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Right Ventricular Myocardial Infarction in Patients With Chronic Lung Disease: Possible Role of Right Ventricular Hypertrophy

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To determine the relation between right ventricular hypertrophy and right ventricular myocardial infarction in patients with chronic lung disease, the records of 28 patients with chronic lung disease, inferior myocardial infarction and significant coronary artery disease (group I) and 20 patients with right ventricular hypertrophy, chronic lung disease without inferior myocardial infarction or significant coronary artery disease (group II) were reviewed. Chronic lung disease was diagnosed by clinical criteria, chest radiographs and pulmonary function tests. All patients had postmortem examinations.

Patients in group I were classified into two subgroups: group Ia (without right ventricular hypertrophy) and group Ib (with right ventricular hypertrophy). Right ventricular wall thickness was 3.3 mm ± 0.5 in group Ia, 6.0 mm ± 1.1 in group Ib and 8.8 mm ± 2.4 in group II (group Ia versus Ib, $p < 0.001$; group Ia versus II, $p < 0.001$; group Ib versus II, $p < 0.001$). Eleven patients (78.6%) in group Ib (chronic lung disease with both right ventricular hypertrophy and inferior myocardial infarction) had right ventricular myocardial infarction compared with only 3 patients (21.9%) in group Ia (chronic lung disease without right ventricular hypertrophy and with inferior myocardial infarction) ($p < 0.008$). Isolated right ventricular myocardial infarction occurred in four patients (20%) in group II (chronic lung disease with right ventricular hypertrophy, but without evidence of infarction of the left ventricle or significant coronary artery disease). There was no significant difference in the extent of anatomic coronary disease in groups Ia and Ib. The cause of death was believed to be directly related to right ventricular myocardial infarction in 6 (33%) of 18 patients; 4 patients were from group Ib and 2 from group II.

Patients with right ventricular hypertrophy as a result of chronic lung disease are prone to right ventricular myocardial infarction in the setting of inferior myocardial infarction. Isolated right ventricular myocardial infarction may occur in patients with chronic lung disease, right ventricular hypertrophy and insignificant coronary artery disease. Both increased myocardial oxygen demand and a decreased supply may play a role in this relation.

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Right ventricular infarction is reported in 5 to 43% of patients with transmural inferior infarction of the left ventricle when studied pathologically (1). Prospective clinical studies (2–5) using echocardiographic and scintigraphic methods have confirmed these pathologic observations. The occurrence of right ventricular myocardial infarction in patients with chronic lung disease and right ventricular hypertrophy has not been studied systematically and remains controversial. Although early studies (6) suggested a possible role of right ventricular hypertrophy in the pathogenesis of right ventricular infarction, a large necropsy study by Isner et al. (7) failed to show an association between these two entities.

The purpose of our study was to determine the relation between right ventricular myocardial infarction and right ventricular hypertrophy caused by chronic lung disease. We retrospectively analyzed 28 patients with significant chronic lung disease, coronary artery disease and a documented transmural inferior myocardial infarction and 20 patients with right ventricular hypertrophy secondary to chronic lung disease but without evidence of inferior myocardial infarction or significant coronary artery disease. These patients were studied for pathologic evidence of right ventricular infarction and the clinical relevance of such an event.

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Methods

Study patients. The autopsy records at the Veterans Administration Medical Center, Nashville, Tennessee during the period from 1980 to 1983 were reviewed to select patients with significant chronic lung disease. This diagnosis was based on clinical and physical findings, history of heavy cigarette smoking, biopsy-proven interstitial lung disease, serial chest radiography and pulmonary function tests. All patients with at least three of these five criteria were included in the retrospective analysis. The diagnosis of significant lung disease was confirmed pathologically at autopsy. The majority of the patients selected had been followed up in a cardiology or pulmonary subspecialty clinic with chronic lung disease being their primary diagnosis.

Pathology. The hearts were evaluated for the presence of right ventricular hypertrophy, defined as 5 mm or greater right ventricular wall thickness uniformly measured at the posterior wall of the right ventricle at the level of the inferior border of the posterior tricuspid valve leaflet. Care was taken to exclude papillary muscle in the measurement (8–11). This method for evaluating right ventricular hypertrophy was chosen over chamber partition and weight and area measurements (12,13). In our experience, the epicardial fat is often extensive over the anterior wall of the right ventricle and it is not uniformly possible to separate fat from myocardium. Epicardial fat infiltrates deeply into the myocardium making mass measurements less accurate. Pathologic evidence of inferior myocardial infarction (by gross and microscopic examination) and the presence of significant anatomic atherosclerotic coronary artery disease (defined as 75% or greater reduction in cross-sectional luminal area of the epicardial coronary arteries after postmortem injection of microvascular dye) were noted (14,15). Patients with valvular heart disease, cardiomyopathy or vasculitis were excluded.

Patient groups. On the basis of the criteria outlined, the patients were classified as belonging to one of the following three groups: group Ia = chronic lung disease without right ventricular hypertrophy and with inferior myocardial infarction; group Ib = chronic lung disease with both right ventricular hypertrophy and inferior myocardial infarction; group II = chronic lung disease with right ventricular hypertrophy but without evidence of infarction of the left ventricular myocardium or significant anatomic atherosclerotic coronary artery disease.

The presence or absence of right ventricular myocardial infarction was then noted. Right ventricular myocardial infarction was classified using the pathologic grading system of Isner and Roberts (7) (grade I = ≤50% of the posterior wall of the right ventricle; grade II = limited to the posterior wall but involved ≥50% of it; grade III = all of the posterior wall and ≤50% of the anterolateral wall; grade IV = all of the posterior wall and ≥50% of the anterolateral wall). Medical records were reviewed for clincal data and relevance of such an event without prior knowledge of autopsy data.

Statistical analysis. Data analysis was performed using Student's *t* test and the chi-square. Student *t* test was used to compare relative right ventricular wall thickness between groups. The chi-square was chosen to compare discontinuous variables, that is, incidence of severe coronary artery disease (≥2 vessel) and incidence of right ventricular myocardial infarction. All results were expressed as mean and standard deviation. A probability value of less than 0.05 was considered significant.

Results

Clinical findings (Table 1, Fig. 1). Forty-eight patients were studied; all were male. There was no difference in age (60 ± 10 years) or race in the three groups. Pulmonary function testing was available in the compensated state within 6 months of death in 17 of these patients and results were compatible with severe airways obstruction. The diagnosis of significant chronic obstructive pulmonary disease was confirmed in 43 patients who manifested at least three of the criteria previously outlined. Of the remaining five patients, alpha$_1$-antitrypsin deficiency was present in one and restrictive lung disease in four patients. Diffusion capacity and results of spirometric testing were consistent with severe restrictive lung disease in those four patients (16,17).

Pathologic findings. Pathologic evidence confirming lung disease was present in all 40 of the 48 patients with pulmonary tissue available for study, manifested by severe emphysematous changes or interstitial fibrosis. The relative severity of lung disease among each of the three groups could not be assessed by our postmortem techniques. Right ventricular wall thickness was 3.3 mm ± 0.5 in group Ia (chronic lung disease without right ventricular hypertrophy and with inferior myocardial infarction), 6.0 mm ± 1.1 in group Ib (chronic lung disease with right ventricular hypertrophy and inferior myocardial infarction) and 8.8 mm ± 2.4 in group II (chronic lung disease with right ventricular hypertrophy but without evidence of infarction of the left ventricle or significant coronary artery disease). These values reached statistical significance: group Ia versus Ib, $p < 0.001$; group Ia versus II, $p < 0.001$; group Ib versus II, $p < 0.001$ (Fig. 1).

Extent of anatomic atherosclerotic coronary artery disease present at autopsy (Table 1). There was no significant difference between groups Ia and Ib; however, group II (chronic lung disease, inferior myocardial infarction with right ventricular hypertrophy) had less coronary atherosclerosis on the basis of experimental design, that is, none of the patients in group II had significant anatomic coronary atherosclerosis as defined previously.

Table 1. Characteristics of 48 Patients Studied

Group Ia					Group Ib					Group II				
Case	Age (yr)	RV (mm)	Severe CAD	RVMI	Case	Age (yr)	RV (mm)	Severe CAD	RVMI	Case	Age (yr)	RV (mm)	Severe CAD	RVMI
1	68	3.0	+	+	15	59	5.0	+	+	29	57	7.0	−	+
2	80	3.0	+	+	16	63	5.0	−	+	30	49	10.0	−	−
3	54	4.0	+	+	17	67	6.0	+	+	31	53	10.0	−	−
4	84	4.0	−	−	18	60	6.0	+	+	32	58	7.0	−	−
5	71	3.0	−	−	19	64	6.0	−	+	33	59	10.0	−	−
6	63	3.0	+	−	20	63	5.0	+	+	34	38	12.0	−	−
7	41	3.0	+	−	21	57	6.0	+	+	35	57	12.0	−	−
8	60	3.0	−	−	22	54	6.0	+	+	36	82	10.0	−	−
9	73	2.0	+	−	23	61	5.0	+	+	37	29	12.0	−	−
10	73	3.0	+	−	24	65	7.0	+	+	38	63	6.0	−	−
11	66	3.0	+	−	25	64	5.0	+	+	39	33	11.0	−	−
12	47	4.0	−	−	26	63	9.0	+	−	40	60	6.0	−	−
13	54	4.0	+	−	27	51	7.0	+	−	41	67	7.0	−	+
14	70	4.0	+	−	28	73	6.0	−	−	42	46	11.0	−	−
Total	65 ± 11	3.3 ± 0.5	10/14	3/14		62 ± 5	6.0 ± 1.1*	11/14	11/14*	43	52	5.0	−	−
										44	58	8.0	−	−
										45	58	5.0	−	−
										46	53	11.0	−	+
										47	76	6.0	−	−
										48	56	10.0	−	+
											56 ± 10	8.8 ± 2.4†	0/20	4/20

*$p < 0.008$, $\chi^2 = 7.0$ (group Ia vs. Ib; †$p < 0.008$, $\chi^2 = 7.0$ (group Ia vs. II, group Ib vs. II). Group Ia = chronic lung disease without right ventricular hypertrophy and with inferior myocardial infarction; group Ib = chronic lung disease with both right ventricular hypertrophy and inferior myocardial infarction; group II = chronic lung disease with right ventricular hypertrophy, but without infarction of the left ventricle or significant coronary artery disease. RV = right ventricular thickness; RVMI = right ventricular myocardial infarction; Severe CAD = coronary artery disease with ≥75% cross-sectional area luminal narrowing by atherosclerosis involving ≥2 vessels; + = positive or present; − = negative or absent.

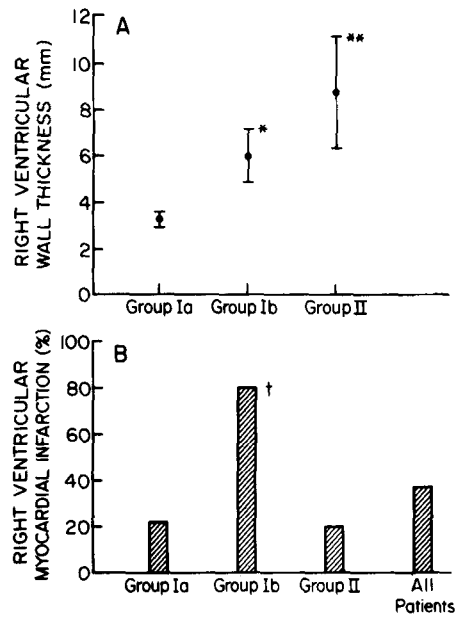

Figure 1. **A**, Right ventricular wall thickness in three groups of patients. Group Ia = chronic lung disease without right ventricular hypertrophy and with inferior myocardial infarction; group Ib = chronic lung disease with both right ventricular hypertrophy and inferior myocardial infarction; group II = chronic lung disease with right ventricular hypertrophy, but without infarction of the left ventricle or significant coronary artery disease (*group Ib versus group Ia, $p < 0.001$; **group II versus group Ib, $p < 0.001$). **B**, Incidence of right ventricular myocardial infarction (†group Ib versus groups Ia and II, $p < 0.008$, $\chi^2 = 7.0$).

Incidence of right ventricular infarction in each of the groups (Table 1, Fig. 1). A total of 18 right ventricular myocardial infarctions were identified; 15 were classified as grade I and 3 were classifed as grade III. Of the latter, two occurred in group Ib patients and one in a group II patient. Patients with inferior myocardial infarction and right ventricular hypertrophy (group Ib) had a significantly higher incidence of right ventricular infarction compared with patients with inferior infarction but without hypertrophy of the right ventricle (group Ia) (11 versus 3, $p < 0.008$, $\chi^2 = 7.0$). There was no significant difference between groups Ia and II in the incidence of right ventricular infarction (three versus four; p = NS).

Significance of right ventricular infarction (Table 2). The cause of death was considered directly related to acute right ventricular infarction in 6 (33%) of 18 patients; 4 were from group Ib and 2 from group II. Three had grade III right ventricular infarction and three had grade I. None of the right ventricular infarctions occurring in group Ia appeared to be directly related to the patient's death. Two of the six patients with right ventricular infarction died immediately after coronary artery bypass surgery (both were in group Ib). Patient 25 could not be weaned from the cardiopulmonary bypass pump. The surgeon noted the right ventricle to be dilated and hypocontractile in comparison with a vigorously contracting left ventricle. Patient 18 experienced cardiovascular collapse immediately after surgery and could not be resuscitated. At postmortem examination, a large, acute, grade III right ventricular infarction was documented. One patient (Case 24) experienced rupture of the right ventricular posterior wall and cardiac tamponade. The other three patients (Cases 15, 19, 48) experienced refractory cardiogenic shock in the setting of acute right ventricular infarction without other explanation for their death.

Discussion

We recently reported a patient (Case 48) with severe restrictive lung disease and right ventricular hypertrophy who died after an isolated grade III right ventricular infarction (18). This led us to investigate whether patients with right ventricular hypertrophy and decreased pulmonary vascular reserve were at increased risk for right ventricular infarction in the setting of an inferior infarction. In this

Table 2. Characteristics of Six Patients Who Died as a Direct Result of Right Ventricular Myocardial Infarction

Case	Age (yr)	Group	Grade RVMI (mm)	RV (mm)	Severe CAD	Comments
48	56	II	III	10.0	–	Cardiogenic shock
29	57	II	I	7.0	–	Cardiogenic shock
25	64	Ib	I	5.0	+	Coronary artery bypass surgery
18	60	Ib	III	6.0	+	Coronary artery bypass surgery
24	65	Ib	I	7.0	+	Right ventricular posterior wall rupture and cardiac tamponade
15	59	Ib	III	5.0	+	Cardiogenic shock

Abbreviations as in Table 1.

study, right ventricular hypertrophy was associated with a significantly higher incidence of right ventricular infarction. This occurred despite a lack of difference in anatomic coronary artery disease demonstrable at necropsy and the presence of transmural inferior myocardial infarction in all 28 patients. The similar extent of anatomic coronary artery obstruction is noteworthy in light of potential differences in collateral blood flow and role of the moderator band artery in determining right ventricular infarct size (19). We also observed that the incidence of right ventricular infarction in patients with right ventricular hypertrophy due to chronic lung disease, but without significant anatomic coronary artery disease (group II), was similar to the incidence in those with chronic lung disease and inferior myocardial infarction but without right ventricular hypertrophy (group Ia). The patients in group II had isolated right ventricular infarction thought to be quite rare (1,20). There was no pathologic evidence of mural thrombus in the left atrium or ventricle of these patients, and histologic sections of the coronary artery did not show evidence of vasculitis. To our knowledge, this is the first report of right ventricular infarction in patients with chronic lung disease and right ventricular hypertrophy without significant anatomic coronary artery disease.

Pathologic studies on right ventricular infarction. Since Wade's necropsy report (6) of 11 patients with right ventricular infarction in 1959, much attention has been focused on this entity, leading to extensive clinical investigation both before and after death. It appears that isolated right ventricular infarction is rare, with an incidence rate ranging from 1.7 to 3.0% in large autopsy series (1,20). However, infarction of the right ventricle is common in patients with left ventricular inferior infarction (average 19%, range 5 to 43) (1,7,14). The incidence of right ventricular infarction in group Ia of our study (21.4%) is consistent with scintigraphic (21) and pathologic data previously cited. However, its incidence in group Ib (78.6%) is much higher than might be expected from other studies.

Several characteristics of patients dying from right ventricular infarction have been identified. There is a high frequency of concurrent inferior left ventricular wall infarction, particularly involving the posterior interventricular septum (7). In addition, most patients have at least a 75% reduction in cross-sectional area of the dominant coronary artery supplying the inferior left ventricular wall (7,13).

The association of right ventricular myocardial infarction with chronic lung disease and right ventricular hypertrophy remains controversial. Wade (6) reported an increased incidence of chronic lung disease, right ventricular hypertrophy and systemic hypertension in patients with pathologic right ventricular infarction. Isner and Roberts (7) were unable to confirm these findings; they noted an association between right ventricular dilation and right ventricular infarction. Horan et al. (13) demonstrated a strong correlation between right ventricular hypertrophy and right ventricular area, the latter an index of right ventricular dilation. Horan and his coworkers referred to these measures of increased right ventricular mass as right ventricular enlargement. They noted 15 patients with gross pathologic right ventricular infarction; 11 of them met criteria for right ventricular enlargement.

Role of right ventricular hypertrophy. In an attempt to investigate the role of right ventricular mass and pressure in the pathogenesis of right ventricular infarction, Ratliff et al. (22) developed a porcine model with pulmonary hypertension and right ventricular hypertrophy by banding the main pulmonary artery trunk. An ameroid constrictor was applied to the right coronary artery to produce infarction of the inferior wall of the left ventricle. These investigators demonstrated a marked increase in susceptibility to right ventricular infarction in pigs with right ventricular hypertrophy due to pressure overload compared with control animals.

Possible pathogenetic mechanisms. Most patients with chronic obstructive lung disease of moderate severity (forced expiratory volume in 1 second and forced vital capacity 65% of predicted) have only a mild increase in pulmonary pressure and pulmonary vascular resistance at rest (23). It may be that transient nocturnal oxygen desaturation (24) or exercise (23), or both, leads to more severe pulmonary hypertension and overt cor pulmonale in some patients with chronic obstructive pulmonary disease. In the patient with cor pulmonale, chronically elevated afterload leads to an increase in right ventricular mass and abnormal compliance. Coronary insufficiency may become manifest in the setting of increased right ventricular mass where a decrease in coronary reserve may already exist. Extravascular compressive forces, owing to the increased mass of the right ventricle and elevated right ventricular filling pressure, may contribute to ischemia. Since patients with chronic obstructive pulmonary disease routinely have high negative intrathoracic pressures, this may further compromise coronary blood flow (25,26). Ultimately, it may be that right ventricular hypertrophy in patients with chronic lung disease is a "marker" for patients who are at risk for developing the clinical syndrome of acute right ventricular infarction, particularly in the setting of transmural inferior myocardial infarction.

Implications. Right ventricular infarction contributes to serum enzyme estimates of infarct size among patients with inferior transmural myocardial infarction and probably accounts for a better prognosis than patients with anterior infarction and similar enzyme elevations (27–29). In our study, death directly related to right ventricular infarction occurred in 33%. This high mortality rate may be the result of selection bias, the retrospective nature of the study or the relatively small number of patients. However, because death directly related to right ventricular infarction occurred only in groups Ib and II, it is reasonable to assume that increased right ventricular mass is the explanation.

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