

# Clinical Meaning of Ascites in Patients with Endomyocardial Fibrosis

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**Objective** - To evaluate the clinical meaning of ascites and the main features of patients with ascites and endomyocardial fibrosis.

**Methods** - We studied 166 patients with endomyocardial fibrosis (mean age 37 years, 114 women) treated over the last 20 years. Ventriculography findings, surgery or necropsy confirmed the diagnosis in all patients. Most patients belonged to New York Heart Association Functional Class III/IV (134, 83.7%). Eighty-one (50.6%) had biventricular, 28 (17.5%) had right ventricular, and 51 (31.8%) had left ventricular involvement. During follow-up, 56 patients died.

**Results** - Ascites was present in 67 (41.8%) patients, and right ventricular involvement was present in 59 (88%). In the comparison between patients with or without ascites, those with ascites had higher mortality (49.2% and 24.7%, respectively). Patients with ascites had a higher incidence of edema (95% vs. 43%), hepatomegaly (5.8cm vs. 4.1cm), mean right atrium pressure (19.3 vs. 12mmHg), and final right ventricle diastolic pressure (18.7 vs. 12.9mmHg). Also, patients with ascites had a longer history of illness (5.1 and 3.9 years, respectively) and had atrial fibrillation more frequently (44.7% vs. 30.1%).

**Conclusion** - Ascites was observed in less than 50% of cases of endomyocardial fibrosis and was associated with greater involvement of the right ventricle and with a longer duration of the disease, thus being a characteristic of a worse prognosis.

**Key words:** ascites, endomyocardial fibrosis, restrictive cardiomyopathy

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Received for publication on 16/11/00  
Accepted on 14/2/01

Endomyocardial fibrosis is a restrictive cardiopathy that may evolve to cardiac failure, which is difficult to control<sup>1-7</sup>. Its detection enables, in most cases, recommendation for surgical treatment, with resection of fibrotic tissue and control of cardiac failure<sup>2-4,8-10</sup>.

Ascites is a very important feature in the diagnosis of endomyocardial fibrosis. When it is associated with peripheral edema, and even in its absence, it is valued as an indication of a restrictive syndrome and must be taken into account as an etiological factor.

The objective of this study was to evaluate the importance of ascites related to its clinical and laboratory characteristics, for the purpose of evaluating whether the presence or absence of ascites identifies patients with different clinical courses and different prognoses.

## Methods

We studied 166 patients with endomyocardial fibrosis followed at the Instituto do Coração-HC/FMUSP since 1978; 114 were women and 46 were men. Age ranged from 5 to 64 years (mean 34.3±13). Diagnosis was confirmed by hemodynamic and angiographic studies in 133 patients, by surgery in 88 patients, and by data obtained in necropsy in 30 patients.

Data obtained through angiographic study or necropsy revealed that 81 patients had biventricular, 28 had right ventricular, and 51 had left ventricular involvement. Based on the findings, involvement was classified as mild, moderate, or severe. Involvement of the right ventricle was considered mild in 52 cases, moderate in 52 and severe in 56 cases. Involvement of the left ventricle was mild in 28, moderate in 82 and severe in 49 cases.

Most patients were symptomatic, and 134 had New York Heart Association (NYHA) functional classes III/IV cardiac failure and 25 had NYHA classes I/II.

During follow-up, 56 (35%) patients died.

Regarding clinical features, 142 (88.8%) had dyspnea, 104 (65.4%) had swelling of the lower limbs, and 112 (70.4%) had

hepatomegaly. In 96 (65.4%), regurgitant systolic murmur was present. Proto-diastolic knock was described in 77 (48.4%) patients. Atrial fibrillation was verified in 58 (36.3%) cases. Ascites was detected by physical examination in 67 (42.1%) patients.

During follow-up, 96 patients underwent echocardiographic study. Because follow-up was long, echocardiographies were performed using different machines and techniques; thus, we will only highlight the measures obtained by M-mode, common to all the cases. Mean left ventricle diameter was 51.9±9.6mm, left atrium diameter was 42.2±9.6mm, and left ventricle ejection fraction was 0.72±0.09.

Hemodynamic study was performed in 130 (31.2%) patients. Mean right atrial pressure was 15.0±7.4mmHg, right ventricular end diastolic pressure was 15.3±7.1 mmHg, left ventricular systolic pressure was 42.9±20.6mmHg, left ventricular end diastolic pressure was 21.8±10.4mmHg and left ventricular systolic pressure was 119.4±19.7mmHg. Tricuspid regurgitation was observed in 98 (61.4%) patients and mitral regurgitation in 102 (63.7%) patients.

According to ventriculographic appearance, the degree of fibrosis was classified as mild, moderate or severe. Fibrosis was considered mild when small changes were observed in ventricular morphology, mainly a restriction in the inflow tract or apex. Moderate fibrosis was characterized by evident reduction in the diastolic ventricular dimension together with endocardial irregularities of the apical region. Severe fibrosis was characterized by a grossly abnormal appearance of the ventricular chamber in diastole (the chamber being reduced in size and acquiring a tubular form owing to the almost complete elimination of the inflow tract and obliteration of the apex).

Patients were followed annually. Those who failed to attend their scheduled follow-up visit were contacted by telephone or letter or by both telephone and letter at least three times. The mean follow-up period was 4.2±4 years. Seventeen patients were lost to follow-up during the first year. Deaths occurred in 56 (34%) patients, 27 among patients treated clinically and 28 among patients treated surgically.

Patients were divided into 2 groups according to the presence or the absence of ascites. We evaluated whether differences existed between the 2 groups regarding clinical symptoms, or in echocardiographic and hemodynamic findings. Kaplan-Meier survival curves were constructed for those with and without ascites. Differences between the curves were analyzed with the log-rank test. Chi-squared analysis was used to test the association between several variables. A p value < 0.05 was considered significant. Statistical analysis was performed using SAS (Statistical Analyses Systems) software.

## Results

Ascites was observed during clinical examination in 67 (42.1%) patients treated at our institution. Table I shows clinical characteristics of patients with or without ascites and table II shows echocardiographic, hemodynamic and ventriculographic data. Patients with ascites were younger than those without it.

**Table I – Clinical profile of patients according to the presence (A+) or absence (A-) of ascites**

Number	A+	A-	p
Age	34±12.8	39.8±12.6	0.0051
Female	48(71.6%)	66(69.9%)	0.892
FC III/IV	67(100%)	68(73.1%)	0.001
FA	37(55.2%)	64(69.5%)	0.064
Dyspnea	60(89.5%)	81(88%)	0.767
Chest pain	7(10.4%)	30(32.6%)	0.001
Hepatomegaly	60(89.5%)	52(56.6%)	0.001
Peripheral edema	64(95.6%)	40(43.4%)	0.001
Proto-diastolic knock	37(55.2%)	40(43.4%)	0.143
Systolic murmur	40(59.7%)	56(69.8%)	0.882
Ventricular involvement (Bi, RV, LV)	42/17/8	39/11/43	0.001
Surgical patients	42(62.6%)	46(49.4%)	0.085
Deaths	34(50.7%)	33(35.4%)	0.0021

FC- NYHA functional class; AF- atrial fibrillation; Bi- biventricular involvement; RV- prevalent involvement of right ventricle; LV- prevalent involvement of left ventricle.

**Table II – Data from echocardiographic, hemodynamic and ventriculographic study, according to the presence (A+) or absence (A-) of ascites**

	A+	A-	p
Left atrium diameter (mm)	42.7±9.2	42.0±8.6	0.7482
Diastolic diameter of LV (mm)	48.3±10	53.5±9.1	0.0131
Ejection fraction of LV (%)	71.8±8.5	72.5±9.4	0.1342
Pressure of left atrium (mmHg)	19.2±6.5	12.0±6.5	<0.0001
Final diastolic pressure of RV (mmHg)	18.6±6.4	12.8±6.6	<0.0001
Systolic pressure of RV (mmHg)	38.7±21.6	46.0±19.5	0.454
Diastolic pressure of LV (mmHg)	20.7±9.3	22.6±11.1	0.3091
Systolic pressure of LV (mmHg)	113.1±16.4	124.1±20.6	0.0010
Tricuspid regurgitation	48(88.9%)	49(59.7%)	0.001
Mitral regurgitation	43(76.8%)	58(69%)	0.317
Fibrosis intensity RV (Mi, Mo, I)	9/23/35	43/29/21	0.001
Fibrosis intensity LV (Mi, Mo, I)	18/33/16	11/49/33	0.037

LV- left ventricle; RV- right ventricle; Mi- mild; Mo- moderate; I- intense.

On physical examination, patients with ascites frequently had more hepatomegaly and peripheral edema and less chest pain than the patients without ascites. The incidence of dyspnea, proto-diastolic knock, and regurgitant systolic murmurs was the same for both groups.

Patients with ascites had left ventricles with lower diameters on echocardiographic examination (48.3mm vs 53.54mm, p=0.0131). In the hemodynamic study, patients with ascites had higher mean right atrial pressure and right ventricular end diastolic pressure, and lower left ventricular systolic pressure. In ventriculography, a greater number of patients had tricuspid regurgitation (p=0.001), and the proportion of patients with a greater intensity of right ventricular fibrosis was higher (p=0.001).

The proportion of patients who underwent surgery was slightly greater among those with ascites (62.6% vs 49.4%), but this difference did not reach statistical significance ( $p=0.085$ ).

Mortality was higher among patients with ascites ( $p=0.0021$ ). Analysis of the Kaplan-Meier survival curves revealed that patients with ascites reached 30% mortality at two years, while those without ascites had a mortality rate of 15% at eight years ( $p=0.00009$ ) (fig. 1).

## Discussion

The main findings of this study include: 1) ascites is frequent in patients with endomyocardial fibrosis (incidence of 42.1%), 2) ascites is usually associated with hepatomegaly and peripheral edema, 3) ascites is related to a greater hemodynamic and morphological involvement of the right ventricle, 4) ascites is associated with the presence of tricuspid regurgitation in the hemodynamic study, 5) presence of ascites is associated with a worse prognosis.

Ascites appears to be a sign frequently found in restrictive cardiomyopathies and is considered an important factor for diagnosis of those entities. It may be present both in constrictive pericardites and in endomyocardial fibrosis, which suggests the need for confirming the diagnosis.

The presence of ascites in patients with endomyocardial fibrosis is mentioned in the majority of articles that discuss the disease<sup>1-7</sup>. It is worth noting that, generally, no special point is made in these articles about stressing its importance; it is presented as another clinical sign of right ventricular involvement. Its incidence ranged between 28% and 100% of reported cases. No concern, in most articles, is shown about verifying whether ascites is important in the follow-up of patients. When we compare our analysis with those in the literature, we observe that in the literature the reported frequency of ascites is greater, because in these studies most patients had biventricular involvement or isolated right ventricular involvement. Analyses of patients with prevalent left ventricular involvement, such as ours,

are rare, because in the majority of the cases, endomyocardial fibrosis is diagnosed because of its congestive manifestations and because of the presence of ascites.

In our data, we have a great number of cases with prevalent involvement of the left ventricle. These patients had chest pain and underwent cineangiography with ventriculography, which facilitates the diagnosis of endomyocardial fibrosis. Ascites was more frequent among patients in whom the disease involved the right ventricle, and the greater the involvement the more frequent the presence of ascites. Thus, in patients with severe fibrosis of the right ventricle, the incidence of ascites was 52%. In those with moderate fibrosis, it was 34%, and in those with mild fibrosis, it was 13%, indicating how important chamber obliteration (fibrosis intensity) is in the restrictive syndrome and in hemodynamic changes that lead to the genesis of ascites.

When we analyzed ascites in relation to the chamber involved, we observed that biventricular involvement was present in 52.5% of patients, right ventricular involvement was present in 60.7% and prevalent involvement of the left ventricle was present in 15.6%. These data show the importance of right ventricular involvement.

If right ventricle involvement is the cause of ascites, why do some patients with endomyocardial fibrosis of the left ventricle have ascites? One hypothesis is that at autopsy we can usually detect involvement of both chambers. In many cases, this involvement is not important enough to determine distortions in the chambers and we cannot identify right ventricular involvement in the clinical or laboratory examinations. These cases are identified as dominant involvement of the left ventricle, but, probably, minimal changes in the right ventricle are enough to explain alterations responsible for the appearance of ascites<sup>11</sup>. In fact, this disease is seldom exclusively univentricular. Another possibility is that ascites is due to an inflammatory process of the peritoneous. Researchers who have observed the high level of proteins and leptocytosis in ascites effusion defend this hypothesis<sup>12</sup>.

Patients with ascites more often had signs related to the involvement of the right chambers, such as hepatomegaly and peripheral edema, usually present in cases of congestive heart failure. Patients with ascites were younger, what could be related to the characteristics of right heart involvement, because since the right ventricle was a smaller muscular mass, it results in earlier symptoms when compared to the left ventricular involvement.

Atrial fibrillation, which is also associated with a worse prognosis, was slightly more frequent among the patients with ascites, but no statistically significant difference existed between the two<sup>13</sup>. The presence of murmur, identifying mitral and tricuspid regurgitation, was more frequent among patients with ascites. The presence of tricuspid regurgitation increases clinical manifestation in cases of cardiac restriction because the ventricles lose the ability to adapt to the volume of regurgitation, as in cases of endomyocardial fibrosis, which explains the higher incidence of ascites in these patients.

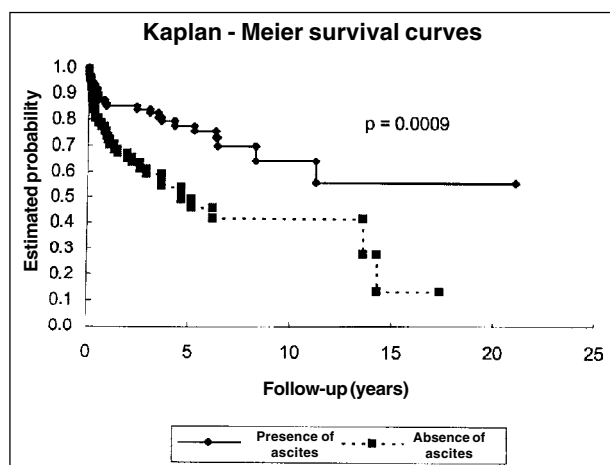


Fig. 1 - Kaplan-Meier survival curves for patients with and without ascites.

Data from hemodynamic examinations confirmed this assessment. Patients with ascites had greater elevation in mean pressure of the right atrium and in the final diastolic pressure of the right ventricle, which indicates greater involvement of the right ventricle. They also show that no relation exists between the presence or absence of ascites and the intensity of the involvement and restriction of the left ventricle, because the final diastolic pressures in the left ventricles were similar in both groups.

Mortality was higher in patients with ascites, which may be because it is a clinical manifestation of right ventricular involvement, which is associated with a worse prognosis, as is reported in the literature<sup>1-7</sup>. Right ventricular involvement characterizes a group with greater cardiac obliteration and a higher frequency of tricuspid regurgitation, both of which are clinical situations that aggravate the evolution of patients with this disease.

We verified that ascites was slightly more frequent in patients referred for surgery, a finding that was probably related to the greater difficulty in clinically controlling these patients, a condition in which surgery is recommended.

Kaplan-Meier survival curves (fig. 1) show that the prognosis of patients with ascites is poorer than the prognosis of those without ascites. These curves differ from the beginning of the study and separate progressively.

The results of this analysis confirm that right ventricular involvement is more harmful to patients and, in those with clinical manifestations such as ascites, surgery must be recommended as early as possible, because it can reverse or minimize hemodynamic alterations that determine this worse evolution, improving the patient's prognosis, according to several studies<sup>2-4,8-10,13</sup>.

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