Should Severe Aortic Stenosis Be Operated on Before Symptom Onset?

Severe Aortic Stenosis Should Not Be Operated on Before Symptom Onset

Prediman K. Shah, MD

“If it ain’t broke, don’t fix it.”
—Thomas Bertram Lance in Nation’s Business, May 1977

Aortic valve stenosis resulting from calcific thickening of a previously normal 3-cusp aortic valve or a congenitally bicuspid aortic valve is a common clinical condition in developed countries, and its prevalence is continuing to increase with aging of the population.1,2 In the Cardiovascular Health Study, which involved 5201 men and women 65 years of age, the prevalence of aortic stenosis was 1.3% in subjects 65 to 75 years of age, 2.4% in subjects 75 to 85 years of age, and 4% in subjects >85 years of age.3 The precise mechanisms involved in the pathophysiology of aortic stenosis and its progression are incompletely understood, but advancing age and atherosclerosis-related risk factors have been implicated in the process.4 In fact, atherosclerotic coronary artery disease is present in nearly 50% of patients with aortic stenosis.5 Studies of valve pathology have suggested a potential role for dyslipidemia, inflammation, and angiogenesis in the process, but pharmacological therapies using statins to reduce dyslipidemia and associated inflammatory processes have yielded inconsistent but largely negative results in terms of reducing the rate of progression of aortic stenosis.6–10 Thus, in the absence of specific and effective disease-modifying medical therapies, surgical aortic valve replacement has been and continues to be the cornerstone of management of severe aortic stenosis. There is general agreement among physicians and surgeons that when severe aortic stenosis is accompanied by 1 or more symptoms, such as chest pain, syncope or near syncope, resuscitated sudden death, shortness of breath, fatigue, effort intolerance, or left ventricular (LV) dysfunction, aortic valve replacement is recommended because of well-established dismal outcome (50% mortality within 3 years) in unoperated symptomatic cases and overall excellent surgical outcomes with relatively low perioperative mortality and morbidity even among octogenarians11–15 (Figures 1 and 2). Thus, despite the absence of data from a randomized clinical trial, symptomatic severe aortic stenosis is considered a class 1 indication for surgery by various professional organizations.16,17 In some, particularly elderly patients, timely surgical aortic valve replacement is not considered because symptoms are mistakenly attributed to comorbid conditions, or the severity of underlying aortic stenosis is underestimated by traditional indices such as aortic valve gradient and peak velocity; this is particularly the case in patients with low-flow, low-gradient with depressed LV ejection fraction but is also true with a recently recognized variant associated with paradoxical low-flow, low-gradient severe aortic stenosis despite normal LV ejection fraction.18–20

Response by Carabello on p 125

In the past few years, less invasive nonsurgical transcatheter transfemoral (and to a lesser extent, transapical) techniques (such as transcatheter aortic valve implantation) for implanting a new bioprosthetic aortic valve inside a diseased
severely stenotic native aortic valve have been developed and tested, with encouraging early results in symptomatic patients considered nonsurgical candidates or at high surgical risk.\textsuperscript{21,22} Thus, in the absence of life-limiting frailty and comorbidity, surgical valve replacement, or in selected cases, nonsurgical transcutaneous bioprosthetic valve implantation, is recommended for symptomatic patients with severe aortic stenosis.

**Figure 1.** The natural history of aortic stenosis, emphasizing a long presymptomatic period and the dismal outcome once symptoms begin. AV indicates average. Adapted from Ross and Braunwald.\textsuperscript{11}

The Case of Asymptomatic Severe Aortic Stenosis

Several observational studies have shown that a large number of patients with severe aortic stenosis deny symptoms for many years, consistent with the well-known presymptomatic phase that had originally been defined by Ross and Braunwald more than 40 years ago.\textsuperscript{11} Admittedly, a certain proportion of the so-called asymptomatic subjects may have subconsciously re-

**Figure 2.** The dramatically favorable outcome of symptomatic aortic stenosis patients undergoing surgical valve replacement is depicted. A, Comparison of percent survival in total male population \(\geq 40\) years of age with that of adult patients with aortic stenosis with and without surgery. Adapted from Ross and Braunwald.\textsuperscript{11} B, Mean survival of patients with symptomatic aortic stenosis with and without surgery. Adapted from Schwarz et al.\textsuperscript{12}
duced their level of activity to low levels, thereby masking their true symptoms or effort intolerance, and their effort intolerance may be unmasked when objectively evaluated with a modified supervised stress test. Thus, physicians taking care of patients with aortic stenosis will frequently face the dilemma of what to do with a patient, especially an elderly patient (≥80 years of age), with physical and echocardiographic signs of severe aortic stenosis who claims to be asymptomatic. Because it is hard to make an asymptomatic subject feel better, preemptive surgery can only be justified when there is clear evidence that surgery actually improves long-term survival compared with watchful waiting and periodic reassessment. Unfortunately, the guidance on this dilemma is not informed by data from any randomized, controlled clinical trial, because no such trials have been conducted. So, what can we glean from a large amount of nonrandomized observational data sets that can provide a reasoned framework for clinical decision making in asymptomatic patients with severe aortic stenosis? The following questions may be posed:

What is the natural history of severe asymptomatic aortic stenosis?

What is the surgical outcome of patients with asymptomatic aortic stenosis?

On the basis of the above, what should be done for the vast majority of patients with asymptomatic severe aortic stenosis?

Are there subsets of patients with seemingly asymptomatic severe aortic stenosis who are at high risk for cardiovascular events?

Does prophylactic surgery improve the outcome of high-risk cases of asymptomatic severe aortic stenosis?

### Natural History of Asymptomatic Severe Aortic Stenosis and Results of Prophylactic Surgery

The 2 major concerns in patients with asymptomatic severe aortic stenosis are the risks of sudden death and the development of symptomatic or subclinical LV dysfunction. The overall incidence of sudden unexpected death in asymptomatic subjects with severe aortic stenosis is ≈0% to 4.1% per year, with approximately an average 1% annual risk.\(^5,14,23\)

The overall risk of sudden death in asymptomatic patients is comparable to or lower than that of surgical mortality. However, within the asymptomatic cohort, progression of the disease and development of symptoms is quite common, with variable rates of symptom development depending on the initial severity of aortic stenosis (Tables 1 and 2).\(^24-26\)

Among patients <70 years of age, the overall surgical mortality associated with isolated aortic valve replacement is ≈1% to 3% (increasing to ≈5%–7% when associated coronary artery disease requires additional intervention), and it is 5% to 15% among older adults, including octogenarians and some nonagenarians.\(^31\) In addition to death, stroke rates of 1.4% to 4.8% have been reported after aortic valve surgery.\(^32,33\) Thus, for the vast majority of asymptomatic patients with severe aortic stenosis, preemptive surgery would be associated with a higher risk of overall death than the natural history of the condition. In addition to surgical mortality, an aortic valve prosthesis, whether biological or mechanical, carries additional risks related to valve degeneration/failure, increased risk of endocarditis, and complications resulting from antithrombotic therapy. Thus, for the vast majority of truly asymptomatic patients with severe aortic stenosis, watchful waiting and periodic reassessment would appear to be a reasonable approach. It is important, however, to emphasize that when patients are followed up in this manner, cardiac surgery should be promptly undertaken when symptoms develop or evidence of LV dysfunction appears with a minimum of delay, because symptomatic patients do incur an increased risk of death (≈2% per month). In the elderly patient with severe aortic stenosis, systemic hypertension and reduced aortic wall compliance are common comorbidities that can add additional afterload to the ventricle beyond that produced by valvular stenosis, and careful and judicious use of antihypertensive drug therapy to maintain optimal blood pressure control may be helpful in preserving LV function.

### Are There Subsets of Patients With Seemingly Asymptomatic Severe Aortic Stenosis Who Are at High Risk for Cardiovascular Events?

As discussed above, a certain proportion of so-called asymptomatic subjects may have subconsciously reduced their level of activity to low levels, thereby masking their true exercise intolerance, and their exercise intolerance may be unmasked when evaluated objectively with a modified stress test performed under supervision (Table 3).

### Role of Treadmill Exercise Testing

Until a few years ago, severe aortic stenosis was considered a contraindication for provocative testing because of the potential for precipitating severe complications. Several small studies over the past decade have examined the potential role of carefully monitored treadmill exercise testing in predicting outcome in seemingly asymptomatic patients with severe aortic stenosis.\(^27,29,30,34–37\) These studies have indicated that a carefully supervised modified Bruce protocol can be safely applied to such patients and that induction of symptoms, ischemic manifestations, serious ventricular arrhythmias, or lack of expected rise in blood pressure and an actual hypotensive response predict an adverse outcome.\(^27,29,30,34–37\) These observational studies have shown that ≈30% of seemingly asymptomatic patients with severe aortic stenosis have an abnormal exercise test,\(^27\) and

### Table 1. Definition of Severity of Aortic Stenosis

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve area, cm²</td>
<td>&gt;1.5 cm</td>
<td>1 to 1.5</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Aortic valve area index, cm²/m²</td>
<td>&gt;0.9</td>
<td>0.6–0.9</td>
<td>&lt;0.6</td>
</tr>
<tr>
<td>Mean gradient, mm Hg</td>
<td>&lt;25</td>
<td>25–40</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Aortic jet velocity, m/s</td>
<td>&lt;3</td>
<td>3–4</td>
<td>&gt;4</td>
</tr>
</tbody>
</table>
in such patients, aortic valve replacement is considered reasonable; however, these data are derived from observational studies and not from any randomized clinical trials and hence are given only a class IIB recommendation by the American College of Cardiology/American Heart Association and European Society of Cardiology guidelines.

Electrocardiographic Criteria for LV Hypertrophy and Strain

Recently, investigators have analyzed electrocardiographic data from 1533 asymptomatic aortic stenosis patients followed up for 4.3 years from the SEAS (Simvastatin and Ezetimibe in Aortic Stenosis) trial, in which patients with aortic stenosis were randomized to treatment with placebo or a combination of simvastatin and ezetimibe. Electrocardiographic criteria for LV hypertrophy and LV strain pattern were related to a poor prognosis in asymptomatic aortic stenosis patients independent of clinical and echocardiographic covariates, which confirms previously reported findings. These observations are intriguing and suggest that patients with asymptomatic severe aortic stenosis with these electrocardiographic findings may merit closer and more frequent follow-up.

Role of Biomarkers

Aortic stenosis increases myocardial diastolic and systolic wall stress, which induces the expression of N-terminal pro-brain natriuretic peptide and brain natriuretic peptide, and thus, increased levels of these biomarkers are found in relationship to severity of aortic stenosis, with good correlation with the aortic valve area and severity of symptoms. In several studies,

### Table 2. Prospective Studies of Outcome in Asymptomatic Aortic Stenosis in Adults

<table>
<thead>
<tr>
<th>Study and Year</th>
<th>No. of Patients</th>
<th>Severity of Aortic Stenosis</th>
<th>Age, y</th>
<th>Mean Follow-Up</th>
<th>Group</th>
<th>Event-Free Survival Without Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kelly et al., 1988</td>
<td>51</td>
<td>V\text{max} \geq 3.6 m/s</td>
<td>63±8</td>
<td>5–25 mo</td>
<td>Overall</td>
<td>59% at 15 mo</td>
</tr>
<tr>
<td>Pellikka et al., 1990</td>
<td>113</td>
<td>V\text{max} \geq 4.0 m/s</td>
<td>40–94</td>
<td>20 mo</td>
<td>Overall</td>
<td>86% at 1 y; 62% at 2 y</td>
</tr>
<tr>
<td>Kennedy et al., 1991</td>
<td>66</td>
<td>AVA 0.7–1.2 cm²</td>
<td>67±10</td>
<td>35 mo</td>
<td>Overall</td>
<td>59% at 4 y</td>
</tr>
<tr>
<td>Otto et al., 1997</td>
<td>123</td>
<td>V\text{max} \geq 2.6 m/s</td>
<td>63±16</td>
<td>2.5±1.4 y</td>
<td>Overall</td>
<td>93±5% at 1 y; 62±8% at 3 y; 26±10% at 5 y</td>
</tr>
<tr>
<td>Rosenhek et al., 2000</td>
<td>128</td>
<td>V\text{max} \geq 4.0 m/s</td>
<td>60±18</td>
<td>22±18 mo</td>
<td>Overall</td>
<td>67±5% at 1 y; 56±55% at 2 y; 33±5% at 4 y</td>
</tr>
<tr>
<td>Amato et al., 2001</td>
<td>66</td>
<td>AVA \geq 1.0 cm²</td>
<td>18–80 (50±15)</td>
<td>15±12 mo</td>
<td>Overall</td>
<td>57% at 1 y; 38% at 2 y</td>
</tr>
<tr>
<td>Das et al., 2005</td>
<td>125</td>
<td>AVA &lt; 1.4 cm²</td>
<td>56–74 (mean 65)</td>
<td>12 mo</td>
<td>Overall</td>
<td>100% at 1 y</td>
</tr>
<tr>
<td>Pellikka et al., 2005</td>
<td>622</td>
<td>V\text{max} \geq 4.0 m/s</td>
<td>72±11</td>
<td>5.4±4.0 y</td>
<td>Overall</td>
<td>82% at 1 y; 67% at 2 y; 33% at 5 y</td>
</tr>
</tbody>
</table>

V\text{max} indicates maximum velocity of shortening of cardiac muscle; AVA, aortic valve area.

Table adapted from Bonow et al.16

in such patients, aortic valve replacement is considered reasonable; however, these data are derived from observational studies and not from any randomized clinical trials and hence are given only a class IIB recommendation by the American College of Cardiology/American Heart Association and European Society of Cardiology guidelines.16,17

**Electrocardiographic Criteria for LV Hypertrophy and Strain**

Recently, investigators have analyzed electrocardiographic data from 1533 asymptomatic aortic stenosis patients followed up for 4.3 years from the SEAS (Simvastatin and Ezetimibe in Aortic Stenosis) trial, in which patients with aortic stenosis were randomized to treatment with placebo or a combination of simvastatin and ezetimibe. Electrocardiographic criteria for LV hypertrophy and LV strain pattern were related to a poor prognosis in asymptomatic aortic stenosis patients independent of clinical and echocardiographic covariates, which confirms previously reported findings. These observations are intriguing and suggest that patients with asymptomatic severe aortic stenosis with these electrocardiographic findings may merit closer and more frequent follow-up.

**Role of Biomarkers**

Aortic stenosis increases myocardial diastolic and systolic wall stress, which induces the expression of N-terminal pro-brain natriuretic peptide and brain natriuretic peptide, and thus, increased levels of these biomarkers are found in relationship to severity of aortic stenosis, with good correlation with the aortic valve area and severity of symptoms. In several studies,
Table 3. Indicators of Adverse Outcome Among Seemingly Asymptomatic Patients With Severe Aortic Stenosis

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Symptoms Present</th>
<th>Symptoms Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal resting ECG with LVH and a strain pattern</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doppler echocardiography variables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very severe AS (jet velocity &gt;4.5 to 5.0 m/s; AVA &lt;0.6 cm²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inappropriate LVH (≥15-mm wall thickness)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced longitudinal strain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced LVEF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal impedance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal exercise test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Induced symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious arrhythmias</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lack of increase in blood pressure (≥20 mm Hg) or drop in blood pressure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Symptom-Free Survival (%) in Asymptomatic Severe Aortic Stenosis

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>3 Months</th>
<th>6 Months</th>
<th>1 Year</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNP</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>&lt;130 pg/mL</td>
<td>100</td>
<td>90</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>&gt;130 pg/mL</td>
<td>94</td>
<td>64</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>NT-proBNP</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;678 pg/mL</td>
<td>100</td>
<td>88</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>&gt;678 pg/mL</td>
<td>92</td>
<td>58</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>

BNP indicates brain natriuretic peptide; NT-proBNP, N-terminal pro-BNP.

Adapted from Bergler-Klein et al.40

Several observational studies have suggested that a number of parameters that can be obtained from 2-dimensional Doppler echocardiography studies during initial or sequential evaluation may portend a particularly adverse prognosis even in asymptomatic subjects (Table 3). These parameters include evidence of very severe aortic stenosis, with an aortic valve area <0.6 cm²; high peak aortic jet velocity of >4.5 to 5 m/s; rapid increase in gradient and velocity (>0.3 m/s per year); extensive valvular calcification; inappropriately increased LV mass; abnormal valvuloarterial load/impedance, also expressed as Zv (ratio of estimated LV pressure and stroke volume index); and reduced LV ejection fraction (<50%). In particular, the presence of very severe aortic stenosis with a peak aortic jet velocity exceeding 5 m/s and especially exceeding 5.5 m/s (regardless of aortic valve area) in asymptomatic subjects has been associated with a particularly poor event-free survival, ranging from 49% to 81% at 1 year, 32% to 48% at 2 years, 15% to 37% at 3 years, and 7% to 21% at 4 years.41 It has been suggested that the presence of any 1 or more of these variables should lead to serious consideration of preemptive surgery.

Should Prophylactic Surgery Be Considered for the Subset of Patients With Asymptomatic Severe Aortic Stenosis Who Have 1 or More Features of High Risk?

As of now, there are no randomized clinical trials addressing the issue of preemptive surgery in high-risk subsets of patients with asymptomatic severe aortic stenosis; however, observational data provide some interesting insights. Kang et al42 reported the results of surgery versus no surgery in a nonrandomized cohort of 197 asymptomatic patients with very severe aortic stenosis and normal LV ejection fraction (aortic valve area <0.75 cm² and peak aortic jet velocity >4.5 m/s), 102 of whom underwent preemptive surgery and 95 of whom were followed up without surgery. During an average follow-up of ∼50 months, the operated group had no operative deaths, no cardiac deaths, and only 3 noncardiac deaths, whereas the conventionally treated group had 18 cardiac and 10 noncardiac deaths. The estimated actuarial 6-year cardiac and all-cause mortality rates were 0% and 2% in the operated group versus 24% and 32%, respectively, in the conventionally managed group (P<0.001).44 From the total group, in 57 propensity score–matched pairs, all-cause mortality was significantly lower in the operated group than in the unoperated group, with a hazard ratio of 0.135 (P=0.008).44 It has been argued that asymptomatic patients with very severe aortic stenosis or those who exhibit 1 or more other features of high risk (Table 3) should be considered for preemptive surgery to avoid the otherwise high mortality and morbidity.43–45,50 However, the evidence base for these recommendations is meager, with small numbers of patients and with a high likelihood of selection bias despite propensity matching, as well as the inclusion of patients who refused surgery when symptoms developed, which contributes to the high mortality in unoperated patients, and the frequent occurrence of noncardiac deaths in nonoperated patients that could not have been prevented by surgery anyway.51 Thus, the recommendations for preemptive surgery are not entirely based on solid ground, and further evaluation, preferably with randomized trials, is needed to
resolve this continuing clinical conundrum. What is a clinician to do? In the absence of clinical trial data, the clinician must monitor high-risk asymptomatic patients at closer intervals (perhaps every 3 months instead of every year as currently recommended by national guidelines) and intervene promptly, without delay, soon after the onset of symptoms or evidence of deterioration of LV function, to catch the patient before adverse events occur. A reasonable alternative to this approach might be to consider preemptive surgery for high-risk patients, provided that the expected institutional and surgeon-specific surgical mortality rates are low and especially if delays in surgery after symptom onset are likely because of a waiting list.

Recently, Gada et al reported results from a decision-analytic model that accounted for not only mortality but also nonfatal adverse effects from aortic valve surgery, as well as costs associated with each surgery. The authors made certain assumptions to execute this model and compared immediate surgery to watchful waiting in asymptomatic severe aortic stenosis patients. The authors concluded that watchful waiting was a better strategy for most asymptomatic patients with severe aortic stenosis, and preemptive surgery was only a better strategy if the expected sudden death rate, in the absence of surgery, would be 13% or higher. However, it is difficult to extrapolate from these model-derived data to the real-life scenario because of various assumptions involved and the lack of accounting for various comorbidities that are common in elderly patients with severe aortic stenosis that can influence outcome.

Percutaneous Transfemoral Implantation of a Bioprosthetic Aortic Valve for Severe Aortic Stenosis: Will That Change the Prevailing Strategy?

Over the past several years, transfemoral transcatheter aortic valve implants have been used in several thousand patients with severe aortic stenosis, and 2 randomized controlled trials have been completed. These studies included symptomatic patients with severe aortic stenosis who were deemed either inoperable or high surgical risks, mostly because of comorbidity. Overall, short-term and intermediate-term follow-up has provided gratifying results with this less invasive intervention, but vascular complication rates and stroke rates are significant enough to give one pause. The short- and long-term risks and benefits of transcatheter aortic valve implantation in asymptomatic patients with severe aortic stenosis remain largely unknown. Therefore, at this time, it does not appear that such a strategy will be optimal for asymptomatic high-risk patients with aortic stenosis, but that could change in the future with improvements in technology that could result in reduced rates of stroke and vascular complications. If and when that happens, the prevailing paradigm of watchful waiting may have to be reconsidered.
Conclusions

For the vast majority of asymptomatic patients with severe aortic stenosis, watchful waiting appears to be the most reasonable strategy (Figure 3). These patients, especially those with 1 or more high-risk features, require close monitoring, with prompt surgical intervention immediately after symptom onset or with evidence of LV function deterioration. In selected cases and selected institutions where surgical mortality and morbidity are very low, high-risk patients may benefit from preemptive surgery, especially if delays in scheduling surgery are expected because of long waiting lists. Improvements in transcatheter valve implant technology in the future, however, may change the thresholds for preemptive intervention. In patients in whom symptomatic status is ambiguous, carefully supervised treadmill testing might uncover serious symptoms justifying preemptive surgery, as currently recommended by guidelines. However, for most asymptomatic patients, for now, “if it ain’t broke, don’t break it or fix it” appears appropriate.

Acknowledgment

The secretarial assistance of Blessie Bulaon is gratefully acknowledged.

Disclosures

None.

References

Response to Shah
Blase A. Carabello, MD

I read with pleasure the opinion offered by Dr Prediman Shah on the management of the patient with severe asymptomatic aortic stenosis. Our 2 treatises are far more notable for their similarities than their differences. We both note the relative lack of evidence on which to base our conclusions. Unfortunately, it is highly unlikely that a large trial randomizing high-risk asymptomatic patients to watchful waiting versus aortic valve replacement (AVR) will ever be performed, leaving the clinician to base management on the few data we have. We both note very similar factors that put the asymptomatic patient at higher risk, including an abnormal exercise test, a high transvalvular jet velocity, and elevated biomarkers. We diverge a bit on what to do with high-risk patients. Dr Shah advocates close follow-up. I would argue that even follow-up at 3-month intervals is inadequate, because with a 2% risk of sudden death per month, once symptoms develop there could be a 6% mortality rate for patients who developed symptoms shortly after an office visit and who waited 3 months to report the change. If the patient called his or her physician immediately on symptom onset, the outcome would likely be good, be a 6% mortality rate for patients who developed symptoms shortly after an office visit and who waited 3 months to report the change. If the patient called his or her physician immediately on symptom onset, the outcome would likely be good,

---

41. Gerber IL, Legget ME, West TM, Richards AM, Stewart RA. Usefulness of serial measurement of N-terminal pro-brain natriuretic peptide plasma levels in asymptomatic patients with aortic stenosis to predict symptomatic deterioration. _Am J Cardiol_. 2005;95:986–901.

---
Severe Aortic Stenosis Should Not Be Operated on Before Symptom Onset
Prediman K. Shah

_Circulation_. 2012;126:118-125
doi: 10.1161/CIRCULATIONAHA.111.079368
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
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:
http://circ.ahajournals.org/content/126/1/118

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ 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_ is online at:
http://circ.ahajournals.org//subscriptions/