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Analysis of aortic size in subjects died due to cardiovascular and non-cardiovascular events: a necropsy study

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Abstract

Aortic size is known to be a predictor for cardiovascular deaths. The purpose of this study was to investigate whether aortic diameters measured on tissue samples obtained during autopsy from subjects that died of cardiovascular disease were bigger when compared to those from subjects deceased from other cause than cardiovascular disease. The study included 91 deceased subjects (average age 56±18.1 years), which underwent autopsy to determine cause of death. Morphological measurements were completed on 364 aortic specimens obtained from four different sites, namely ascending aorta, aortic arch, distal thoracic aorta and abdominal aorta. Aorta showed the tendency to decrease in diameter from ascending aorta to abdominal aorta, the latter presenting with the smallest diameter. All studied aortic diameters were found to be larger in the cardiovascular population (p<0.01).

Keywords: aorta, diameter, cardiovascular cause of death, morphometry.

Introduction

Currently, cardiovascular diseases are responsible for over one third of deaths worldwide and due to present spectacular changes in life expectancy, it is estimated a long-term increase in frequency both in developed countries and in the developing ones.

In Romania, cardiovascular disease remains the leading cause of death, with a rate of about 740 cases per 100 000 inhabitants, although a small decline in percentage was noticed during the last decade [1].

Understanding the cause–effect relationship between cardiovascular events and aortic morphology is crucial in routine clinical practice.

Although multiple studies have demonstrated that deviation from normal aortic distensibility represents an independent predictor of all-cause and cardiovascular mortality in apparently healthy subjects [2], patients with essential hypertension [3], type 2 diabetes [4], kidney disease [5], fewer studies have analyzed the connection between aortic size and cardiovascular events. In one study, Newman *et al.* showed that the presence of small, uncomplicated abdominal aneurysms determines higher risk for total and cardiovascular mortality [6].

The purpose of the study was to compare aortic diameter in two distinct populations, divided by cardiovascular or non-cardiovascular cause of death.

Materials and Methods

Studied population and study design

This study analyzed human aortic samples obtained from 91 deceased subjects who underwent necropsy for diagnosis in the Department of Pathology, Emergency County Hospital, Craiova, Romania.

There were no eligibility criteria for inclusion in this study and all subjects were enrolled regardless of pathology leading to death.

Study participants were divided according to the cause of death established by corroborating necropsy diagnostic with clinical data in two groups: the CV group, including the cases whose cause of death was a cardiovascular disease. In addition, the NCV group whose cause of death was a non-cardiovascular disease.

This prospective study followed a comparison design and was carried out as a single-center study. It was divided into two sections: the study of clinical data and the study of pathological data.

Studied material

Study material was represented by patient's clinical documents (medical charts and autopsy protocols) and morphological analysis of human aortic tissue collected during necropsy.

The specimens consisted of aortic tissue rings obtained by transversal sectioning of the vessel at four different levels, as following (Figure 1):

- the ascending aorta (AscAo): slicing at 2–3 cm below the sinotubular junction;
- the aortic arch (AoArch): slicing in the close proximity of the left subclavian artery;
- the distal thoracic aorta (DTAo): slicing at the midway between the aortic arch and the diaphragm aortic hiatus;

▪ the abdominal aorta (AbdAo): slicing close to the emergence of renal arteries.

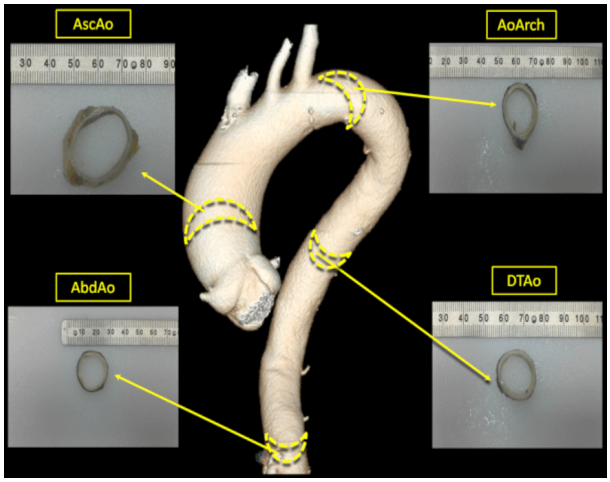

Figure 1 – ***Sites of sampling.***

Quantitative morphological measurements

For the measurement of aortic diameters, a software designed in MATLAB programming environment (Math Works) was developed and used (Figure 2).

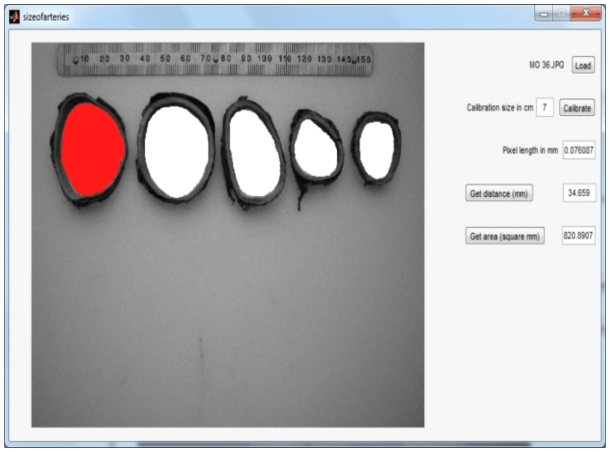

Figure 2 – ***MathWorks software window.***

The program allowed tracing manually the internal perimeter of the aortic samples (lumen was marked with a single color). After color filling, a mathematical algorithm was used to determine the area of the arterial lumen in each image after prior calibration using the ruler within the picture.

Estimated diameter of each aortic segment was calculated using the formula:

$$\text{Diameter} = \text{SQRT}\ (4 \times \text{determined Area}/\pi)$$

where SQRT represents square root.

Statistical analysis

All preliminary data on clinical and pathological parameters were introduced into database tables in Microsoft Excel module of the Microsoft Office XP Professional software package compatible with all statistical analysis programs that we used for data interpretation. These parameters were divided into: (a) **parameters defining the clinical profile** (gender, age, cause of death), and (b) **parameters defining the morphological profile** (site of sampling, internal diameter of the aortic samples).

For numerical parameters, the lowest value (V_{MIN}), the highest value (V_{MAX}), average value (AV), the half range value (HRV) calculated as (V_{MAX} + V_{MIN})/2 and standard deviation (STDEV) were determined. Differences within and between groups were analyzed using paired and unpaired Student's *t*-test.

For graphical representation, V_{MIN}, AV + STDEV, AV, AV - STDEV and V_{MIN} were used.

The graphs showing the evolution patterns of different assessed parameters and the comparisons between them were done with the "Graph" tool included in the "Word" and "Excel" modules of the Microsoft Office XP Professional software package.

Results

Clinical data

Cause of death

All subjects underwent complete examination for diagnosis of the underlying cause of death, which was established in all cases. The overall rate of NCV deaths was higher than the CV deaths in the studied group (Figure 3).

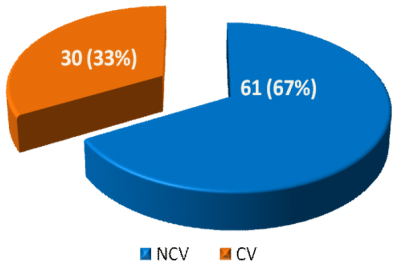

Figure 3 – ***Comparison between distribution based on clinical status in studied groups.***

In the CV group, diagnosis included ischemic heart disease (*n*=8), hemorrhagic and ischemic cerebrovascular stroke (*n*=7), congestive heart failure (*n*=5), massive pulmonary thromboembolism (*n*=4), valvular infectious endocarditis (*n*=2), and other causes (*n*=4). Regarding the NCV group, the greatest proportion of necropsies was carried out for a forensic reason (car accidents, suicide or polytraumatisms).

Gender distribution

The number of males was greater than that of females in both studied groups, with a ratio of 1.72 in the CV group and a ratio of 1.44 in the NCV group (Figure 4).

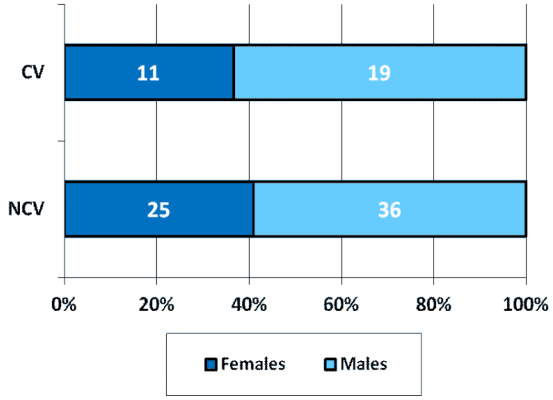

Figure 4 – ***Comparison between gender distribution in the studied subgroups.***

Age distribution

Subjects in the CV group were older than those that constituted the NVC group. The age dispersion of all subjects varied within wide ranges of values, whose lowest limit was eight years (in the NCV group) and highest limit 82 years (in both groups) (mean 56±18.1 years) but had different patterns of distribution in the two groups.

Thus, while in NCV group, the whole range of values was larger and the interval comprising the majority of values also more "extended" around an AV significantly higher than the corresponding HRV, which displaced the interval towards the higher limit of the range, in CV group, both the whole range and the interval comprising the majority of values were smaller, the latter due to a smaller STDEV, and the AV was significantly higher than that of the former group and almost equal to the corresponding HRV, thus defining a more compact group. These differences were confirmed statistically by the Student's *t*-test (Table 1, Figure 5).

Table 1 – ***Statistical parameters of age in studied groups***

Parameter	NCV	CV
Highest age [years]	82	82
AV + STDEV	71.3	75.9
AV	52.4	**65**
HRV	45	63.5
AV - STDEV	33.5	54.2
Lowest age [years]	8	45
STDEV	18.9	10.9
Student's t-test	***p*<0.001**	

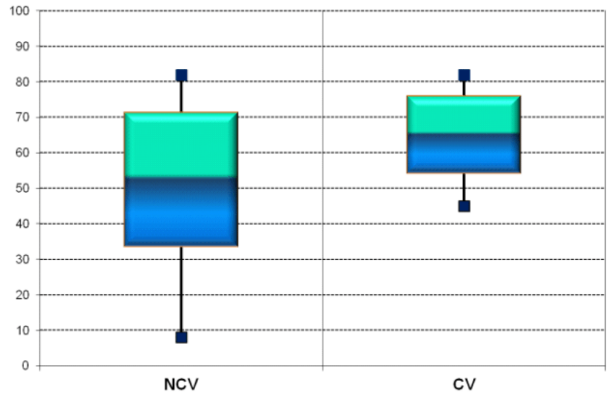

Figure 5 – ***Comparison between age distribution in studied groups.***

Morphological data

Ascending aorta

The largest AscAo diameter was measured on samples obtained from an 80-year-old female in the CV group and the smallest diameter was found in an 8-year-old girl of the NCV group. In both groups, the interval comprising the majority of values was more condensed that the whole range of values due to smaller STDEV values and displaced towards the lower limit of the ranges because of an AV value smaller than the corresponding HRV. However, the AV value of AscAo diameter was higher in CV group as compared to NCV group, difference confirmed statistically by the Student's *t*-test (Table 2, Figure 6).

Table 2 – ***Statistical parameters of AscAo in studied groups***

Parameter	AscAo [mm]	
	NCV	***CV***
V_{MAX}	36.6	39
AV + STDEV	27.6	29.4
AV	22.4	**25**
HRV	24.25	**28.1**
AV - STDEV	17.2	20.6
V_{MIN}	11.9	17.2
STDEV	5.2	4.4
Student's t-test	***p*=0.02**	

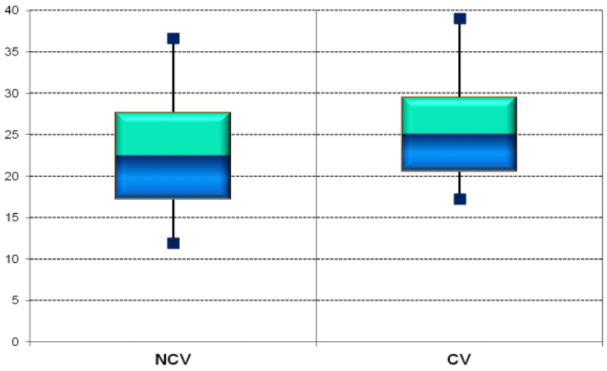

Figure 6 – ***Distribution of AscAo diameters in studied subgroups.***

Aortic arch

Both the largest and the smallest AscAo diameters were measured on samples obtained from the NCV group, the former in a 75-year-old male and the latter in the 8-year-old girl. In both groups, the interval comprising the majority of values was obviously more condensed that the whole range of values due to smaller STDEV values.

The interval comprising the majority of values was displaced towards the lower limit of the ranges in both groups because of AV values smaller than the corresponding HRVs. The AV value of AoArch diameter was, as in AscAo, higher in CV group as compared to NCV group, difference confirmed statistically by the Student's *t*-test (Table 3, Figure 7).

Thoracic aorta

In the case of thoracic aorta determinations, the situation concerning the largest and the smallest diameters was similar with that observed in the case of aortic arch, both values being observed on samples obtained from the NCV group, the former in a 81-year-old male and the latter in the 8-year-old girl. In both groups, the interval comprising the majority of values was obviously more condensed that the whole range of values due to smaller STDEV values.

The interval comprising the majority of values was displaced towards the lower limit of the ranges only in NCV group because of AV value smaller than the corresponding HRV.

In the CV group, the same interval was more condensed than in the NCV group, due to a smaller STDEV and displaced almost in the middle of the whole range of values.

The AV value of DTAo diameter was here too higher in CV group as compared to NCV group, difference confirmed statistically by the Student's *t*-test (Table 4, Figure 8).

Table 3 – *Statistical parameters of AoArch in studied groups*

Parameter	AoArch [mm]	
	NCV	***CV***
V_{MAX}	28	27.4
AV + STDEV	20.5	21.7
AV	16.7	**18.8**
HRV	18.85	20.25
AV - STDEV	12.8	15.8
V_{MIN}	9.7	13.1
STDEV	3.8	3.0
Student's t-test	***p*=0.01**	

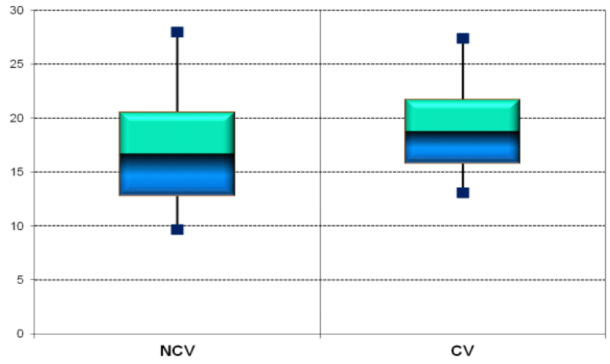

Figure 7 – *Distribution of AoArch diameters in studied subgroups.*

Table 4 – *Statistical parameters of DTAo in studied groups*

Parameter	DTAo [mm]	
	NCV	***CV***
V_{MAX}	23.1	20.7
AV + STDEV	17.2	17.7
AV	14.2	15.5
HRV	15,85	15.8
AV - STDEV	11.3	13.3
V_{MIN}	8.6	10.9
STDEV%	3.0	2.2
Student's t-test	***p*=0.04**	

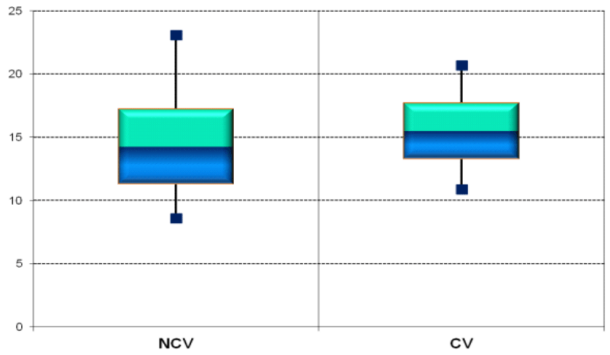

Figure 8 – *Distribution of DTAo diameters in studied subgroups.*

Abdominal aorta

In the case of abdominal aorta determinations, the situation concerning the dispersion, the concentration of the majority of determinations and the AV values is similar to that observed in the previous aortic segment (the thoracic one), the only difference being an obvious higher value of the AV than in CV group as compared with the NCV group (Table 5, Figure 9).

Table 5 – *Statistical parameters of AbdAo in studied groups*

Parameter	AbdAo [mm]	
	NCV	***CV***
V_{MAX}	21.0	18.3
AV + STDEV	15.4	16.5
AV	12.5	14.4
HRV	13.9	14.28
AV - STDEV	9.7	12.3
V_{MIN}	6.9	10.3
STDEV%	2.9	2.1
Student's t-test	***p*=0.0018**	

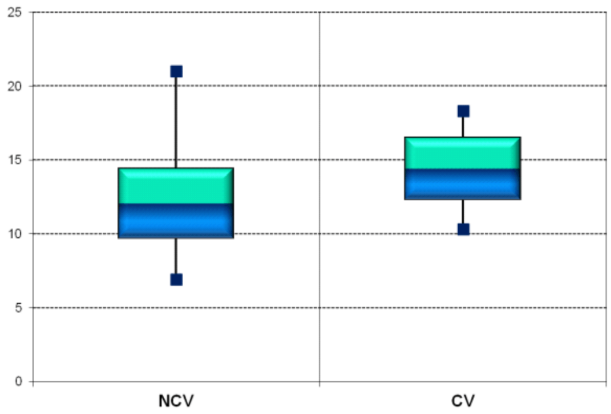

Figure 9 – *Distribution of AbdAo diameters in studied subgroups.*

Discussion

This study is, to the best of our knowledge, the first study that measured aortic size in four different sites on specimens obtained after necropsy from two distinct populations, divided by cardiovascular or non-cardiovascular cause of death.

Expansion of the risk factors among young adults along with the population aging phenomenon contribute to an increase of the percentage of deaths due to cardiovascular events in a wider range of ages even if imaging technology and medical care showed a spectacular progress in the last decades. Therefore, as expected, the mean age was, in our study higher in the CV group as compared with the NCV group.

In our study group, males had a higher CV death rate than females and a higher death rate by a CV disease than by a NCV disease.

One interesting observation coming from our results was that aorta showed an obvious decreasing trend in its size starting from AscAo segment towards the AbdAo segment in both groups of cases (Table 6, Figure 9). However, it should also be emphasized that none of the studied subjects met the criteria for diagnosing aortic aneurysm.

Considering the effect of age throughout the life over aortic size [7–10] and that the AV age in the CV group was higher, another interesting observation was that in all segments, the values of the determined internal diameter were higher in the CV group as compared with the NCV group, difference that was validated also from statistical point of view (Table 6, Figure 10).

Table 6 – *Statistical parameters of AbdAo in studied groups*

Parameter	NCV	CV
AscAo [mm]	22.4	**25**
AoArch [mm]	16.6	**18.7**
DTAo [mm]	14.2	**15.5**
AbdAo [mm]	12.5	**14.4**
Student's t-test	***p*=0.0057**	

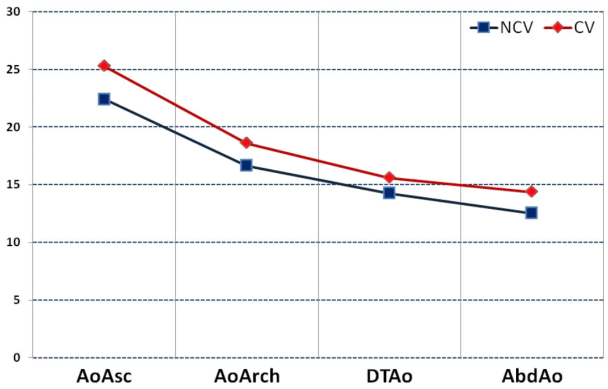

Figure 10 – *Comparison of aortic diameters in the studied subgroups.*

Conclusions

Merging information derived from the statistical analysis of the studied parameters, we could conclude that aortic arterial wall has different pathways of remodeling depending on the dominant pathological process that could determine the death but possibly also on the gender and age of the patient. The reduced number of subjects limited the possibility of a statistical multivariate analysis regarding the influence of multiple parameters (age, gender, specific diagnosis of death) on aortic diameters. However, this study is just a preliminary one, which will be continued with the analysis over a larger group of subjects.

Acknowledgments

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Author contribution

The authors had equal contributions in the achievement of the research, the design, the editing and the writing of this article.

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