

Early Recurrence of Carcinoid Valvulopathy after Valve Replacement

Jerome S. Zacks¹, Ester Cánovas¹, Ronald Lavine², Richard R.P. Warner¹
 1. Mount Sinai Hospital, Center for Carcinoid and Neuroendocrine Tumors, New York City, 2. Beth Israel Med Center, New York City

Background and Objectives

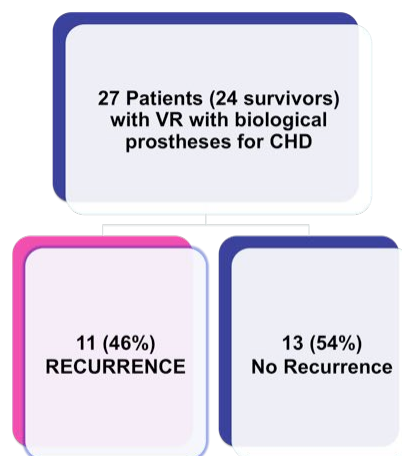
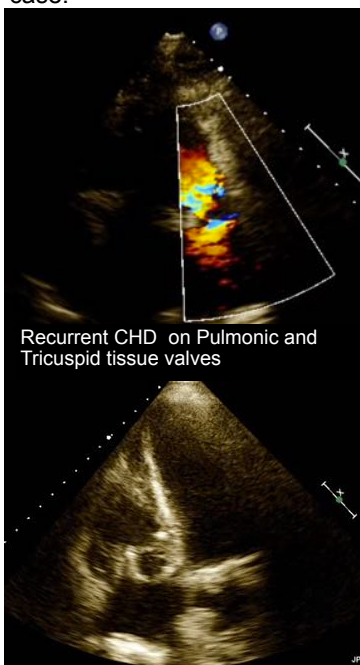
While valve replacement reduces mortality in carcinoid heart disease (CHD), bioprosthetic valves may suffer the same fibrosis as native valves **if serotonin remains elevated**. Mechanical valves do not undergo fibrosis but require lifelong anticoagulation. This study aimed to evaluate the incidence, risk factors and time of clinically significant CHD **recurrence**. Clinically significant CHD recurrence was defined as moderate or severe prosthetic dysfunction due to leaflet thickening and/or retraction absent on pre-discharge echocardiogram after valve replacement (VR) with **tissue** valves.

Methods

From January 2001 to November 2013, 27 consecutive patients (30% female; mean age 62±9 years) with carcinoid syndrome, liver metastases and CHD underwent VR with biologic prosthetic valves for severe valve dysfunction and right heart failure. Twenty-two patients (82%) presented with isolated right-sided valve disease whereas 5 (18%) had concomitant left-sided disease. **Thirty-day perioperative mortality was 11%** (n=3). Clinical, laboratory and echocardiographic follow-up data was prospectively collected among survivors (24).

Results

Of the 24 survivors, 11 (46%) had clinically significant recurrent disease on follow-up. (6 patients moderate and 5 severe dysfunction). 4 (16%) had moderate to severe RV dysfunction. Four patients (36%) manifested functional class ≥ III. Median time from the initial surgical procedure until **clinically significant recurrence** was 16 months (Range: 11-25). Despite all attempts at tumor reduction and serotonin receptor blockade, **biomarker levels before and after surgery remained high** (Table 1). Higher median peak levels of Chromogranin A on follow up were found to be a significant marker for recurrence (2339.4ng vs. 485.6ng, p=0.004). We did not find a statistically significant difference between Serotonin or 24 urine 5HIAA levels between groups before surgery or on follow-up. 2 patients underwent successful reoperative surgery with mechanical valves, 2 received percutaneous balloon valvuloplasty, and 1 was deemed inoperable due to severe tumor burden. Pathology confirmed carcinoid etiology in each case.



<i>Biomarkers Levels Before surgery</i>	CHD Recurrence	No CHD Recurrence	P
Serotonin serum ng/mL	961	1068	0.65
Serotonin Peak plasma ng/mL	1331	1244	0.76
Chromogranin A Peak	615	901	0.6
Chromogranin A 24 h urine(mg/L)	1081	976	0.86
Peak 5HIAA	503	190	0.40
	216	378	0.26

<i>Biomarkers Levels After Surgery</i>	CHD recurrence	No CHD recurrence	P
Serotonin serum ng/mL	841	899	0.81
Serotonin serum Peak	1338	1114	0.47
Chromogranin A plasma ng/mL	1212	384	0.18
Chromogranin A Peak	2339	485	0.004
5HIAA 24 h urine (mg/L)	127	423	0.13
Peak 5HIAA mg/24h	216	378	0.26

Conclusions

We have found a high incidence (46%) of **clinically significant** CHD recurrence soon after VR (median time of 16 months) attributable to a failure to reduce serotonin to normal levels after implantation of tissue valves. High levels of Chromogranin A on follow up were found to be the only significant predictor for recurrence. Because of the devastating consequences of clinically significant valve deformity, it is important to use echocardiography to search for **subclinical** (mild) prosthetic valve changes which should signal the urgency to further reduce serotonin; such changes can be detected as early as 4 months following bioprosthetic valve implantation. A multidisciplinary approach is advisable to control tumor activity, reduce biomarkers and make the critical decisions concerning valve prosthesis selection. Although **tissue** valves might eliminate the need for chronic anticoagulation, perhaps **mechanical** prosthetic valves should be considered in this challenging setting.