Clinical and Echocardiographic Characteristics of Papillary Fibroelastomas
A Retrospective and Prospective Study in 162 Patients

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Background—Cardiac papillary fibroelastoma (CPF) is a primary cardiac neoplasm that is increasingly detected by echocardiography. The clinical manifestations of this entity are not well described.

Methods and Results—In a 16-year period, we identified patients with CPF from our pathology and echocardiography databases. A total of 162 patients had pathologically confirmed CPF. Echocardiography was performed in 141 patients with 158 CPFs, and 48 patients had CPFs that were not visible by echocardiography (<0.2 cm), leaving an echocardiographic subgroup of 93 patients with 110 CPFs. An additional 45 patients with a presumed diagnosis of CPF were identified. The mean age of the patients was 60±16 years of age, and 46.1% were male. Echocardiographically, the mean size of the CPFs was 9±4.6 mm; 82.7% occurred on valves (aortic more than mitral), 43.6% were mobile, and 91.4% were single. During a follow-up period of 11±22 months, 23 of 26 patients with a prospective diagnosis of CPF that was confirmed by pathological examination had symptoms that could be attributable to embolization. In the group of 45 patients with a presumed diagnosis of CPF, 3 patients had symptoms that were likely due to embolization (incidence, 6.6%) during a follow-up period of 552±706 days.

Conclusions—CPFs are generally small and single, occur most often on valvular surfaces, and may be mobile, resulting in embolization. Because of the potential for embolic events, symptomatic patients, patients undergoing cardiac surgery for other lesions, and those with highly mobile and large CPFs should be considered for surgical excision. (Circulation. 2001;103:2687-2693.)

Key Words: fibroelastoma ■ echocardiography ■ cardiovascular event

Cardiac papillary fibroelastoma (CPF) is a rare primary cardiac neoplasm of unknown prevalence. Since the introduction of echocardiography, the diagnosis of these tumors in living patients has been reported sporadically. The largest report of pathologically confirmed CPF includes only 17 patients. Echocardiographically, this entity has been described as a small, well-delineated, pedunculated mass with a predilection for valvular endocardium. Case reports have associated CPF with coronary, cerebral, pulmonary, and retinal artery emboli, although the frequency with which this occurs is not well-established.

With improved echocardiographic resolution due to higher frequency transducers and new imaging modalities, small, ill-defined valvular lesions are increasingly recognized. Physicians must be able to decide how to manage such patients with either incidental echocardiographic findings or symptoms that may be attributable to these masses. Therefore, the purpose of this study was to (1) confirm the clinical, pathological, and echocardiographic characteristics of CPF; (2) report the risk of embolic and other complications among patients with presumed CPF; and (3) develop a management strategy for patients with presumed or a definite diagnosis of CPF.

Methods

Study Population
We used the echocardiography and pathology databases at the Cleveland Clinic Foundation between March 1, 1983 and March 31, 1999 to identify patients with a presumed or confirmed diagnosis of CPF. A total of 162 patients with pathologically proven CPF were identified through the pathology database. Twenty-one patients did not undergo transesophageal echocardiography (TEE) or transthoracic echocardiography (TTE), leaving 141 patients with 158 pathologically confirmed CPFs who underwent echocardiography. TTE was available for 126 patients, and TEE was available for 107 patients. Patients ranged in age from 5 to 86 years (mean, 60±16 years), and 65 (46.1%) were male. From this group, echocardiography identified 93 patients with 110 CPFs, of which 26 patients with 30 CPFs were identified prospectively and 67 patients with 80 CPFs were identified retrospectively.
Because all cases were identified retrospectively through the pathology and echocardiography databases, the term prospective refers to the presence of a lesion consistent with CPF identified by echocardiography before surgical confirmation. In this group, CPF may have been identified before or after an embolic event. The retrospective group consists of patients with CPF in whom presurgical echocardiography did not detect a lesion before surgical detection.

A total of 48 patients had CPFs confirmed by pathological examination that were not visible on echocardiograms because these CPFs were extremely small (<0.2 cm). An additional 45 patients with presumed CPF were identified by the echocardiography database and followed for symptoms that may be attributable to CPF. During the study period of >16 years, 109,502 patients had echocardiograms recorded in our database.

Study Methods
Clinical information was obtained from the patients’ medical records, which included data from cardiac catheterization and surgical and pathology reports. Clinical events assessed included transient ischemic attacks, stroke, myocardial infarctions, angina (typical chest pain), and dyspnea. Transient ischemic attacks were attributed to the CPF if patients had no significant carotid or aortic atheroma and no atrial fibrillation or valvular heart disease. Myocardial infarctions, angina, or both were attributed to the CPF if the patient had no significant coronary obstruction.

Echocardiographic studies were reviewed retrospectively from stored VHS videotapes by 2 experienced echocardiographers who were blinded to the presence and location of the tumors. The largest dimension of the tumor, its location, and the length and mobility of a stalk were measured using off-line measurement calipers on an echocardiographic machine (Hewlett Packard Sonos 1500). Associated valvular abnormalities were also assessed.

Clinical follow-up data were obtained from clinical visits, mail surveys, or telephone interviews of patients or their families. The primary clinical end points were embolic events, myocardial infarction, and death over the follow-up period.

A separate case-control study was undertaken to determine the accuracy of echocardiography for the diagnosis of CPF. This group consisted of 86 patients matched by age and valve type that included 41 control patients with no suspicion of CPF and 45 patients with pathological confirmation of CPF (from the group of 93 patients with echocardiographically detectable CPF). All patients underwent surgery and had pathological inspection of their valves. An experienced, blinded echocardiographer reviewed these studies to determine the presence and location of CPF.

Statistical Methods
Data are presented as mean±SD. χ² testing was used to compare differences in the location and mobility of CPFs. ANOVA was used to compare the size of the tumors and their location. Linear regression was used to determine the size of tumors measured by echocardiography and by pathology. P<.05 was considered statistically significant.

Results
Pathological Characteristics
Gross Appearance
CPF have a characteristic frond-like appearance and resemble a sea anemone, especially when placed in saline (Figure 1).

Histology
The tumor is covered by endothelium that surrounds a layer of acid mucopolysaccharide and an inner vascular core of connective tissue (Figure 2). The amount of collagen, smooth muscle cells, and elastic fibers is variable within the connective tissue matrix.

Concomitant Lesions
Of the 141 patients with proven CPFs by echocardiographic studies, 98 (69.5%) had CPFs associated with cardiac valvular disease; among them, 37 patients (37.8%) had rheumatic valvulitis, and 61 (62.2%) had fibrosis and/or calcification. Twelve patients had 19 tumors in the chambers, which were isolated lesions; 31 patients had associated hypertrophic cardiomyopathy, aortic aneurysm, or congenital heart disease.

Echocardiographic Characteristics
Morphology/Appearance
Tumors appeared round, oval, or irregular on echocardiography but were generally well-demarcated and homogenous in appearance. When image quality was optimal, a “speckled appearance” with “stippling” around the perimeter could be seen.2
Accuracy
From the case-control study, the sensitivity and specificity of TTE were 88.9% and 87.8%, respectively, with an overall accuracy of 88.4% for the detection of CPF $\geq 0.2$ cm. A positive diagnosis for the presence and location of a tumor was correct in 40 of 45 patients. A negative diagnosis was consistent with pathology data in 36 of 41 patients. When CPF $\leq 0.2$ cm were included in the analysis, the overall sensitivity of TTE was 61.9% and that for TEE was 76.6%.

Location
Among the 110 CPFs seen by echocardiography, 49 (44.5%) were on the aortic cusp (24 on the right, 6 on the left, and 19 on the noncoronary cusp), with 40 tumors present on the aortic side of the valve and 9 on the ventricular side. Forty tumors (36.4%) were on the mitral leaflets (23 on the anterior and 17 on the posterior leaflet), with 32 on the left atrial surface and 8 on the left ventricular surface (Table 1). Significantly more tumors occurred on the valves than in the chambers (91 of 110, 82.7%, versus 19 of 110, 17.3%; $P<0.001$).

Size
The size of the tumors ranged from 2 to 28 mm (mean, $9\pm4.6$ mm; median, 8 mm) for the largest dimension. A total of 99% were $\leq 20$ mm. The masses in the cardiac chambers were larger than those on the aortic or mitral valves ($12.0\pm4.6$ mm versus $8.5\pm4.4$ mm in diameter, respectively; $P<0.001$). Tumors diagnosed prospectively were larger than those diagnosed retrospectively. Examples of CPFs are shown in Figures 3 and 4. The largest diameters of CPF were compared in a random sample of 45 patients by pathology and echocardiography with good correlation ($r=0.87$, $P<0.001$; Figure 5).

Stalks and Mobility
Of 110 tumors, 48 (43.6%) had a stalk from 1 to 3 mm in length, and all of these were mobile. No tumors without stalks were mobile. All 19 CPF in the chambers were mobile, as were 29 of the 91 on a valvular surface (31.9%).

Numbers
Single lesions were detected by echocardiography in 85 patients (91.4%). Multiple CPFs (range, 2 to 8) were detected...
in 8 patients (8.6%). One patient had 8 tumors observed in various locations on the right and left sides of the heart.

Valvular Function
Of the 26 patients with a prospective diagnosis and pathological confirmation, 23 had CPFs on valves with normal function. In no patient was the CPF thought to be responsible for valvular dysfunction. Of the 67 patients with a retrospective diagnosis and pathological confirmation, 62 had severe valvular disease, and all of these patients had CPFs on the dysfunctional valve. The CPFs in this latter group were smaller and tended not to be mobile (Table 1).

Clinical Features
Table 2 lists the clinical features of patients with pathologically diagnosed CPF in comparison with the group with presumed CPF. During a follow-up period of 11 ± 22 months, among 26 patients with a prospective diagnosis of pathologically confirmed CPF, 23 patients had symptoms that could be attributable to embolization. Three of 45 patients with presumed CPF had symptoms that could be attributed to possible embolization of the tumor (incidence, 6.6%). The mass could no longer be detected in 2 patients at follow-up, and these patients remained asymptomatic. Four patients were lost to follow-up.

Follow-Up Data
Echocardiographic follow-up data were available for 64 of 141 patients (45.4%) after surgical excision. The average follow-up time was 630 ± 903 days (range, 10 to 3639 days; median, 130 days). No mass was detected by echocardiography in any patient during the follow-up period.

Clinical follow-up data were available for 110 of the 141 patients (78%). The average follow-up time was 2269 ± 893 days (range, 10 to 4176 days; median, 1221 days). Thirty-nine patients died of disease processes unrelated to CPF (36 died of congestive heart failure, 2 of cancer, and 1 of pneumonia). The remaining 71 patients were in stable condition, without symptoms related to emboli, during the follow-up period.

Figure 3. A papillary fibroelastoma attached to the aortic side of the noncoronary cusp of the aortic valve, as seen by TEE in the midesophageal short-axis.

Figure 4. A papillary fibroelastoma in the right ventricular outflow tract, as shown by TEE. This tumor at its largest dimension was 1.8 cm.

Figure 5. Comparison of tumor size measured by pathology and echocardiography in a subgroup of 45 patients showing a good correlation of echocardiography for tumors ≥ 0.2 cm. Solid line represents regression; dashed line is line of identity.
Tumors arising from the right atrium are described in only 3 cases.3,48 It is readily apparent that the lower rate of right-sided detection is likely due to a lack of symptoms from right-sided embolization and under-reporting due to uncommon excision of right-sided valves or entry to the right heart. This common location of the tumor suggests a potential for dynamic coronary ostial obstruction leading to myocardial ischemia.

Mitrale valve was the next most common location of involvement in published data, with tumors occurring on the anterior or posterior leaflets, the chordae, and the papillary muscles.1,4,10,21–36 When an atrioventricular valve is involved, the tumor was most often on the atrial side of the valve, as found in our study.4 Along the valve leaflet, the most common site of occurrence was in the midportion, well away from the free edge or the annulus.4 There are also occasional reports of tricuspid37–41 and pulmonic valvular CPF,42,43 and in our study, all of the masses in chambers were mobile. Stalks and mobility were present in most patients with a prospective diagnosis of CPF; therefore, as expected, these traits may be associated with the likelihood of embolization.

### Echocardiographic Characteristics

We found that there are typical echocardiographic features of CPF. These include the following: (1) the tumor is round, oval, or irregular in appearance, with well-demarcated borders and a homogeneous texture; (2) most CPFs are small (99% were <20 mm in the largest dimension); (3) nearly half of CPFs had small stalks, and those with stalks were mobile; (4) CPFs may be single or multiple lesions and are most often associated with cardiac valvular disease. These echocardiographic characteristics have not been reported previously in a large group of patients, but they are consistent with published case descriptions.2,6,11–29

### Tumor Locations

Approximately 90% of the CPFs reported in the literature were attached to valves,3,4 and the majority were on the aortic valve.1 For the aortic valve, no predilection for the tumor to appear on the aortic or the ventricular side has been reported.4 In the present study, 49 of the 110 CPFs (44.5%) were attached to the aortic valve, predominantly on the aortic side. This common location of the tumor suggests a potential for dynamic coronary ostial obstruction leading to myocardial ischemia.

### Discussion

Diagnosis of CPF

As previously described, we found that CPFs were usually <20 mm in their largest diameter. The largest reported CPF is 40 mm.49 The mobility of CPFs has also been a typical feature, with 17 of 18 tumors having independent mobility and an identifiable stalk in one analysis.2 In our study, all of the masses in chambers were mobile. Stalks and mobility were present in most patients with a prospective diagnosis of CPF; therefore, as expected, these traits may be associated with the likelihood of embolization.

Clinical Features

The findings of our study were consistent with prior studies with regard to the clinical profile and presentation of patients with CPF. As in other reports that have detected CPF in neonates and patients as old as 92 years,3,11,30,50 we found a wide distribution of age. Although CPFs are often diagnosed incidentally, neurological events,7,21,26,51,52 sudden death,53,54 angina,8 acute myocardial infarction,5,14,15,23,54 pulmonary emboli,9 and retinal artery embolism10 related to CPF have been reported. In the present study, CPFs were diagnosed incidentally in many patients with another underlying cardiovascular disease who were asymptomatic. Among the patients who had prospectively diagnosed CPF, underlying heart disease was uncommon, and detection occurred related to a search for the cause of the symptoms. This fact suggests that isolated tumors may easily “shed into the blood stream,” whereas tumors fixed by a combined lesion are not easily shed.

The potential for suspected CPF to cause symptomatic embolization was also demonstrated in this study. After follow-up of 45 patients with the echocardiographic diagnosis of CPF, stroke occurred in one patient (48-year-old woman) who had a mobile CPF on the mitral anterior leaflet and no other cardiovascular disease. Transient ischemic attacks occurred in 2 patients: one of them a (34-year-old woman) had a mobile CPF on aortic noncoronary cusps and no other valvular disease.

Diagnosis

With the increased use of 2D TTE, CPF are detected during life and are occasionally found in patients without symptoms.5,33 Echocardiography is a convenient and noninvasive diagnostic technique and should be the first choice of tests to search for CPFs.45,52 TEE is an important tool for delineating the extent and anatomic attachment of these small tumors because only this technique allows optimal high-resolution imaging. However, many CPF go undetected by echocardiography. The reasons echocardiography may fail to diagnose tumors include the following: (1) the tumor was masked by an associated lesion; (2) the tumor was too small to be seen; (3) the examination was not done carefully with a sufficient index of suspicion; or (4) there were no significant characteristics to differentiate the CPF from the degenerative valve disease.

### Postsurgical Follow-Up

To our knowledge, there is no information regarding recurrence of CPF after surgical excision as detected by echocar-
diography. In the present study, 64 patients (42.4%) had echocardiographic follow-up at an average 630 days after surgery. No patients were found to have recurrent CPF, although most studies used TTE.

Limitations
The presence of a patent foramen ovale in patients with CPF who had an embolic event was not determined. Because paradoxical embolism through a patent foramen ovale cannot be excluded, the incidence of embolism due to CPF may be overestimated.

Management
On the basis of our findings and a review of the literature, we recommend the following guidelines for the assessment and management of patients with CPF. Patients with events that may be embolic in nature and are not explained by other cardiovascular or neurological diseases should undergo TTE and TEE if necessary to exclude cardiac sources of emboli, including CPF. A mass seen by echocardiography should be characterized by size, shape, location of attachment, mobility, presence of a stalk, and multiplicity. Although the differential diagnosis may still include vegetations (infective or noninfective), thrombi, degenerative valve tissue, and other benign tumors, these lesions can often be differentiated by clinical information, blood cultures, and laboratory tests. Because the presence of a stalk and associated mobility is a significant predictor of embolic risk, patients with presumed CPF, especially if left-sided, should undergo TEE to determine if a stalk is present.

Decisions regarding the primary surgical excision of CPF depend on the size, location, mobility, and potential or strength of association of the tumor with symptoms. Excision of isolated right-sided CPFs is indicated only for large mobile tumors, including those that result in obstruction or embolization that is hemodynamically significant. The presence of a patent foramen ovale with a sizeable right-to-left shunt is an additional consideration for management of right-sided CPF. Asymptomatic patients with small, left-sided, nonmobile (no stalk) CPFs are usually observed. However, larger (≥1 cm) CPF, especially if mobile, should be considered for excision, especially if other cardiovascular disease is detected or the patient is young, with low risk of surgery and a high cumulative risk for embolization. Patients with residual tumors who have had an embolic event should similarly be considered for excision, depending on the risks of surgery and other cardiovascular indications. Isolated CPF excision of aortic or mitral valve lesions can often be performed through a minimally invasive approach, with no damage to the valve. Incidentally detected CPF in patients undergoing cardiac surgery should generally be removed unless they add substantial time and risk to the operation that cannot be justified based on size, location, and mobility. No data exist to evaluate the efficacy of anticoagulation or antiplatelet therapy for patients with CPF, although it is speculated that deposition of thrombotic material on the tumors may add to the risk of microembolization.

Summary
The echocardiographic characteristics of CPF have been confirmed in a large series and allow for differentiation from ill-defined masses seen on routine studies. Although symptoms related to fibroelastomas are uncommon, there is a potential for serious morbidity, particularly among patients with large, mobile, left-sided lesions. Therefore, the presence of tumors should be determined in patients with symptomatic unexplained cardiac or neurological events. Consideration for surgical excision should be given to those patients, whether asymptomatic or symptomatic, especially those with a high cumulative risk of embolization and a low risk for surgery.

Acknowledgment
Supported in part by grant NCC9-60 from the National Aeronautics and Space Administration, Houston, Tex.

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Circulation. 2001;103:2687-2693
doi: 10.1161/01.CIR.103.22.2687

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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