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3 **TITLE:** Zonal variation in atherosclerotic aorta: Is it a fact?

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18 **Short Running Title:** Zonal variation in atherosclerotic aorta

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21 submission.

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33 **ABSTRACT**34 **Aims**

35 The diameter of ascending aorta changes in different stages of cardiac cycle in
36 normal, dissected and aneurysmal aorta. The differences in size of arch of aorta
37 during cardiac cycle in atherosclerotic patients are not well established. Here we
38 studied the long and short axis diameter of arch of aorta in atherosclerotic patients to
39 assess the differences in diameter in different stages of cardiac cycle.

40

41 **Methods**

42 This study involved evaluation of retrospective data, for patients who underwent
43 retrospectively gated cardiac CT examinations for various indications. Zones 0-4
44 were identified from CT scan as per Shin Ishimura's division of arch of aorta. The
45 short axis and long axis, along with the average of the two, were obtained both in
46 systole and diastole, at the same level. The measurements were taken from outer
47 wall to outer wall of the aorta.

48

49 **Results**

50 Data from 27 patients (11 females and 16 males) was reviewed. The age range was
51 50-89 years. A total of 135 zones were identified and axial diameters (short and long
52 axes) were measured. The average zone variation between the long axis and short
53 axis diameter during systole and diastole did not exceed 1mm (max = 2.9mm, min =
54 0.0mm) for any zone. The largest difference in average variation was noted in zone
55 4; 0.58mm, although this was not statistically significant.

56

57 **Conclusion**

58 Our study suggested that the variation of atherosclerotic aorta is minimal in different
59 phases of cardiac cycle. This should be considered for endovascular intervention in
60 atherosclerotic arch of aorta.

61

62 **Keywords:** Aorta, atherosclerosis, endograft, imaging, CT SCAN.

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64

65 INTRODUCTION

66 Ishimaru has described the division of arch of aorta in 2001 [1]. This innovation has
67 significant clinical implication in mapping of landing zone for endograft. It not only
68 helps to evaluate the arch of aorta during the treatment but also assists in monitoring
69 the outcome of treatment in follow up scan. Proximal placement of endograft on a
70 sufficient long segment of healthy aorta (landing zone) is vital for successful
71 endovascular management of aneurysm of arch of aorta. Figure 1 shows the division
72 of zone 1, 2, 3 distal to each branch of aortic arch and zone 4 correlates to the
73 straight part of thoracic aorta upto the lumbar region of abdominal aorta and zone 0
74 is proximal to the arch innominate branch.

75 Aortic distension is a physiological phenomenon, occurring in different phases of
76 cardiac cycle due to vessel wall elasticity or compliance [2]. The aortic displacement
77 is most prominent near the heart due to transmission of kinetic movement of
78 pericardium during cardiac cycle. [3]. Winkessel's principle shows that distension of
79 aorta during systole and recoil in diastole reduces the pulse pressure and maintains
80 the continuous blood flow throughout its length. This elastic property of the aorta
81 allows the vessel to work as a buffering chamber [4]. Two different disease
82 processes affect the aortic wall elasticity: arteriosclerosis and atherosclerosis.
83 Arteriosclerosis is progressive loss of elasticity and distension of the vessel wall due
84 to aging [5]. Atherosclerosis happens due to inflammatory process followed by lipid
85 accumulation resulting in structural weakness in tunica media [6].

86 Over last three decades, endovascular grafting has become the mainstay of
87 treatment for thoracic and abdominal aortic aneurysm. To size the optimal
88 endograft, multi-detector computerised tomography and magnetic resonance
89 angiography are used to assess the anatomy of diseased aorta. MDCT has high
90 spatial resolution with high specificity and sensitivity both for diagnosis and sizing [7,
91 8]. It offers accurate depiction of branch vessel anatomy along with aneurysm and
92 dissection configuration [9, 10]. However, MDCT involves high levels of ionising
93 radiation and iodinated contrast causes nephrotoxic changes leading to contrast
94 induced nephropathy [11, 12]. Another limitation of MDCT is motion artefact usually
95 present in the aortic root and ascending aorta. Some studies suggest that the degree
96 of motion artefact is most pronounced in proximal aorta zone 0-zone 1 during systole

97 and diastole [13]. Upto 17.8% difference in diameter occurs during different phases
98 of cardiac cycle. ECG gated CT scan utilises MCDT in correlation with cardiac cycle
99 requiring higher radiation dose. It can be performed in two ways: retrospective and
100 prospective. Retrospective gating uses continuous modulated or unmodulated X-ray
101 throughout cardiac cycle (R-R interval), whereas prospective gating takes images at
102 approximately 70% cardiac cycle (late diastolic phase) [Figure 2].

103 Endograft sizing is vital to ensure adequate functioning and to minimise potential
104 complication. Most clinicians oversize the endograft by 10-15% [14]. Alongside size,
105 as opposed to abdominal aortic aneurysms (AAA's), the thoracic aorta, particularly
106 the aortic arch with a natural curvature can be problematic when sizing and planning
107 for endovascular repair [15]. Furthermore, the morphological and hemodynamic
108 characteristics of the thoracic aorta need to be considered. Undersizing as well as
109 oversizing can lead to complications such as migration, collapse, pseudocoarctation,
110 infolding and endoleaks (particularly type1) [16, 17]. Furthermore, the pressure or
111 radial force exerted by some stent graft designs, along with excessive oversizing,
112 can lead to further deterioration of already diseased aortic walls. The decision
113 regarding the degree of oversizing is still debatable. Most clinicians oversize the
114 measurement by 10-20%. Excessive oversizing have shown conflicting results, with
115 the possibility of greater associated increased tendency for specific complications
116 [17-19].

117 The purpose of this study was to assess the expansile differences during the cardiac
118 cycle, in the various Ishimura zones of the aortic arch. We focused on patients that
119 have atherosclerotic disease and not have previously undergone endovascular
120 repair procedures.

121

122 **MATERIALS AND METHODS**

123 This study involved prospective evaluation of retrospective data, for patients who
124 underwent retrospectively gated cardiac CT examinations for various indications.
125 Individuals with evidence of atherosclerotic disease, identified by the presence of
126 atherosclerotic plaques, calcification of the vessel wall, and elevated serum levels of
127 cholesterol or lipids, were included. Patients with acute aortic syndrome, previous
128 aortic rupture, and connective tissue disorders were excluded as these patient

129 groups may have reduced aortic compliance leading to confounding data. All scans
130 were performed with retrospective CT cardiac gating. Standard axials were acquired,
131 at 0.75mm thin slices, using a dual source Seimans CT scanner, without the usage
132 of β -blockers. Contrast used for these procedures was; 90ml of 350 strength Iodine
133 (optiray covidiene) at the rate of 5ml/sec followed by 30ml of normal saline chase at
134 4ml/sec using a pump injector. The standard set of axial data was analysed using
135 the VOXAR 3D workstation (equipment/software). Oblique sagittal slices were
136 obtained from the standard axial slices were used to derive true axial projections
137 orthogonal to aortic centreline as shown Figure 3. The short axis and long axis,
138 along with the average of the two, were obtained both in systole and diastole, at the
139 same level. The measurements were taken from outer wall to outer wall of the aorta.

140

141 RESULTS

142 Data from 27 patients (11 females and 16 males) was reviewed. Of these, 20 had
143 calcification in the arch and 7 had calcification either within the coronary arteries or
144 the aortic valves. The age range was 50-89 years. A total of 135 zones were
145 identified and axial diameters (short and long axes) were measured. The average
146 zone variation between the long axis and short axis diameter during systole and
147 diastole did not exceed 1mm (max = 2.9mm, min = 0.0mm) for any zone (Table 1).
148 The largest difference in average variation was noted in zone 4; 0.58mm, although
149 this was not statistically significant. There was no significant difference in aortic
150 diameter variation during cardiac cycle for any zone (Table 2).

151

152 DISCUSSION

153 This study demonstrates that the expansile nature of the aorta, during the cardiac
154 cycle, is reduced when the artery becomes atherosclerotic. The results showed no
155 statistically significant variation in aortic diameter in any of the individuals observed.
156 The maximum variation seen in both the long axis and short axis is in zone 4 (p-
157 value = 0.46 and 0.48, respectively). We could not find any specific reason for
158 greater expansile nature in zone 4. Indeed our expectations were that zone 4 may
159 have the least distensibility being furthest from the heart. It might be related to the
160 atherosclerotic nature of the disease and plaque distribution. In a study by Parodi et

161 al the variation in dimensions between systole and diastole in the descending
162 thoracic aorta were noted similar to our study which also revealed a near significant
163 variation in size in zone 4 [20]. Future studies in this area will be able to justify this
164 finding and show any distinct comparison between the anatomical zones of the aorta
165 or demonstrate anatomical anomaly. As mentioned in the results, the p-values for
166 long and short axes in zone 0 and zone 1 have shown the least significance.

167 The introduction of electrocardiographic (ECG) cardiac-gating CT, both prospective
168 and retrospective, has enable reduction of movement artefact. As mentioned, the
169 main implication that exists with using MDCT imaging is ionising radiation exposure
170 which in the younger atherosclerotic patients is relevant due the risk associated with
171 the amount of X-ray radiation exposure leading to lifetime risk of developing cancer
172 [21]. This aspect applies particularly to the organs within the region being scanned,
173 for instance effective dose radiation form a 64-slice MDCT of the chest for female
174 breast tissue is 10-30 times greater than that received from mammography
175 screening [21]. This issue is carefully considered when introducing CT-gating, as
176 relative exposure can increase dramatically. Many studies have observed the
177 efficacy and use of specific types of CT gating techniques, questioning quality over
178 radiation exposure.

179 Retrospective gating involves continuous, intensity-modulated, x-ray imaging
180 throughout the cardiac cycle (R-R interval), whereas perspective gating invokes on a
181 step-and-shoot model, where around 26% of the cardiac cycle (late diastolic phase)
182 is imaged [22, 23]. Numerous studies have focused on the effective dose
183 implications and quality of images produced [24, 25, & 26]. There has been little
184 difference, in terms of image quality, between the two techniques . However, some
185 studies reveal marked differences in effective dose, up to 77% less radiation
186 exposure in prospective gating [26]. Though this is the case, there are limitations
187 imposed on prospective gating, including image quality which is severely affected if
188 heart rate is >70bpm. This statement, regarding quality, is particularly notable with
189 images of the coronary arteries and not with the aorta. It should be noted that the
190 implications for using ECG gating are not limited to aortic malformations. Indeed
191 some authors discuss a triple rule-out technique, allowing emergency imaging
192 evaluation of the pulmonary and coronary arteries, as well as the thoracic aorta, in

193 response to chest pain. This technique is performed with retrospective gating, as
194 opposed to prospective, due to relative speed acquired to image these areas whilst
195 the contrast is still present.

196 This finding is crucial for clinicians when performing endovascular repair, in relation
197 to landing zone choice. Currently the use of retrospective cardiac CT-gating, in
198 endograft repair, allows to acquire the relevant information needed to select the
199 most appropriate endograft size. The results in this study, however, demonstrate
200 that the difference in the aortic diameter, throughout the cardiac cycle, is not
201 significant enough to affect endograft sizing, in the zones of the arch of aorta as
202 compared to descending aorta.

203 Furthermore, since the majority of the clinicians who perform this procedure oversize
204 the aortic diameter by 10-20%, to achieve better endograft apposition to aortic wall,
205 for the endograft used, the discrepancy between the aortic sizes would seem
206 insignificant. This prospect is important to consider in terms of diagnostic benefits
207 against patient risk. Another important consideration is motion artefact, caused by
208 cardiac movement. This can affect the quality of the axial images produced in normal
209 CT scans particularly when observing zones 0 and 1, as they are closest to the
210 heart. Indeed we have considered this aspect in the clinical setting. When significant
211 motion artefact generated during CT scanning, we recommend that prospective
212 cardiac CT-gating is performed to limit image distortion. Though we appreciate that
213 the level of radiation, using prospective CT-gating, is higher than that of normal spiral
214 CT scanning it is significantly lower than the volume of radiation used for
215 retrospective CT-gating.

216

217 **Limitations**

218 The study was carried out with retrospectively ECG gated CT SCAN in
219 atherosclerotic patients. This was a retrospective study with a small group of
220 patients, the implications to perform higher quality studies is, however, questionable
221 due to the ethical implications concerning ionising radiation. Certain variables were
222 not considered, including patient medication such as beta blockers, smoking history
223 (which reduces expansible nature of blood vessels), and low cardiac output patients
224 related to cardiac failure or aortic stenosis (low cardiac output would not cause large

225 distension of the aorta). Finally, the study did not evaluate pre and post stenting
226 procedures for the patients. This needs to be documented in the study as it can have
227 significant effect on the results.

228

229 **CONCLUSION**

230 We conclude that routine cardiac gating, both CT and MRI, is not required for
231 endovascular repair of arch in atherosclerotic patients. For stent in or near zone 0,
232 the use of prospective CT gating allowing for a more accurate depiction of the aortic
233 walls is substantial, whilst acquiring lower radiation dose than retrospective CT
234 gating. Current oversizing by 10- 20% would be sufficient to compensate for the
235 minimal changes that occur during aortic distension in different phases of cardiac
236 cycle.

237

238 **CONFLICT OF INTEREST**

239 None

240

241 **AUTHOR'S CONTRIBUTIONS**

242

243 Anupama Barua: editing, writing.

244 Christopher Dadnam: Data collection, analysis

245 Sapna Puppala: Project idea and final revision

246

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TABLES

EARLY VIEW

350 Table 1: Zonal size variation between diastole and systole for both long and short
 351 axis

352

Ishimaru zone	Average variation (mm)	Maximum variation (mm)	Minimum variation (mm)
0	0.17	1.9	0.15
1	0.0	2.9	0.05
2	0.38	2.5	0.0
3	0.24	2.1	0.0
4	0.58	2.2	0.1

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373 Table 2: Mean axial length of the zones and calculated p values

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Ishimaru zone	SA systole (mm)	SA diastole (mm)	P value	LA systole (mm)	LA diastole (mm)	P value
0	32.36	32.65	0.7	34.72	34.78	0.9
1	29.52	29.46	0.94	31.96	32.02	0.93
2	27.80	27.42	0.65	30.71	30.33	0.64
3	26.20	26.12	0.92	29.02	28.61	0.63
4	26.49	25.94	0.48	28.04	27.42	0.46
SA – short axis, LA – long axis						

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FIGURE LEGENDS

398 Figure 1: The Ishimura zones.

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400 Figure 2: The retrospective and prospective ECG gated CT SCAN

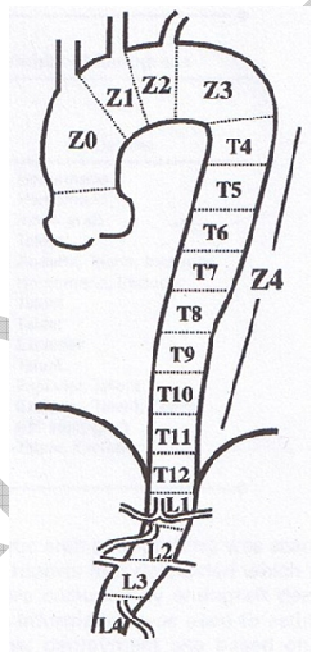
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402 Figure 3: The methodology used to obtain true axial slices from the original data
403 using VOXAR 3D workstation. The raw axial data is used to reformat the oblique
404 saggitals from which true axials were obtained.

405

406 **FIGURES**

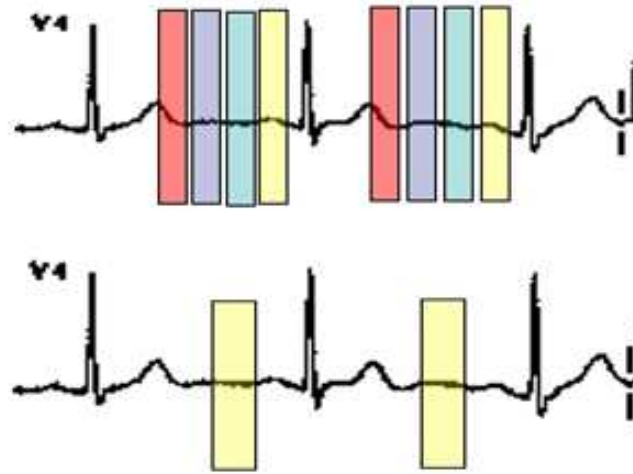
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410 Figure 1 Shows the Ishimura zones.

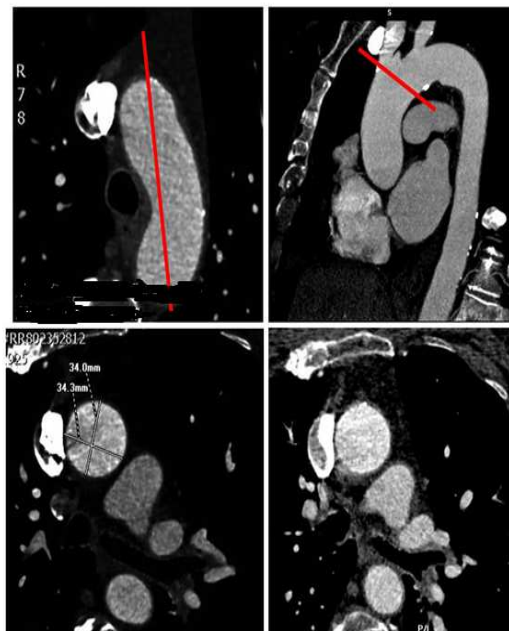


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