Features of Carcinoid Heart Disease Identified By Two- and Three-Dimensional Echocardiography and Cardiac Magnetic Resonance Imaging.

Sanjeev Bhattacharyya MB ChB MRCP 1, Christos Toumpanakis MD PhD 2, Margaret Burke MD FRCPath 3, Andrew M Taylor MD FRCP FRCR 4, Martyn Caplin Bsc(Hons) MD FRCP 2, Joseph Davar MRCP MD PhD 1

1 Carcinoid Heart Disease Clinic, Department of Cardiology, Royal Free Hospital, London, UK
2 Neuroendocrine Tumour Unit, Royal Free Hospital, London, UK
3 Department of Pathology, Harefield Hospital, Harefield, Middlesex, UK
4 Centre for Cardiovascular MR, UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, UK

Journal Subject Codes: [19] Valvular heart disease; [30] CT and MRI; [31] Echocardiography

Address for Correspondence:
Dr. J Davar
Department of Cardiology,
Royal Free Hospital, Pond Street,
London, NW3 2QG, UK.
Phone: 0207 794 0500 Fax: 0207 472 6881
E-mail: joseph.davar@royalfree.nhs.uk
ABSTRACT

Background: Carcinoid heart disease is a rare form of valvular heart disease (VHD). We sought describe the spectrum of carcinoid heart disease identified by echocardiography and cardiac magnetic resonance imaging.

Method and Results: 252 patients with carcinoid syndrome underwent a range of investigations including two-dimensional (2D) transthoracic echocardiography (TTE), three-dimensional (3D) TTE and transoesophageal echocardiography (TEE) and cardiac magnetic resonance imaging (CMR). 52 patients had evidence of carcinoid heart disease. Involvement of the tricuspid, pulmonary, mitral and aortic valves were found in 47(90%), 36(69%), 15(29%) and 14(27%) respectively. Myocardial metastases were found in 2 (3.8%) of patients. Several patterns of disease were identified depending on the extent and severity to which each leaflet and its associated sub-valvular apparatus was affected. 13 out of 15 (87%) patients with left sided carcinoid involvement had a patent foramen ovale. Three patients with severe degree of shunting had severe valvular regurgitation. Patients with mild/moderate degree of shunting had mild or moderate valvular regurgitation. 3D TTE/TEE provided detailed anatomical information particularly for the TV and PV. CMR allowed complimentary assessment of VHD and delineation of myocardial metastases. Gallium-68 octreotate positron emission tomography (PET) identified neuroendocrine metastases.

Conclusion: Carcinoid heart disease is a heterogeneous disease with a wide spectrum of echocardiographic findings. A multi-modality approach is needed in patients with this complex pathology.

KEY WORDS: valves, heart disease, carcinoid
BACKGROUND

Carcinoid tumours occur in between 2.5 and 5 cases per 100,000 of the population. Carcinoid syndrome is thought to occur when the tumour metastases to the liver allowing high levels of 5-hydroxytryptamine (5-HT) to reach the systemic circulation. Manifestations of the syndrome include flushing, diarrhoea, bronchospasm and the development of carcinoid heart disease (1).

5-HT is thought to promote deposition of plaques composed of myofibrocytes onto the endocardial surfaces of the heart. Cardiac involvement is commonly manifested by the development of right sided valvular dysfunction. Characteristic changes include thickening of valve leaflets/cusps which become retracted and eventually immobile, resulting in a combination of valvular regurgitation and stenosis (2, 3).

Significant advances in echocardiography, including the development of transoesophageal (TEE) and three-dimensional (3D) echocardiography, have allowed greater understanding and assessment of valve pathology (4). Secondly, newer imaging modalities such as cardiac magnetic resonance (CMR) imaging have emerged which may allow complimentary assessment of cardiac pathology (5).

The purpose of this study is to describe the echocardiographic features of carcinoid heart disease identifying features of both early and advanced disease and to ascertain the value of advanced echocardiographic techniques and other imaging modalities.

METHODS

Patients
Patients with carcinoid syndrome were consecutively and prospectively enrolled between April 2006 and December 2008. The diagnosis of carcinoid tumour was based on histological examination of either primary tumour or liver metastases biopsy. The protocol was approved by the institution’s ethics committee. All patients gave written, informed consent.

**Echocardiography**

All patients underwent comprehensive two-dimensional (2D) transthoracic echocardiography (TTE). Additional 3D TTE was performed after the 2D study from 2008 onwards. 3D TEE was performed where transthoracic windows were not suitable for full evaluation of heart valves and there was clinical suspicion of valvular heart disease or as part of pre-operative assessment prior to valve surgery.

**Two-dimensional echocardiography**

Two-dimensional TTE were performed in all patients using commercially available echocardiography machines (Siemens Acuson C512 and Philips iE33). Valve morphology and function was evaluated in several views. Valve regurgitation severity and quantification were assessed and graded according to The American Society of Echocardiography (ASE) guidelines (6). Valve stenosis was quantified according American College of Cardiology Guidelines (7). Pulmonary stenosis was graded (according to peak gradient across valve) as mild (<25mmHg), moderate (25 - 50mmHg) or severe (>50mmHg). Tricuspid stenosis was graded (mean gradient across valve) as mild (1 - 5mmHg), moderate (5 - 8mmHg) or severe (>8mmHg). Right and left ventricular function and sizes were assessed and calculated according to ASE guidelines(8).

All echocardiograms were reviewed by two cardiologists experienced in echocardiography (SB, JD). The abnormalities described are based on the consensus of
the two reviewers. Carcinoid heart disease was defined as the presence of characteristic thickening, reduced excursion or retraction of valvular leaflets (with associated evidence of valvular stenosis or regurgitation), or the presence of myocardial metastases, in the absence of other aetiologies.

**Contrast Echocardiography**

All patients were assessed for the presence of a patent foramen ovale using “microbubble” contrast at rest and with cough and Valsalva manoeuvre. The presence of patent foramen ovale was defined as the presence of at least 3 microbubbles in the left atrium within 3 cardiac cycles of contrast visualisation in right atrium. The degree of shunting was classified as mild if 3-9 microbubbles appeared, moderate if 10 to 30 microbubbles appeared and large if more than 30 microbubbles appeared (9).

**Three-dimensional transthoracic echocardiography**

Three-dimensional TTE was performed using Phillips iE33 equipped with X3-1 transducer (Philips Medical Systems, Andover, Massachusetts) after 2D examination was complete. Full volume, 3D zoom and live datasets were obtained from parasternal, apical views and subcostal views. Full volume acquisition was performed over 5 cardiac cycles with breath hold. Image rendering was performed after the procedure. Pyramidal datasets were cropped along x,y,z axes or manually using the cropping plane of choice. Gain settings, smoothing and brightness were adjusted to optimise visualisation of valve and valvular apparatus.

**Transoesophageal echocardiography**

Transoesophageal echocardiography was performed using Phillips iE33 equipped with a X7-2t transducer. Multi-plane 2D TEE evaluation was completed followed by acquisition of a 3D dataset. A live 3D zoom and full volume dataset was obtained. Images were rendered in the same way as for transthoracic echocardiography.
Cardiac magnetic resonance imaging

CMR was undertaken using commercially available 1.5 Tesla MR scanners. Steady state free precession and gradient echo pulse sequences were used to assess valve morphology, ventricular function and to detect valvular regurgitation. By using phase contrast sequences, the forward and regurgitant volumes were calculated from phase-encoded velocity maps. Delayed enhancement gadolinium images were acquired to assess myocardial involvement.

Statistical Analysis

Data are expressed as either median and (first – to – third quartile) or number and percentage. The Mann-Whitney U test was used to compare continuous variables between groups. The Chi squared test was used to compare groups regarding categorical variables; when a cell frequency was less than five, the Fisher exact test was used. All tests of significance were two sided. A probability value (p) of <0.05 was considered statistically significant. Statistical analysis was performed using StatsDirect Version 2.5.7 (StatsDirect, United Kingdom).

RESULTS

Two hundred and fifty-two patients were recruited over the study period and underwent 2D TTE. Fifty-two patients were found to have abnormalities consistent with carcinoid heart disease. 100 patients (40 patients with carcinoid heart disease) underwent additional 3D TTE. Twenty-two patients with carcinoid heart disease underwent 3D TEE and 10 patients with carcinoid heart disease had a CMR study.

There were no significant differences in age, sex, tumour characteristics or treatments received between those patients with or without carcinoid heart disease. Significantly higher levels of urinary 5-hydroxyindolacetic acid and plasma Chromogranin A were found in patients with carcinoid heart disease (Table 1).
Right ventricle, atrium and tricuspid valve

Abnormalities of the tricuspid valve were found in 47 (90%) patients with carcinoid heart disease. The mildest changes were thickening of the valve leaflets and subvalvular apparatus. The normal concave curvature of the leaflets was diminished causing them to become straightened. The dynamic motion of the leaflet during diastole was altered. The leaflets moved in a stiff “board like” fashion rather than the normal undulating motion. Only trivial or mild centrally directed tricuspid regurgitation was noted.

Thickening of the valve leaflets was associated with thickening of the chordae and papillary muscles. Chordae may become fused and shortened. This was associated with greater degrees of retraction and reduction excursion of the valve cusps. The extent to which each leaflet and subvalvular apparatus was affected was variable and produced several patterns of disease (Figure 1).

In the most severe cases leaflets were fixed, retracted and did not co-apt. This was associated with severe tricuspid regurgitation with a characteristic “Dagger shaped Doppler” profile and mild or moderate tricuspid stenosis (median gradient 3.5mmHg (interquartile range 2.9mmHg – 4.3mmHg). RV was dilated in 28 (93%) patients with severe tricuspid regurgitation (median 3.9cm (interquartile range 3.6cm – 4.2cm). The right atrium was enlarged in all patients with severe tricuspid regurgitation (median 26cm² (interquartile range 22cm² – 27cm²) (Figure 1).

Three dimensional TTE visualisation of the tricuspid valve allowed an en-face view of the valve from either atrial or ventricular side to be obtained. In 22 patients, all three leaflets were thickened and fixed in a semi-open position. This caused a large area of non-coaptation. Detailed delineation of sub-valvular structures was obtained. Gross thickening, shortening and fusion of chordae together with papillary muscles was
observed (Figure 2). The ability to visualise all three leaflets simultaneously allowed comparison between leaflets. Three patients had involvement of an isolated septal leaflet. This leaflet was thickened, retracted and fixed with preservation of mobility of anterior and posterior leaflets. This caused mal-coaptation of the cusps. Typically the tip of unaffected leaflet met the body of the affected leaflet. This was associated with a moderate, eccentrically directed jet of tricuspid regurgitation.

2D and 3D TEE assessment of the tricuspid valve allowed visualisation of valve leaflets in all patients who had poor transthoracic windows. Eighteen (90%) of patients with carcinoid heart disease who underwent TEE had thickened right ventricular endocardium with probable deposition of carcinoid plaque (Figure 2).

**Pulmonary valve**

Abnormalities of the pulmonary valve were found in 36 (69%) of patients with carcinoid heart disease. Changes in valve morphology were similar to the tricuspid valve. With mild involvement, valve cusps were diffusely thickened which caused them to become straightened. With more severe disease varying degrees of retraction and reduction in excursion of valve cusps was seen. In severe cases valve cusps were fixed, retracted and thickened with severe pulmonary regurgitation. The characteristic sharp deceleration slope of severe pulmonary regurgitation was seen. The peak velocity through the pulmonary valve ranged from 1.6 to 3.8 metres per second (Figure 1).

3D TTE allowed identification of all three pulmonary valve cusps simultaneously. In two patients 3D TTE demonstrated marked thickening of a single cusp of the pulmonary valve (demonstrating probable carcinoid plaque deposition) with the other two cusps unaffected (Figure 3). These abnormalities were not on identified on 2D images. Additionally 3D TTE allowed the anatomical relationship between all three leaflets and...
endocardial surfaces as well as the degree of coaptation of the cusps to be assessed. In patients with severe disease 3D TTE demonstrated constriction of the pulmonary valve annulus with thickened, partially retracted and fixed pulmonary cusps causing non-coaptation of the cusps and significant stenosis. Post-stenotic dilatation of the pulmonary artery was seen. In three patients the arterial surfaces of the pulmonary valve cusps were grossly thickened to the extent they completely filled the valve sinus. This made it difficult to demarcate the valve cusps from underlying endocardium (Figure 3).

3D TEE provided anatomic information regarding relationship of the all three pulmonary valve cusps including the relationship of cusps to the ventricular walls, mobility and thickness as well as allowing assessment of pulmonary valve annulus constriction and visualisation of right ventricular outflow tract and pulmonary artery.

**Left sided heart valves and foramen ovale**

Fifteen (29%) patients had left sided valvular involvement. Thirteen (87%) of these were associated with a patent foramen ovale. The two patients with left sided disease but without patent foramen ovale both had multiple bronchial carcinoid metastases. Three patients with a severe degree of shunting on their bubble contrast had severe mitral and/or aortic valve regurgitation. The remaining 10 patients with mild or moderate degree of shunting had mild or moderate mitral or aortic regurgitation.

**Aortic Valve**

Aortic valve involvement was seen in 14(27%) cases of carcinoid heart disease. Diffuse thickening of valve cusps was identified together with mild aortic regurgitation. One patient had gross thickening of the non coronary cusp with mild thickening of right coronary cusp. Two patients had severe aortic regurgitation. Visualisation of the valve cusps was poor on 2D TTE but they were clearly thickened. On 2D TEE gross
thickening, retraction of all three leaflets which were almost fixed leading to non-
coaptation of the leaflets was found (Figure 4).

**Mitral Valve**

Mitral valve involvement was seen in 15 (29%) patients with carcinoid heart
disease. Similar to the aortic valve, patients had diffuse thickening of both leaflets
although one patient had a nodular like involvement. Trivial or mild mitral regurgitation
was present.

Three patients had grossly thickened papillary muscles and shortened chordae.
This caused tenting of the mitral valve leaflets and associated severe mitral regurgitation.
Although leaflet mobility was restricted no significant stenosis was seen. 2D and 3D TEE
enabled detailed assessment of the sub-valvular apparatus and visualise valve anatomy.
(Figure 4).

**Myocardial metastases**

Myocardial metastases were detected in 2 (3.8%) of patients with carcinoid heart
disease. One patient with valvular involvement had a 1.2cm X 10mm metastasis in the
right atrium and one patient without valvular involvement had multiple metastases in the
inferior (3.3cm X 2.2cm) and anterior walls (4.1cm X 2.9cm and 3.4cm X 5.6cm) as well
as basal septum of the left ventricle. Two dimensional TTE and TEE allowed
visualisation of the cardiac masses. However only an estimate of their diameter could be
obtained as it was difficult to demarcate the mass from surrounding myocardium. Three
dimensional TTE demonstrated better delineation of the mass to adjacent structures.
CMR allowed identification of location, number, size and relationship of cardiac
metastases to surrounding structures. Gallium-68 octreotate positron emission
tomography (PET) demonstrated avid focal uptake in the two masses suggesting
metastastic spread (Figure 5).
Cardiac Magnetic Resonance Imaging

Ten patients with carcinoid heart disease underwent CMR (Figure 6). Eight patients had dilated RV and 2 patients had impaired RV function. CMR demonstrated thick, fixed, retracted leaflets which did not co-apt in all 10 patients. Quantification of tricuspid regurgitation was severe in all cases. One patient had mild tricuspid stenosis.

Eight out of ten patients had thickened pulmonary valve cusps with restricted motion. All of these patients had either mild or moderate pulmonary stenosis. Five of these patients had mild pulmonary regurgitation and three had moderate pulmonary regurgitation. No patient demonstrated myocardial involvement on late gadolinium enhancement imaging.

Pathological Correlation

Twenty-one patients with carcinoid heart disease underwent cardiac valve replacement surgery. Gross morphological and histological examination of the excised valves was performed in all patients. The identification of carcinoid heart disease in individual valves by echocardiography correlated with findings at pathological examination.

In one patient with severe right sided valvular dysfunction, echocardiography demonstrated diffuse thickening of MV leaflets and chordae with trivial regurgitation (Figure 4C +D). At the time of surgery, visual inspection identified features of carcinoid heart disease in this valve, therefore MV replacement was performed in addition to TV and PV replacement. Histological examination confirmed the diagnosis. In one patient (with bronchial in addition to liver metastases) with severe left sided valvular dysfunction, echocardiography demonstrated mild thickening and retraction of PV and TV. This was associated with mild PS and moderate TR. The patient underwent
replacement of all 4 valves. Histological examination confirmed carcinoid involvement of all valves.

**DISCUSSION**

This study describes the features of carcinoid heart disease encompassing the spectrum of disease from early to advanced disease and encompassing both two dimensional and three dimensional echocardiography as well as CMR and PET imaging.

Echocardiography remains pivotal in the investigation of patients with carcinoid syndrome and suspected carcinoid heart disease. The classical features of advanced carcinoid heart disease typically involving the tricuspid valve and pulmonary valve have been well-described (3, 10, 11). However the spectrum of disease is wide.

In this study we have identified several patients with diffuse thickening of valve leaflets or isolated thickening of a single valve leaflet without significant reduction in leaflet mobility or the development of valvular regurgitation. Histological examination in two of these patients demonstrated changes typical of carcinoid heart disease. Therefore, these findings may represent the early stages of carcinoid heart disease.

We have demonstrated greater involvement of the sub-valvular apparatus and valve leaflets can lead to a wide heterogeneous array of appearances and functional consequences. These findings are in keeping with previous necropsy studies (12), where the location, extent and pattern of “plaque” deposition on valvular and sub-valvular structures is highly variable with both focal and diffuse patterns of plaque deposition described.

Advanced techniques such as 3D TTE or 3D TEE are helpful in identifying and assessing valve pathology, particularly in the pulmonary and tricuspid valve, as all
leaflets may not be visualised on 2D echocardiography. The ability to crop images and change the plane of view allowed detailed assessment of the sub-valvular apparatus and delineation of the relationship between valve leaflets to each other and surrounding structures and the endocardium.

CMR can be a valuable adjunct in the investigation of these patients particularly where echocardiographic windows are poor or structures such as the pulmonary value are difficult to visualise. Morphological features of severe carcinoid heart disease can be delineated with assessment of valvular regurgitation, stenosis and quantification of ventricular volumes. CMR enables measurement of size of metastases and is able to offer information regarding extension into extracardiac structures which is not available on echocardiographic techniques.

Cardiac metastases from carcinoid tumour are rare. In this study 4% of patients had cardiac metastases. Although echocardiographic and CMR techniques may be able to accurately identify and characterise the mass they are not able to elucidate whether it is a carcinoid metastases or another primary cardiac tumour. Carcinoid tumours express several somatostatin receptors, particularly receptors 2 and 5. Gallium-68 octreotate PET utilises a somatostatin analogue labelled with gallium-68 tracer. Neuroendocrine tumour cells will take up the somatostatin analogue and this will be visible on PET as it is labelled with Gallium-68. Recent data suggest greater than 97% sensitivity and 92% specificity of Gallium-68 octreotate PET for metastatic deposits in patients with neuroendocrine tumours (13).

A limitation of the present study is pathological correlation was not available in all patients. This was because patients with mild abnormalities or those with progressive carcinoid tumour would not undergo valve replacement surgery. The number of patients studies may seem relatively small, however, given the relative rarity of the condition this
represents one of the largest cohorts of carcinoid patients studied and a full range of pathology has been described.

**CONCLUSIONS**

Carcinoid heart disease is a heterogeneous disease with a wide spectrum of echocardiographic findings. An integrated approach using multiple modalities should be adopted in patients at risk of developing carcinoid heart disease in order to identify pathology and assess severity of disease.

**Conflicts of Interest/Disclosure:** None
REFERENCES


Table 1. Baseline Demographics

<table>
<thead>
<tr>
<th></th>
<th>Carcinoid Heart Disease</th>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present (n = 52)</td>
<td>Absent (n = 200)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>64 (55 - 69)</td>
<td>64 (58 - 71)</td>
<td>0.4</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>28 (54%)</td>
<td>98 (49%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Duration of diagnosis (months)</td>
<td>5 (1 - 6)</td>
<td>4 (3 - 6)</td>
<td>0.42</td>
</tr>
<tr>
<td>Tumour Grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>48 (92%)</td>
<td>194 (97%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Intermediate</td>
<td>4 (8%)</td>
<td>6 (3%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Presence of Liver Metastases</td>
<td>50 (96%)</td>
<td>171 (86%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Chromogranin A (pMol/L)</td>
<td>1000 (655 - 1000)</td>
<td>140 (56 - 484)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Urinary 5-hydroxyindolacetic acid (μMol/24 hours)</td>
<td>800 (399 - 1490)</td>
<td>42 (0 - 205)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Therapies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatostatin Analogue</td>
<td>48 (92%)</td>
<td>161 (81%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Interferon</td>
<td>2 (4%)</td>
<td>8 (4%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>6 (12%)</td>
<td>13 (7%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Surgery</td>
<td>19 (37%)</td>
<td>98 (49%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Targeted Radionuclide</td>
<td>18 (35%)</td>
<td>52 (26%)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Data are expressed as median and interquartile range or number (%). Picomoles per litre (pMol/L), Micromoles (μMol).
FIGURE LEGENDS

Figure 1. Two dimensional transthoracic echocardiogram. Right atrium (RA), right ventricle (RV), right ventricular outflow tract (RVOT), pulmonary artery (PA).

A. Diffuse thickening of septal and anterior tricuspid valve (TV) leaflets (arrow) and chordae. Leaflets are “stiffened” and “board like” and lose their normal curvature. Good excursion of the leaflets was present. Trivial/mild tricuspid regurgitation was present.

B. Fixed, thickened septal leaflet of tricuspid valve tethered to ventricular endocardium (arrow). Anterior leaflet, although thickened had good excursion (dashed arrow). The tip of anterior leaflet meets body of septal leaflet in diastole causing an eccentric jet of moderate tricuspid regurgitation.

C. Tricuspid valve (TV) leaflets (arrow) are thickened, fixed and retracted. This patient had “free flowing” severe tricuspid regurgitation. Both right atrium and right ventricle are dilated.

D. Mild thickening of pulmonary valve cusps. The cusps are “straightened” and lose their normal curvature.

E. Grossly thickened, fixed, and retracted pulmonary valve (PV) cusps (arrow) which do not co-apt.

F. Continuous wave Doppler demonstrating pulmonary stenosis (PS) with a peak gradient of 58 mmHG and peak velocity of 3.8 metres per second and the steep deceleration slope of severe pulmonary regurgitation (PR).

Figure 2. Three dimensional Transthoracic Echocardiogram.

A. View from the right atrium. Visualisation of anterior, septal and posterior tricuspid valve (TV) leaflets (arrow). Thickened tricuspid valve leaflets fixed and retracted towards ventricular walls.
B. Thickening, shortening and fusion of chordae tendinae (dashed arrow) and grossly thickened papillary muscles (arrow).

C. Resected tricuspid valve of patient in panel B. Papillary muscle encased in carcinoid “plaque”. Thickening and fusion of chordae tendinae. Histology confirmed plaque composed of myofibroblasts.

D. View from the right ventricle apex. Thickened tricuspid valve (TV) leaflets (arrow) fixed in a semi-open position. Large area of non-coaptation.

E. Transoesophageal echocardiogram demonstrating carcinoid involvement of tricuspid valve (TV) (arrow). Thickened endocardial surface of the right ventricle with carcinoid plaque deposition (black dashed arrow).

**Figure 3.** Three dimensional echocardiography of pulmonary valve. Right ventricular outflow tract (RVOT), pulmonary artery (PA).

A. Thickened, fixed and retracted pulmonary valve (PV) cusps (arrow) coupled with constriction of pulmonary valve annulus causing severe pulmonary stenosis. Pulmonary valve (PV) cusps do not co-apt leading to a large area of non-coaptation (dashed arrow).

B. Post stenotic dilatation of the pulmonary artery (dashed arrow) in a patient with carcinoid involvement of the pulmonary valve (PV) and severe pulmonary stenosis. Pulmonary valve sinus obliterated and fused with valve cusp (arrow).

C. Resected pulmonary valve of patient in panel B. Gross, nodular thickening of valve cusp causing obliteration of valve sinus (arrow). The normal cusp (*) just being discernable on the ventricular surface of the nodule. Inset upper right. Histopathological examination. Thickening of valve cusp is due almost entirely to deposition of myxoid tissue on the arterial surface of the cusp (arrow) which has otherwise retained its normal structure and shape (*) (Alcian Blue – Elastic Van Gieson). Inset lower right. Myxoid
tissue is due to proliferation of myofibroblasts, shown here as brown-staining spindle cells with an antibody to smooth muscle actin (arrow). The cusp itself (*) does not stain with this antibody (Streptavidin-biotin, SMA mab @ dilution 1:100, Dako Ltd).

D. Carcinoid plaque deposition on anterior cusp of pulmonary valve (PV) (arrow) with preserved mobility. Other two cusps unaffected.

**Figure 4.** Left sided Carcinoid Heart Disease. Left ventricle (LV), left atrium (LA), aorta (Ao), right atrium (RA), right ventricle (RV).

A. Two dimensional transoesophageal echocardiogram demonstrating fixed, thickened and retracted aortic valve (AV) cusps (arrow). This was associated with severe aortic regurgitation.

B. Two dimensional tranoesophageal echocardiogram demonstrating diffusely thickened mitral valve (MV) (arrow) and sub-valvular involvement of mitral valve chordae (dashed arrow).

C. Two dimensional transthoracic echocardiogram. Diffusely thickened mitral valve leaflets, chordae and papillary muscles. Minimal mitral regurgitation was noted.

D. Resected mitral valve of patient in panel C. Papillary muscle encased in white “carcinoid plaque”. Thickened and partially fused chordae tendinae. Histology confirmed plaque composed of myofibroblasts.

**Figure 5.**

A. Tranoesophageal echocardiogram demonstrating large mass in mid to distal inferior wall of the left ventricle (arrow).

B. Three dimensional transthoracic echocardiogram showing well demarcated, rounded mass (arrow) in the posterior wall of left ventricle (LV).
C. Cardiac Magnetic Resonance demonstrating two well demarcated masses in the mid infero-lateral wall extending to the apex (dashed arrow). Masses are limited to myocardium with no extra cardiac extension.

D. Gallium 68 Octreotate PET demonstrating focal avid uptake of tracer in the region of the two masses (arrow) suggesting metastatic carcinoid tumour.

Figure 6. Cine Cardiac Magnetic Resonance Imaging.

A. 4 Chamber View (Systole). Dilated right atrium and ventricle. Thickened, fixed and retracted tricuspid valve leaflets (arrow) with associated subvalvular involvement (dashed arrow).

B. Thickening, retraction and reduced excursion of the pulmonary valve leaflets (arrow).

C. Phase contrast flow map (short axis view in systole). Severe tricuspid regurgitation demonstrated by black retrograde jet (arrow).
Features of Carcinoid Heart Disease Identified By Two- and Three- Dimensional Echocardiography and Cardiac Magnetic Resonance Imaging
Sanjeev Bhattacharyya, Christos Toumpanakis, Margaret Burke, Andrew Taylor, Martyn Caplin and Joseph Davar

*Circ Cardiovasc Imaging.* published online November 17, 2009;
*Circulation: Cardiovascular Imaging* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/early/2009/11/17/CIRCIMAGING.109.886846

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation: Cardiovascular Imaging* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation: Cardiovascular Imaging* is online at:
http://circimaging.ahajournals.org//subscriptions/