SB³C2021
Summer Biomechanics, Bioengineering and Biotransport Conference
June 14-18, Virtual

IN VIVO ANALYSIS OF AORTIC HEMODYNAMICS BY COMBINING 4D FLOW MRI AND COMPLEX NETWORKS THEORY

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INTRODUCTION

Ascending aorta (AAo) aneurysm is a common aortic disease which consists of a localized dilation of the AAo and which carries a considerable risk of life-threatening events, such as aortic dissection. Since a dilation of the AAo usually presents with altered hemodynamics and aortic insufficiency, an accurate knowledge of the aortic blood flow is required to reveal possible links between hemodynamic features, dilation progression and related risks. In this exploratory study, the Complex Networks (CNs) theory was applied for the first time to an *in vivo* dataset of 4D flow MRI acquisitions of human aorta, aiming at exploring the spatiotemporal heterogeneity of large scale/dominant aortic flow features, as well as its association with AAo dilation. A total of ten patients, five presenting with no AAo dilation and five with dilated AAo, underwent 4D flow MRI [1], covering the thoracic aorta with a spatial resolution of 2.5x2.5x2.5 mm. The time-resolved phase velocity data were used to build a correlation-based CN for each subject [2]. The persistence length of the correlation of velocity data along the cardiac cycle was quantified and its association with AAo dilation, kinetic energy, flow jet angle, and pulse wave velocity was explored.

METHODS

The study population comprises five patients presenting with AAo dilation (one of them with bicuspid aortic valve, BAV), and five with no AAo dilation (one with BAV). All the enrolled patients also present with mild-to-severe aortic valve dysfunction. Full details on 4D flow MRI acquisition protocol and data processing are exhaustively reported elsewhere [1,3]. The study was approved by the ethics committee of the Vall d'Hebron Hospital and informed consent was obtained from all participants. The lumen of each thoracic aorta was semi-automatically segmented from an angiography derived from 4D flow MRI data using ITK-Snap and its centerline was computed using VMTK (www.vmtk.org). Anatomical landmarks were identified from co-registered 2D cine images and used to ensure a consistent spatial extent across all cases. For each patient and each voxel pertaining to the aorta, time-resolved velocity magnitude waveforms were obtained, as reported elsewhere [1]. 3D velocity data were exported using in-house Matlab code (MathWorks Inc, USA) and used to build a CN.

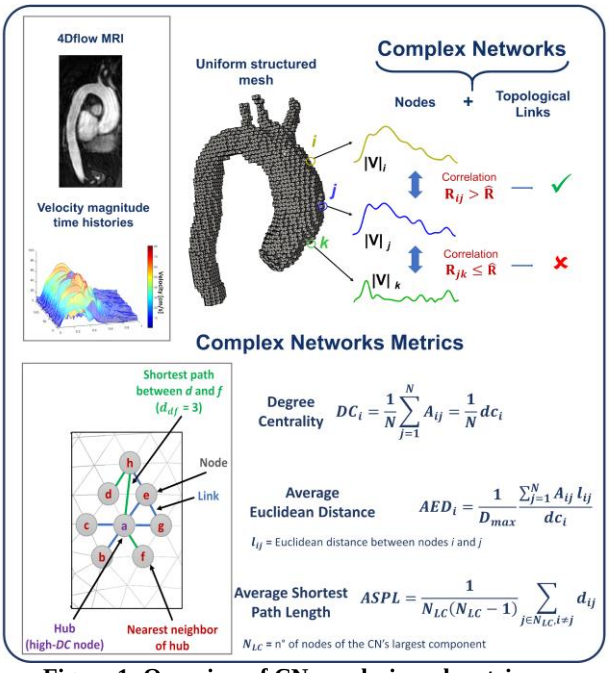

Figure 1: Overview of CNs analysis and metrics.

In detail, each node of the CNs is defined by the voxel where the velocity magnitude |**V**| time history along the cardiac cycle is acquired and two nodes are connected by a topological link $\{i, j\}$ if the Pearson correlation coefficient R_{ij} between the time histories at nodes *i* and *j* is greater than a threshold value $\hat{R}$ (**Fig. 1**) [2]. In this study, the median value of the correlation coefficients between |**V**| time histories derived from patient-specific CFD simulations carried out on a dataset of healthy aorta models was adopted as threshold value ($\hat{R}$=0.87). Each patient's network was characterized by its adjacency matrix A_{ij} containing the information on each node connections [2]. The topological structure of the networks built from *in vivo* data was characterized by three CNs metrics [2] (**Fig. 1**): (1) the *degree centrality* (DC_i) of node *i*, defined as the number of nodes of the CN connected to node *i* expressed as a percentage of the number of voxels in the model; (2) the *normalized average Euclidean distance* (AED_i) between node *i* and all its nearest neighbors, expressed in terms of number of maximum patient-specific AAo diameters D_{max}; (3) the *average shortest path length* ($ASPL$) of the network, defined as the average length of the shortest path d_{ij} connecting two generic nodes *i* and *j* in the CN (**Fig. 1**). DC is a measure of the homogeneity/heterogeneity of |**V**| time history acquired at each voxel with respect to the whole fluid domain, whereas AED and $ASPL$ quantify for each patient the anatomical and topological persistence length of the correlation between |**V**| time histories in the aorta, respectively [2]. The impact of clinically-relevant features on the heterogeneity of the aortic hemodynamics was evaluated by exploring the existence of associations between CNs metrics and kinetic energy (KE), flow jet angle (FJA) [4], pulse wave velocity (PWV) [5] and AAo maximum diameter (D_{max}).

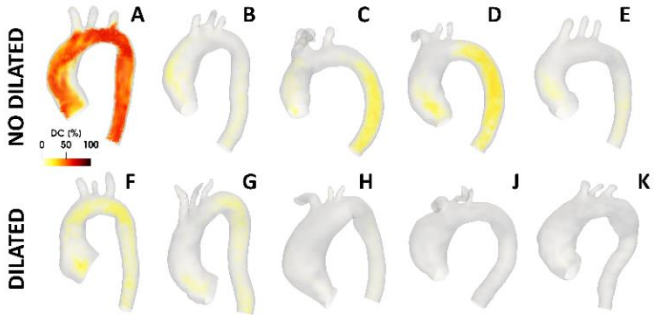

Figure 2: DC volumetric maps.

RESULTS

The volumetric maps of DC in **Fig. 2** clearly highlight a large interindividual variability in the heterogeneity of |**V**| time history shapes. The CN built on patient A is characterized by a dense pattern of connections between nodes in the entire aortic domain, confirmed by the DC values around 50%. The other patients present sparse, scarcely connected networks, reflecting from very poor (as in dilated patients H, J and K, **Fig. 2**) to moderate homogeneity (in particular no dilated patients C and D). The AED maps (data not shown) highlight that, in general, the anatomical length of the correlation of |**V**| time histories is higher in the descending aorta, whereas it reaches a minimum the ascending aorta, especially in patients with dilated AAo. A significant, negative correlation emerges between AED median values and D_{max} (**Fig. 3a**), suggesting that AAo dilation can play a major role in disrupting hemodynamic similarity in velocity magnitude waveforms not only in the AAo, but involving the entire thoracic aorta. In parallel, a near significant positive trend (p_{value}=0.06) emerges between KE and AED, suggesting that high peak kinetic energy values might contribute to increase the anatomical length of the correlation persistence (**Fig. 3b**).

The opposite effects of aortic dilation and blood flow kinetic energy also emerge in the moderate but significant associations with the topological correlation persistence length, expressed by $ASPL$ (**Fig. 3c** and **3d)**. Finally, CNs metrics were not significatively correlated with FJA and PWV at this stage of the investigation, probably because of the scarcely stratified dataset.

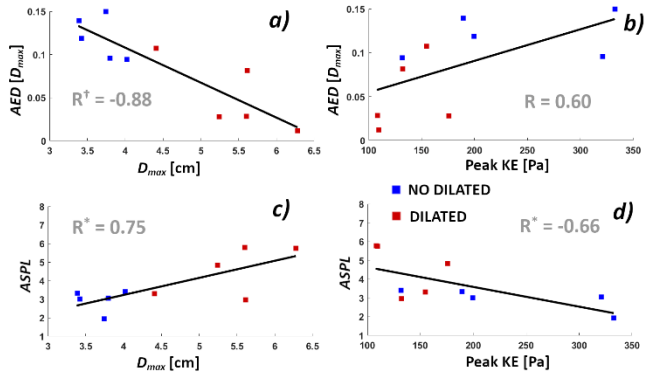

Figure 3: Associations between CNs metrics and clinically-relevant features. For each CN, AED is expressed as the median value of all nodes. (*p_{value} < 0.05; †p_{value} < 0.001)

DISCUSSION

In this study, the CNs theory is applied to *in vivo* 4D flow MRI velocity data to investigate the spatiotemporal heterogeneity of aortic velocity magnitude waveforms shape along the cardiac cycle, and the existence of possible associations between CNs metrics and quantities of clinical interest is explored. The main findings suggest that the physiological Euclidean and topological length of persistence, which are supposed to characterize the physiological aortic intravascular hemodynamics, might be more markedly disrupted in patients with larger maximum AAo diameter (high D_{max} values reduce the anatomical extension of the correlations, AED, and increase the topological separation between nodes, $ASPL$). This is consistent with a recent study on CFD models of ascending thoracic aorta aneurysms, highlighting how the aortic dilation disrupts the correlation persistence of velocity-based waveforms, breaking the topological connections between nodes, especially in the region where a marked change in the mechanical properties of the aortic wall occurs [6]. Conversely, it is suggested that the amount of fluid kinetic energy, representative of the large scale flow features, might play a beneficial role in preserving physiological homogeneity in blood velocity magnitude waveforms shape. In conclusion, this first *in vivo* application of CNs theory to cardiovascular flows looks promising in disentangling the complex 4D aortic hemodynamics. The combined use of D_{max} and CNs distance metrics may allow a finer risk stratification for AAo disease in future applications on larger datasets.

ACKNOWLEDGEMENTS

Guala A. has received funding from the Spanish Ministry of Science, Innovation and Universities (IJC2018-037349-I).

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