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CARDIAC AMYLOIDOSIS IN THE ELDERLY: A QUANTITATIVE STEREOLOGIC STUDY

Santosh Mehta*, Marcelino G. Reyes, Thomas Tosch,
William Thomas, Jr., and Albert I. Rubenstone

Departments of Pathology, Oak Forest Hospital*, Oak Forest,
Illinois and Mt. Sinai Hospital, Chicago, Illinois, U.S.A.

ABSTRACT:

Thirty-nine autopsied patients with senile cardiac amyloidosis were studied by technics of stereology to assess the severity of amyloid deposits in the left ventricle. Volume density of amyloid in the section correlated with the weight of the heart in 21 patients with congestive heart failure but not with the age, presence or absence of hypertension, diabetes, cause of death or the severity of coronary arteriosclerosis. Our findings indicate that the weight of the heart of elderly patients with congestive heart failure and amyloid deposits in the left ventricle can be useful in predicting the severity of amyloidosis in the left ventricle.

INTRODUCTION:

Although senile amyloidosis of the heart is a well known pathologic entity, very little is known about its severity. In particular, it is not clear if it increases with age or how it relates to sex, race, presence or absence of hypertension, diabetes or congestive heart failure, cause of death, severity of coronary arteriosclerosis or the weight of the heart. In this study, we estimated the severity of senile amyloidosis with technics of stereology and found that the severity of amyloidosis of the left ventricle increased with the weight of the heart of patients with congestive heart failure.

MATERIALS AND METHODS:

Thirty-seven cases of cardiac amyloidosis were seen on retrospective study of 408 autopsies performed on patients ranging in age from 59 to 96 years at Oak Forest Hospital. Two cases were added from the files of Mount Sinai Hospital. At the time of autopsy, the following information was abstracted from the medical chart: 1) age; 2) sex; 3) race; and 4) presence or absence of hypertension, diabetes and congestive heart failure. The fresh unfixed heart was weighed and the severity of coronary arteriosclerosis was then subjectively estimated from the degree of narrowing of the lumen as: mild (less than 25%), moderate (less than 50%), and severe (more than 50%). Lastly, a cause of death was determined from the clinical and autopsy findings.

TABLE I: CLINICAL AND AUTOPSY FINDINGS AND SEVERITY OF AMYLOIDOSIS

Findings			Severity of Amyloidosis ($mm^3/100\ mm^3$) Range	Median	Mean ±s.e.	Correlation
Age 82.3 ± 1.4 (n = 39) 59-96, 85			< 0.5 - 53.0	8.8	14.1 ± 2.4	None
Sex						
Male	24	62%	< 0.5 - 53.0	8.8	15.9 ± 3.3	None
Female	15	38%	< 0.5 - 50.0	1.5	11.2 ± 7.6	
Race						
White	20	51%	< 0.5 - 50.0	1.5	16.3 ± 3.6	None
Black	19	49%	< 0.5 - 53.0	4.9	11.7 ± 3.2	
Hypertension						
Present	11	29%	< 0.5 - 45.9	3.4	10.0 ± 4.1	None
Absent	27	71%	< 0.5 - 53.0	8.0	15.9 ± 3.1	
Diabetes						
Present	4	11%	< 0.5 - 27.0	5.0	14.1 ± 5.5	None
Absent	34	89%	< 0.5 - 53.0	8.0	14.2 ± 2.7	
Congestive Heart Failure						
Present	21	55%	< 0.5 - 53.0	10.5	16.7 ± 3.7	None
Absent	17	45%	< 0.5 - 50.1	4.9	11.1 ± 3.2	
Cause of death						
Cardiovascular	12	31%	< 0.5 - 42.2	2.0	9.8 ± 4.1	
Neoplasms	13	33%	< 0.5 - 53.0	15.9	18.8 ± 4.8	None
Others	14	36%	< 0.5 - 50.0	11.5	13.3 ± 3.6	
Coronary Atherosclerosis						
Mild	11	28%	< 0.5 - 45.9	8.9	16.0 ± 4.7	
Moderate	12	31%	< 0.5 - 53.0	9.5	18.9 ± 5.5	None
Severe	16	41%	< 0.5 - 30.0	2.1	9.2 ± 2.6	

One section was taken from the free wall of the left lateral ventricle of each heart, fixed in formalin, dehydrated in alcohols, embedded in paraffin, cut in serial or step sections at 4 microns and stained with hematoxylin and eosin, crystal violet and congo red stains. In the hematoxylin and eosin preparation, amyloid consisted of hyalin amorphous material between the muscle fibers and less commonly in the wall of the blood vessels. These deposits stained metachromatically (purple) with crystal violet and showed green birefringence in congo red sections viewed with polarized light.

Because sections stained with crystal violet gave a sharper contrast and better resolution than congo red, we used the crystal violet stained sections for the stereologic estimates. The sections mounted on glass slides were projected from a 35 mm slide projector on a white board lined with a grid of squares. The upper right hand corner of the squares of the grid was used to count the points hitting amyloid and myocardium. Each section was counted twice by the same observer (SM) by moving the image on the board six inches sideways and the points hitting amyloid and myocardium were counted and averaged. Volume density of amyloid was calculated using a derivation of Delesse's equation V/V = P/P where P/P is the point fraction or total amyloid

TABLE II

CORRELATION OF HEART WEIGHT AND SEVERITY OF AMYLOIDOSIS

	Range	Median	Mean ±s.e.	Correlation
Congestive Heart Failure (n = 21)				
Heart weight (gms)	250 - 800	375	434 ± 32	r = + .746
Amyloidosis (mm^3/100 mm^3)	<0.5 - 53.0	10.5	16.7 ± 3.7	p<0.001
No Congestive Heart Failure (n = 17)				
Heart weight (gms)	230 - 575	310	331 ± 20	None
Amyloidosis (mm^3/100 mm^3)	<0.5 - 50.0	4.9	11.1 ± 3.2	

points divided by total amyloid and myocardial points counted (Weibel and Bolender, 1973). V/V was multiplied by 100 and expressed as $mm^3/100mm^3$ of section. Results were analyzed using standard statistical tests programmed on an Apple II Plus computer.

RESULTS:

Table I compares the severity of amyloidosis with the clinical and autopsy findings described below.

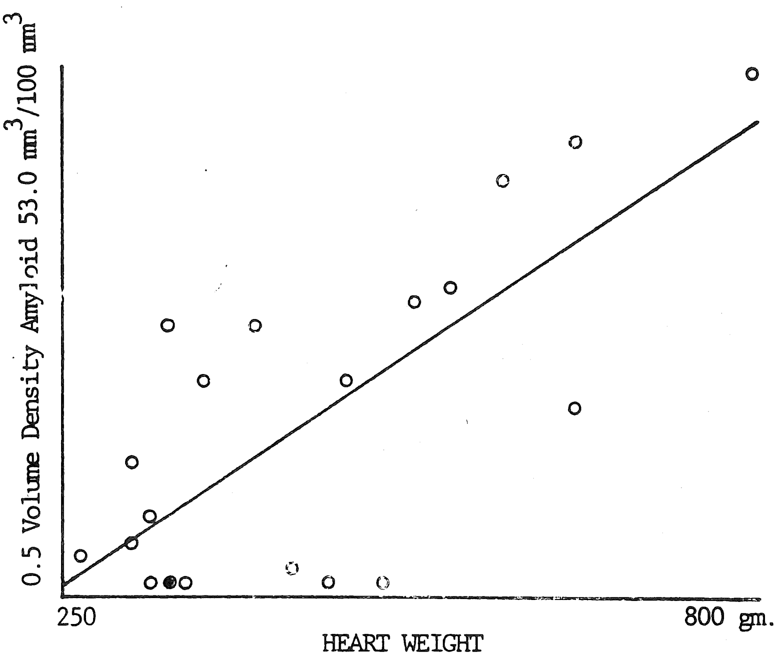
Volume density of amyloid in the section in the thirty-nine patients which had a range of $< .05$ to 53.0, median of 8.8 and mean + std err of 14.1 + 2.4 $mm^3/100mm^3$ did not correlate with the age, sex or race of the patients. Also in 38 patients with available information, volume density of amyloid in the section did not correlate with the presence or absence of hypertension, diabetes or congestive heart failure. Severity of amyloidosis also did not correlate with the cause of death which we divided into cardiovascular, neoplastic and other causes or with the severity of coronary arteriosclerosis.

Table II compares the severity of amyloidosis and the weight of the heart of patients with and without congestive heart failure. Volume density of amyloid in the section was positively correlated with the weight of the heart of 21 patients with congestive heart failure ($r = +.746$, $p < 0.001$) (Figure), but not with the heart weight of 17 patients without congestive heart failure. Also, hearts of those with congestive heart failure weighed more than those without congestive heart failure. [$F(1,37) = 6.47$, $p < 0.05$].

DISCUSSION:

Our study shows that quantitative stereologic estimates of the severity of senile amyloidosis of the left ventricle do not appear to be related to the age, sex, race, presence of hypertension, diabetes or congestive heart failure

Figure, Scattergram showing that the volume density of amyloid in the section increases with the weight of the heart in 21 elderly patients with congestive heart failure.



SLOPE = 0.8 INTERCEPT - 19.85

CORRELATION = +.746 P < .001

N=21

or to the cause of death or severity of coronary arteriosclerosis. Buerger and Braunstein (1960) who subjectively estimated the severity of senile cardiac amyloidosis in their patients also found no correlation between severity and the age, the presence of congestive heart failure or severity of coronary arteriosclerosis. However, these authors along with Pomerance (1966) also reported that their subjective estimates of the severity of amyloidosis did not correlate with the weight of the hearts of their patients, and that cardiomegaly in their patients probably resulted from causes other than amylodiosis. These authors' findings, therefore, differed from our observation that the severity of amyloidosis of the left ventricle increased with the weight of the heart in patients with congestive heart failure. These authors felt that cardiomegaly in amyloidosis was probably related to other cardiac factors. This difference in their findings and ours could be due to technics used to estimate the severity of amyloidosis and possibly because neither of the two authors directly compared the severity of amyloidosis and the heart weight of patients with congestive heart failure.

However, in our study of two groups of patients with and without congestive heart failure, the mean of amyloid deposits in the left ventricle did not differ in severity. Thus, it would appear that congestive heart failure in senile amyloidosis can result not only from amyloidosis but from other causes as well. Pomerance (1966) had suggested that severe amyloidosis of the heart can cause congestive heart failure in a significant number of patients.

We conclude that in elderly patients with congestive heart failure and amyloid deposits in the left ventricle, the heart weight can be useful in predicting the severity of amyloidosis of the left ventricle. We believe that this finding could be important to the practicing pathologists who can expect to see senile amyloidosis of the heart in about 10% of patients who die after 60 years of age (Wright and Calkins, 1975).

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Reprints requests to SM, Department of Pathology, Oak Forest Hospital, 15900 South Cicero Avenue, Oak Forest, Illinois 60452.