making that a physician already uses on many occasions [1]. Towards such an approach, the purpose of this study was to build a decision tree that classifies AAAs into high versus low growth rate groups, based on demographic, morphometric, thrombus-based, biomechanic, and biologic characteristics that can all be measured from 3D imaging data and routine blood sample analysis.

METHODS

Thirty-four patients with diagnosed AAA, with at least one follow-up examination, were included in the study. In total, 24 characteristics from 5 categories (morphometric, thrombus related, biomechanic, biological, and demographic) were analyzed. Among those, the recently introduced asymmetry thrombus deposition index (ADTI) was also included, since a posterior thrombus deposition was found to associate with low growth rate with a specificity of ~90% [2]. Blood analysis results were available for 17 patients.

The growth rate was linearly extrapolated from the difference in maximum AAA diameter between the first and last CT scans. The cases were divided into high and low growth rate based on the cohort's median growth rate (3.2 mm/year).

Morphometric	***Thrombus***	***Biomechanical***
1. Max Diameter (D_{max}) 2. Neck Diameter (D_{neck}) 3. Normalized diameter (D_{max}/D_{neck}) 4. Tortuosity (L/H) 5. Length of AAA (L_{AAA}) 6. Saccular Index (D_{max}/L_{AAA}) 7. Surface Area of AAA (S) 8. Volume of AAA (V) 9. Aorta-Neck Angulation 10.Neck-AAA Angulation	1. Volume of ILT (V_{ILT}) 2. Relative ILT volume (V_{ILT}/V) 3. Max ILT thickness 4. ATDI ("+1" anterior, " -1" posterior deposition)	1. Peak Wall Stress (PWS) 2. Neck vs. body PWS location 3. Anterior vs. posterior PWS location 4. Max Rupture Potential Index (RPI)
Biological	***Demographic***	
1. Creatinine 2. Platelets 3. Cholesterol	1. Gender 2. Age 3. Family History	

Table 1. List of patient and AAA characteristics. (L: length of aorta's centerline from renal arteries to aortic bifurcation, H: Distance between the two endpoints of the centerline (renal to bifurcation)

Morphometric and thrombus related markers were measured using vascular modelling toolkit [REF] after reconstructing the 3D image by segmenting the external and lumen surface of the aorta using ITK-snap [REF]. For the measurement of AAA length (centerline), the AAA sac was defined as the part of infra-renal aorta with diameter more than 3 cm. Aorta-neck and neck-AAA angulation were measured

in the imaging software Evorad Workstation (Evorad SA, Athens, Greece).

Estimation of wall stress distribution at peak systole (120 mmHg) was performed in Workbench (*ANSYS* Inc., Berkeley, CA, *USA*), after tetrahedral mesh generation in ICEM CFD v.12.0.1 (*ANSYS* Inc., Berkeley, CA, *USA*). Hyperelastic material models for wall [3] and for ILT [4] were adopted.

Statistical analysis was performed in WEKA [5], an open source machine learning software used for data mining. The highest ranked attributes were selected with chi-square statistics with respect to growth rate class and a J48 decision tree algorithm with ten-fold cross validation was used to develop a model based on the data. A kappa statistics (κ) was also calculated.

RESULTS

The highest ranked attributes were ATDI, gender, anterior vs. posterior PWS location, neck vs. body PWS location, and relative ILT volume. The lowest ranked attribute was D_{max}. The highest ranked feature, ATDI, was also the feature with the highest information gain thus making it the first in the decision tree, which consisted of ATDI, relative ILT volume, and neck-AAA angulation (Figure 1). Twenty-six out of the 34 cases were correctly classified yielding a prediction accuracy of 76.5% with κ=0.53.

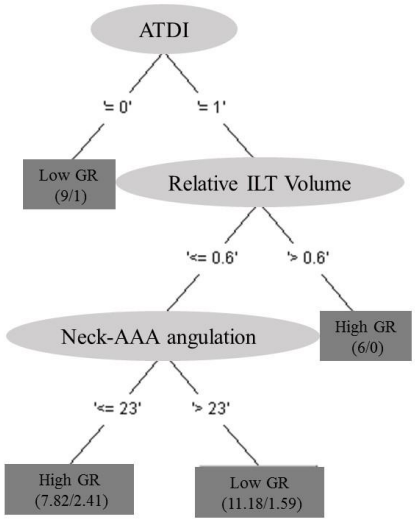

Figure 1. Model learned by J48 decision tree.

DISCUSSION

With the ongoing improvement of imaging techniques, the establishment of screening programmes and the ageing population, the amount of data has greatly been increased. In order to narrow the gap between data collection and data comprehension and decision making, machine learning algorithms can build models for rupture risk assessment, that are not only appealing to physicians, but also capture the multifactorial nature of AAAs.

Shum et al. were recently the first to use a classification model to discriminate between ruptured and non-ruptured AAAs from a set of geometric features from 76 patients resulting in a decision tree model with 86.6% accuracy and κ=0.37. While the accuracy was high and the model promising, we believe that a multimodal approach, where several parameters from different categories are taken into consideration, would provide a more accurate rupture risk assessment, This is because the different categories of risk markers can potentially have a complementary role to each other. For example, biomechanics analysis provides the wall stress distribution, while blood analysis provides information about the biological activities (inflammation, thrombus formation, enzymatic activities) that may reflect the state of the degraded wall and presumably its strength. By integrating all these risk markers in one statistical model we will be able to achieve a more complete picture of the aneurysm state and predict more accurately its growth rate.

This study shows that the growth rate can be predicted with the knowledge of thrombus eccentric deposition in the sac, its relative volume, and the neck-AAA angulation with an accuracy of 76.5%. When a larger patient cohort is acquired, and more blood markers (such as C-Reactive protein, fibrinogen, D-dimer) are incorporated in the model, the decision tree may have more or different leafs and potentially increase its accuracy. A low κ (=0.53) was so far unavoidable due to the small data size.

Although the patient cohort was small, this study presents a set of lead candidates, and demonstrates proof-of-principle for a more extensive follow-up study, providing the basis for the development of an integrated, multidisciplinary approach to the diagnosis, management and treatment of AAA.

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Vmtk
Itl-snap