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Does the Gender Imply A Certain Predilection as Regards the Morphology of Left Atrial Appendage in Egyptians?

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ABSTRACT
Background: Left atrial appendage (LAA) has different shapes, sizes, and relations to different adjacent structures, all of these may be extremely important when interventional procedures related to left atrium are done. There is a growing data about variations in LAA morphology in relation to gender and in different populations.
Objective: So in our study we evaluated LAA morphologies and identified the proportion of its different subtypes in Egyptians. **Patients and methods:** We analyzed retrospectively the data of 101 consecutive Egyptian patients who underwent multidetector computed tomography (MDCT) in our university specialized hospital from August 2019 to February 2020. **Results:** All images were evaluated for LAA morphology and volume. Windsock morphology existed in 32% of patients followed by chicken wing in 25% of patients. Cauliflower morphology was reported in 23% of patients whereas 20% of patients had cactus morphology. There was a significant gender difference, as female patients had predominantly cauliflower and cactus morphologies (P<0.05). Left atrial appendage volume showed a statistically significant positive correlation with advanced age and significant negative correlation with left ventricular ejection fraction.
Conclusion: Egyptians had LAA predominantly windsock morphology in males and cactus morphology in females.
Keywords: Egyptians, Left atrial appendage, MDCT, Morphology.

INTRODUCTION
The left atrial appendage is identified anatomically from the left atrium by the narrowest part of the appendage which separates and also connects it into the left atrium [(1)]. It has structural, and biological features discrete from the left atrium proper [(2)]. LAA has dissimilar shapes, sizes, and relations to different adjacent structures, all of these may be extremely important when interventional procedures related to the left atrium are done [(3)].In the past, the left atrial appendage (LAA) has been conveyed to be a rather irrelevant portion of the cardiac anatomy but recently it may have a significant correlation with the pathogenesis of LAA thrombus formation. The pathogenesis for LAA thrombus formation is probably linked to blood stagnation within a long, blind-ended trabeculated pouch[(2)]. In a study using multidetector computed tomography (MDCT) and cardiac magnetic resonance (CMR), the shapes of the LAA were classified into 4 morphological types: "chicken-wing" "cactus", "windsock", and "cauliflower" [(4)] (Fig. 1).

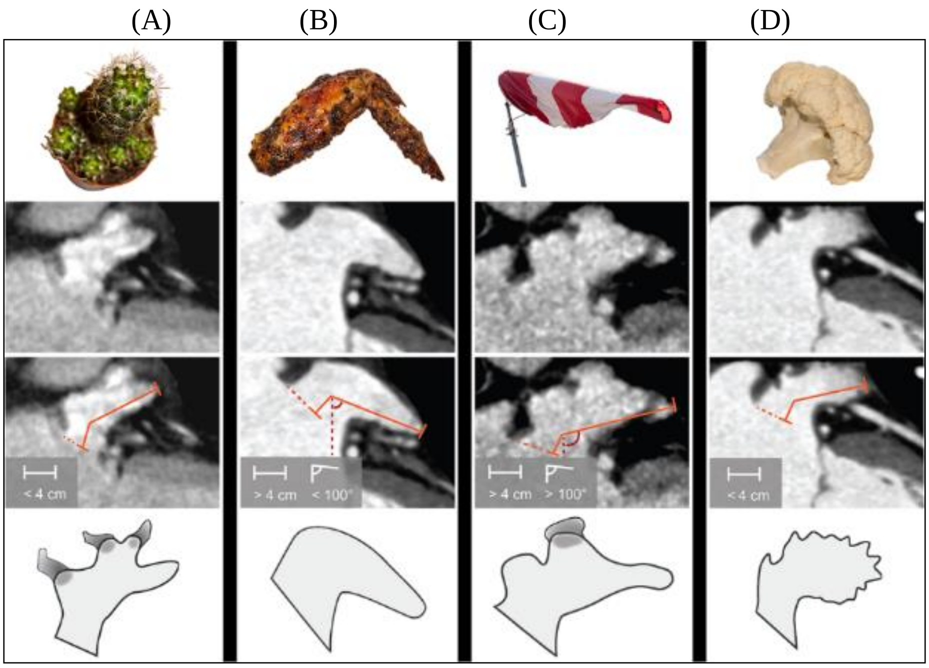

Figure (1): LAA morphology types based on Wang's classification with Kimura's quantitative limit, (A) Cactus (B) Chicken wing (C) Windsock (D) Cauliflower[(4)].

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The aim of the present work is to identify the prevalence of different morphological subtypes of left atrial appendage in Egyptian patients undergoing multi-slice CT coronary angiography and the possible modifying factors affecting it.

PATIENTS AND METHODS

We analyzed retrospectively the data of 101 consecutive Egyptian patients who underwent multi-detector computed tomography (MDCT) in our university specialized hospital from August 2019 to February 2020.

Patients who have congenital or acquired heart disease affecting left atrium and patients who had LAA surgical closure/excision or occlusion device were excluded from the analysis.

A precise revision of their hospital medical records was done with emphasis on the following data: age, gender, history of hypertension, diabetes mellitus, dyslipidemia, and previous revascularization.

Ethical approval: The study followed the ethical considerations according to the Ethical Committee of the Faculty of Medicine of our University.

MDCT:

Cardiac CT imaging was performed using 128-slice multidetector SEIMENS scanner (Siemens Healthcare, Erlangen, Germany). Axial source images, two and three-dimensional data sets were evaluated. Three-dimensional reconstruction images were performed to clearly visualize the cardiac structures with detailed cross-sectional analysis. For the three-dimensional images, the volumetric CT data sets were processed on a separate work station with multi-planar reformatting and volume rendering. All images were assessed and evaluated for LAA morphology and volume.

LAA morphology:

LAA morphology was assessed and categorized according to the classification of **Wang *et al.*** [6] into the four different morphological, **(Fig. 2)** showing different morphological sub-types of left atrial appendage according to Wang model using multidetector computed tomography (MDCT) in our study.

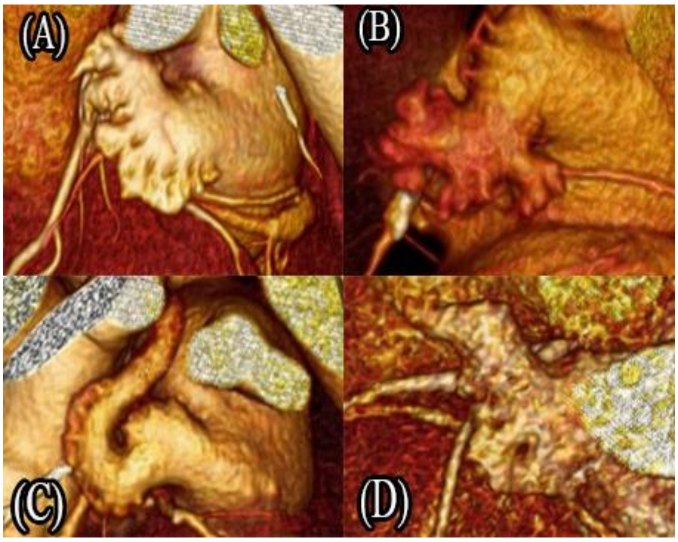
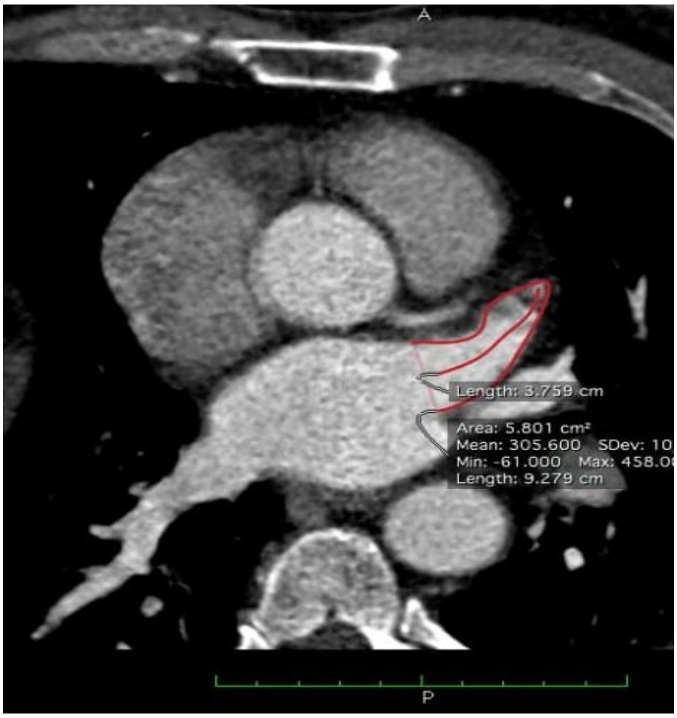


Fig. (2): (A) Cauliflower Morphology - (B) Cactus morphology -(C) Chicken Wing morphology- (D) Windsock morphology.

LAA volume: LAA volume was measured by multi-detector computed tomography by using three-dimensional reconstructed images and modified axial images (Fig. 3).



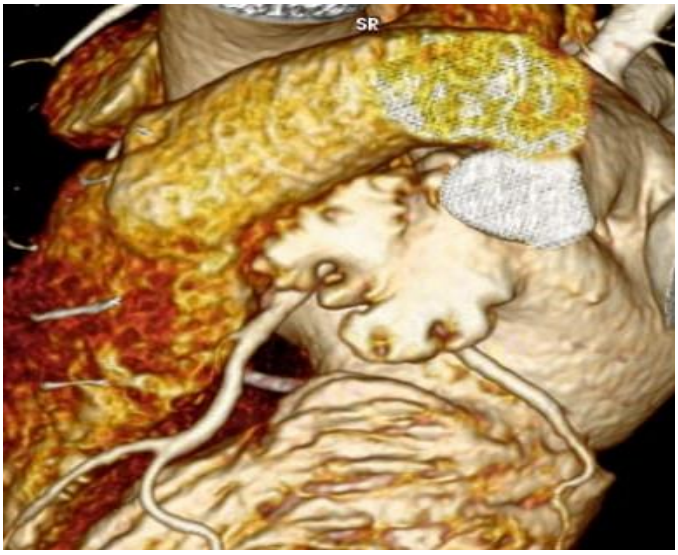


Fig. (3): Showing LAA volume measured by multi-detector computed tomography by using three-dimensional reconstructed images and modified axial images.

LAA length: LAA length was measured by multi-detector computed tomography by using three-dimensional reconstructed images and modified axial images (Fig. 4).

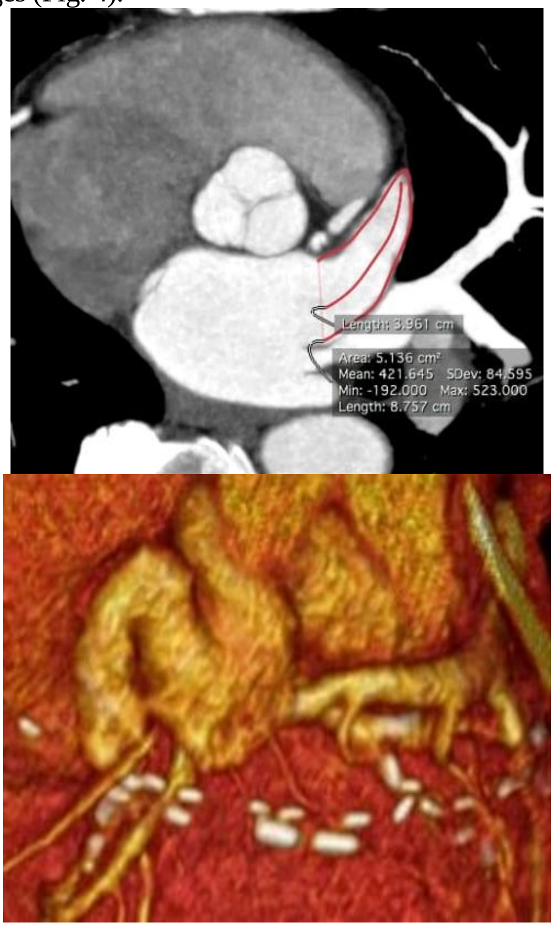


Fig. (4): Showing LAA length measured by multi-detector computed tomography by using three-dimensional reconstructed images and modified axial images.

Left atrial volume: Left atrial volume was measured by multi-detector computed tomography by using three-dimensional reconstructed images and modified axial images.

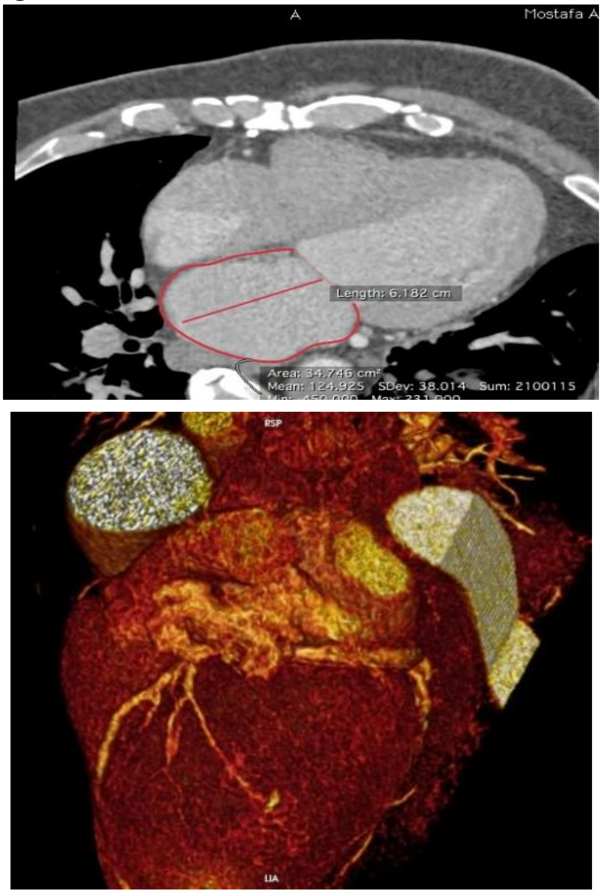


Fig. (5): Showing Left atrial volume measured by multi-detector computed tomography by using three-dimensional reconstructed images and modified axial images.

Statistical analysis

Data were collected, revised, coded, and entered into the Statistical Package for the Social Sciences (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations, and ranges when their distribution was found parametric and as median and interquartile rage (IQR) when nonparametric. Also qualitative variables were presented as numbers and percentages.

The comparison between groups regarding qualitative data was done by using Chi-square test. The comparison between groups with quantitative data and parametric distribution was done by using one way ANOVA. Univariate analysis was used to assess factors related to LAA volume. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: $P > 0.05$: Non-significant. $P < 0.05$: Significant. $P < 0.01$: Highly significant.

RESULTS

The demographic and clinical data of the patients are shown in table 1.

Table (1): Demographic Data and Clinical characteristics of study sample

		No. = 101
Age	Mean ± SD Range	54.31 ± 10.64 28 – 84
Age <60 **Age≥60**		65 (64.4%) 36 (35.6%)
Sex	Male Female	70 (69.3%) 31 (30.7%)
EF (%)	Mean ± SD	57.07 ± 12.33
DM	No Yes	58 (57.4%) 43 (42.6%)
HTN	No Yes	41 (40.6%) 60 (59.4%)
Dyslipidemia	No Yes	68 (67.3%) 33 (32.7%)

The left atrial and left atrial appendage dimensions are shown in table 2.

Table (2): Showing left atrial and left atrial appendage dimensions

		No. = 101
LA diameter (cm)	Median (IQR)	4.39 (3.89 - 5.09)
LA volume (ml)	Median (IQR)	105.24 (82.05 - 125.87)
LAA orifice	Median (IQR)	2.65 (2.22 - 3.26)
LAA volume (ml)	Median (IQR)	10.80 (5.8 - 14.91)
LAA length (cm)	Median (IQR)	3.67 (3.14 - 4.31)

Only gender showed a significant impact on the LAA morphology distribution (Table 3).

Table (3): Shows the relation of different parameters on LAA morphology

		LAA morphology				**Test value**	**P-value**	**Sig.**
		Cauliflower	**Cactus**	**Chicken wing**	**Windsock**			
		No. = 23	**No. = 20**	**No. = 26**	**No. = 32**			
Age	Mean ± SD Range	55.87 ± 13.79 34 – 84	53.45 ± 8.84 36 – 71	51.77 ± 11.34 28 – 74	55.81 ± 8.29 40 – 70	0.913•	0.438	NS
Age<60		12 (52.2%)	13 (65.0%)	20 (76.9%)	20 (62.5%)	3.330*	0.344	NS
Age≥60		11 (47.8%)	7 (35.0%)	6(23.1%)	12 (37.5%)			
Sex	Male Female	16 (69.6%) 7 (30.4%)	12 (60.0%) 8 (40.0%)	21 (80.8%) 5 (19.2%)	30 (93.8%) 2 (6.2%)	9.537*	0.023	S
EF (%)	Mean ± SD Range	56.26 ± 14.01 25 – 72	5.80 ± 12.06 30 – 71	58.85 ± 11.04 35 – 73	57.00 ± 12.65 20 – 75	0.278•	0.841	NS
DM	No Yes	14 (60.9%) 9 (39.1%)	12 (60.0%) 8 (40.0%)	17 (65.4%) 9 (34.6%)	15 (46.9%) 17 (53.1%)	2.296*	0.513	NS
HTN	No Yes	8 (34.8%) 15 (65.2%)	5 (25.0%) 15 (75.0%)	12 (46.2%) 14 (53.8%)	16 (50.0%) 16 (50.0%)	3.846*	0.279	NS
Dyslipidemia	No Yes	11 (47.8%) 12 (52.2%)	14 (70.0%) 6 (30.0%)	21 (80.8%) 5 (19.2%)	22 (68.8%) 10 (31.3%)	6.206*	0.102	NS
CAD (no. of vs)	0 1 2 3	9 (39.1%) 3 (13.0%) 5 (21.7%) 6 (26.1%)	8 (40.0%) 5 (25.0%) 3 (15.0%) 4 (20.0%)	10 (38.5%) 7 (26.9%) 0 (0.0%) 9 (34.6%)	14 (43.8%) 6 (18.8%) 7 (21.9%) 5 (15.6%)	9.501*	0.392	NS

Non-significant: NS, Significant: S, *:Chi-square test, •: One Way ANOVA test

By analysing the effect of LAA morphology on different parameters of LA and LAA on the, only LAA length varies among different LAA sub-types as shown in table (4).

Table (4): Shows the impact of different LA and LAA parameters on LAA morphological subtypes**.**

		LAA morphology				value	ig.
		Cauliflower	Cactus	:hicken wing	Windsock		
		No. = 23	No. = 20	No. = 26	No. = 32		
\ diameter (cm)	edian (IQR)	08 (3.93 - 7.95)	79 (3.99 - 5.15)	32 (3.83 - 4.9)	56 (3.79 - 5.21)	.569	\IS
A volume (ml)	edian (IQR)	97.36 56.23 - 125.36)	106.19 81.22 - 118.96)	98.53 5.56 - 121.37)	110.44 99.54 - 138.21)	.279	\IS
LAA orifice	edian (IQR)	.6 (2.32 - 3.53)	65 (2.28 - 3.33)	5 (2.11 - 2.92)	.8 (2.29 - 3.28)	.357	\IS
AA volume (ml)	edian (IQR)	).5 (5.9 - 14.92)	65 (5.6 – 13.45)	37 (4.6 - 12.4)	2.1 (8.2 - 15.97)	.054	\IS
AA length (cm)	edian (IQR)	.2 (3.01 - 3.46)	25 (2.99 - 3.51)	08 (3.46 - 4.7)	26 (3.99 - 4.77)	0.001	IS

Non-significant: NS, highly significant: HS

The age and dyslipidemia had a significant positive direct correlation with LAA volume. On the other hand, ejection fraction had a negative direct correlation with LAA volume. As shown in table (5) and table (6).

Table (5): Shows the effect of different parameters on LAA volume.

		LAA volume (ml)		P-value	Sig.
		Median (IQR)	Range		
Sex	Male Female	10.45 (5.7 – 14.91) 11.6 (6.6 – 14.92)	2.8 – 35.29 3.6 – 25.8	0.477	NS
Age	<60 ≥60	10.40 (5.5 – 13.52) 12.5 (7.25 – 19.71)	2.8 – 35.29 4.50 – 26.68	0.018	S
DM	No Yes	10.75 (5.7 – 14.2) 11.3 (5.8 – 16.1)	2.9 – 35.29 2.8 – 26.68	0.361	NS
HTN	No Yes	10.4 (5.7 – 12.6) 11.48 (5.82 – 15.57)	3.2 – 35.29 2.8 – 26.68	0.428	NS
Dyslipidemia	No Yes	10.25 (5.4 – 13.06) 13.88 (8.34 – 16.11)	2.8 – 35.29 4.25 – 26.68	0.028	S
CAD (No. of vessel)	0 1 2 3	9.68 (5.8 – 14.92) 12.4 (10.5 – 14.91) 11.9 (6.6 – 14.3) 8.3 (4.17 – 13.93)	2.8 – 26.17 4.9 – 35.29 5.1 – 22.17 3.3 – 23.82	0.186	NS
LAA morphology	Cauliflower Cactus Chicken wing Windsock	10.5 (5.9 – 14.92) 8.65 (5.6 – 13.45) 6.37 (4.6 – 12.4) 12.1 (8.2 – 15.97)	4.1 – 22.88 3.2 – 26.68 2.8 – 35.29 5.1 – 26.17	0.054	NS
Numbers of pulmonary veins	3 4 5	7.01 (5.37 – 10.16) 11.19 (6.1 – 15.4) 5.57 (4.25 – 14.74)	5.04 – 12 2.8 – 35.29 2.9 – 20.44	0.174	NS

Non-significant: NS, Significant: S

Univariate analysis to elucidate the correlation between different variables and LAA volume, showed that advancing age has a significant positive correlation with LAA volume, and estimated LVEF had a significantly negative correlation with LAA volume. As shown in table (6).

Table (6): Association between left atrial appendage volume and age, left ventricular functions and left atrium dimensions.

	LAA volume (ml)	
	r	P-value
Age	**0.304****	**0.002**
EF (%)	**-0.205***	**0.039**
LA diameter (cm)	**0.517****	**<0.001**
LA volume (ml)	**0.550****	**<0.001**
LAA orifice	**0.315****	**0.001**

DISCUSSION

LAA morphology varies in size, shape, and the number of lobes. Based on these features, the LAA has been classified into 4 main morphologies: Windsock, chicken-wing, cactus, and cauliflower [(6)]. These morphologies may influence an individual's risk of cardio-embolic stroke, the risk being highest in cauliflower morphology, and least in chicken-wing morphology. This variation in risk arises from a difference in contractility in the morphologies since low contractility predisposes to thrombi formation [(7)].

In the current study, retrospective analysis of LAA morphologies on Egyptian people revealed that the non-lobulated forms of LAA morphology were predominant. Windsock followed by chicken wing were more common as compared to the lobulated forms (cactus and cauliflower morphologies).

These findings were supported by another study done by **El Zinini *et al.*** **[8]** on Egyptian population where data were collected from another pool of private CT attendees. They found that the windsock was the most common morphology among Egyptian patients.

Was there any racial influence on LAA morphology?

We went across literature dealing with racial differences as regards LAA morphology, which revealed a bunch of information. **Korhonen *et al.*** **[9]** investigated the morphology of LAA in 111 patients in Finland with acute ischemic stroke of cryptogenic or cardiogenic etiology other than known atrial fibrillation. The windsock morphology was the most common (47.7) followed by the chicken-wing (23.4) followed by the cauliflower (19.8%). The cactus left atrial appendage morphology was the least common (9.0%).

Another study by **Di Biase *et al.*[10]** was done on 932 Italian patients who were planned to undergo catheter ablation for atrial fibrillation, the chicken-wing LAA morphology was found to be the most common. The distribution of different left atrial appendage morphologies was chicken-wing (48%), followed by cactus (30%), windsock (19%), followed by cauliflower (3%).

In a study by **Bai *et al.*[11]** was done on 200 non-valvular atrial fibrillation patients in the USA who were prepared to undergo radio-frequency ablation, the chicken-wing LAA morphology was also found to be the most common. The distribution of different left atrial appendage morphologies was (31.7%, 25.4%, 22.2% and 20.6% respectively).

Hirata *et al.* **[12]** investigated in Japanese LAA morphology, the chicken-wing LAA morphology was found to be the most prevalent, followed by the windsock and cactus morphologies, with the cauliflower morphology being the least prevalent.

A study that was carried out by **Kong *et al.*** **[13]** on 219 Chinese patients who underwent catheter ablation for fibrillation, the different LAA morphologies were distributed as follows: chicken wing (52.2%), windsock (23.9%), cauliflower (13.0%), and cactus (10.9%).

An autopsy study was done by **Mumin *et al.*** **[14]** on 91 black Kenyan hearts. They found that the cauliflower, chicken wing, and windsock morphologies were more frequent and present in almost similar prevalence. Cactus morphology was the least frequent.

On the other hand, our findings were contradicted by a study conducted by **Fukushima *et al.*** **[15]** in 2015 on 96 Japanese patients with paroxysmal atrial fibrillation. They found that the cactus LAA morphology was the most prevalent type. The different LAA morphologies were distributed as follows: cactus (38.5%), windsock (32.3%), cauliflower (16.7%), and chicken-wing (12.5%). This contradiction may suggest that racial differences may play role and as well as the exclusion of AF patients in the present study.

So, multiple studies declared that the American, Finnish and Turkish populations have similar results to the Egyptian patients. As shown in table (7).

Table (7): Prevalence of LAA morphology types in various populations

	Population	Chicken wing	Windsock	Cauliflower	Cactus
El Zinini *et al.* (2017)[8]	Egyptian	25.7%	31.7%	22.8%	19.8%
Mumin *et al.* (2018)[14]	KENYAN	27.4%	28.6%	29.7%	14.3%
Di Biase *et al.* (2012)[10]	Italian	48%	19%	3%	30%
Wang *et al.* (2010)[6	American	18.3%	46.7%	29.1%	5.9%
Korhonen *et al.* (2015)[9]	Finish	10%	67.5%	25%	20%
Fukushima *et al.* (2016)[15]	Japanese	12%	32.3%	16.7%	38.5%
Ucerler *et al.* (2013)[16]	Turkish	12%	38%	26%	24%

Is there any gender difference as regards LAA morphology?

In the present study, the distribution of the four different LAA morphologies was evaluated in correlation with gender. A significant relationship between LAA morphology and gender was noticed. The cactus was the most predominant morphology among females then cauliflower morphology. This finding was supported by the other study carried on Egyptian patients. **El Zinini *et al.*** **[8]** found a significant correlation between gender and LAA morphology as females were more likely to have cactus morphology while the chicken-wing morphology was the least common.

Rafał *et al.* **[17]** confirmed a significant variability in LAA morphology and volumes with a tendency to have lower values in females. As regards LAA morphology the two lobed morphology was predominant while three-lobed appendages were less common and more common in men. He stated that this anatomical variability seems to be clinically significant and may affect the course of the coagulation process inside the appendage.

Our findings are contradicted by the study of **Nikitin *et al.*** **[18]** who concluded that there were no sex-related differences between men and women in any of the indices of LAA morphology and function measured with B-mode echocardiography. This contradiction may be due to the use of different imaging modalities in assessing LAA parameters in both studies, with the CT evaluation is more accurate.

Additively a study by **Mumin *et al.*** [14] declared that cauliflower was the most prevalent morphology in males compared with females who had the chicken-wing morphology as the most prevalent morphology. Cactus morphology was the least prevalent in both genders. However gender difference as regards the LAA morphologies was not statistically significant (P value= 0.537).

LAA morphologies with multiple lobes (windsock and cactus) were more common in males than females (46% vs. 35%). Men also had longer left atrial appendage lengths than women as declared by **Korhonen *et al.*** [9].

Boucebci *et al.* [19] reported that men had longer left atrial appendage lengths with no significant differences between males and females in the left atrial appendage number of lobes or morphology.

Korhonen *et al.* [9] referred this discordance between different studies regarding gender-associated differences in left atrial appendage morphologies to the different amounts of pericardial fat since the association between gender and left atrial appendage morphology was lost after adjusting the results with body surface area. A larger amount of pericardial fat could be associated with a higher number of adipocytes contributing to more remodeling in the left atrium.

In the present study, the median of left atrial volume calculated from 3-dimensional reconstruction images in our study was 105.25 ml (IQR) (82.05-125.87), with a wide range of 39.2 to 210 ml. This finding is supported by **Korhonen *et al.*** [9], who did a study on 111 patients revealing a mean left atrial volume of 95.3 ml ± 31.2.

In this work, the median of left atrial appendage volume calculated from 3-dimensional reconstruction images in our study was 10.80 ml (IQR (5.8-14.91) with a wide range of 2.8 to 35.29 ml.

These LAA measurements were larger than that found by **Wang *et al.*** [6] who found that the mean left atrial appendage volume to be 8.8 ml ± 5.6 and.

Also our results revealed smaller LAA volumes than that stated by **Kimura *et al.*** [4]**,** (16.1 ml ± 7.5) and **Korhonen *et al.*** [9] study 10.2 ml ± 3.3.

In the present work, the median of left atrial appendage length was 36.7 mm (IQR) of (31.4-43.1) with a range of 18.6 to 43.3 mm which was smaller than that measured by **Wang *et al.*** study, who found the mean left atrial appendage length to be 45.8 mm ± 12.1[6].

These data carried on a special race showed that a smaller mean LAA volume and length may be present in the Egyptian population and reinforces the racial difference.

In the present study, the median left atrial appendage volume was largest in the windsock morphology, followed by the cauliflower and cactus morphologies, and was smallest in the chicken wing morphology.

On the other hand, our finding is contradicted by **Hirata *et al.*** [12] who studied the impact of age on the LAA morphologies, and found no significant association in patients with sinus rhythm, but showed a significant increase in the chicken wing morphology in older age groups in the atrial fibrillation group of patients.

Hirata *et al.* [12] findings may be explained by aging in atrial fibrillation patients affecting properties of the left atrial appendage wall and therefore affecting remodeling. However, it is an observation that needs to be further assessed.

In this work, age had a significant direct relation to LAA volume. This finding is supported by **Korhonen *et al.*** [9] who stated that, after adjusting LAA volume by body surface area values, a positive correlation was identified between LAA volume and age.

Also a study was done by **Boucebci *et al.*** [19] stated that LAA volume was found to display an age-related association. Aging might modify the properties of the LAA wall along with other components of the cardiovascular system, this remodeling increases the risk of thrombosis. These reasons might explain the higher prevalence of embolic events in elderly patients.

Moreover, **Nikitin *et al.*** [17] found a tendency for an increase in left atrial diameter with age. The elder population had higher left atrial volume indices.

Also, **Hirata *et al.*** [12] suggested that there is a strong relationship between age and left atrial appendage volume in both study groups either sinus rhythm or atrial fibrillation.[12]

In the present study, a significant correlation existed between the presence of dyslipidemia and LAA volume. This finding is supported by **Zemrak *et al.*** [20] who stated that although a statistically significant relation between left atrial volume and dyslipidemia was found, this finding is unlikely to be of clinical significance. On the other hand, **Korhonen *et al.*** [9] found no significant correlation between LAA volume and dyslipidemia. Fat deposition over LAA and diastolic dysfunction in dyslipidemic patients may give an illustration of why left atrial appendage tend to be larger in dyslipidemic patients.

In this work, Left ventricular systolic function had a statistically significant negative relationship with left atrial appendage volume. This is supported by **Mahilmaran *et al.*** [21] who established that patients with left ventricular dysfunction got left atrial appendage dysfunction as demonstrated by lower emptying and filling velocities, which might increase the incidence of thrombus formation.

CONCLUSION

Egyptian people as many other races had predominantly the windsock and chicken wing LAA morphologies. Female gender had a more lobulated form of LAA morphology than males that may increase the risk of thromboembolism. Increasing age and decreased left ventricular ejection fraction significantly affect LAA volume which may predispose to thromboembolism through LAA remodeling.

RECOMMENDATIONS

Larger studies all over Egypt that involve different governorates are needed. Studies to compare the association between different atrial arrhythmia and thromboembolism risk and LAA morphology and volumes are also needed.

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