Cost-Effective Use of Echocardiography in Children With Kawasaki Disease

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ABSTRACT. *Objective.* **To determine whether a third echocardiogram, performed 6 months to 1 year after the onset of Kawasaki disease (KD), as recommended by current American Heart Association guidelines, identified any case of coronary artery abnormalities when previous echocardiograms were normal.**

Methods. **Children diagnosed with KD were identified by searching our institution's database. Cases were included in the study if diagnosed between June 1988 and December 1996 and if at least two echocardiograms were documented, including at least one study between 2 weeks and 2 months from the onset of KD and another in follow-up. The patients' charts were reviewed and videotapes of the echocardiograms were reviewed if reports were unclear or contradictory. McNemar's test for discordant pairs was used for statistical analysis. Additionally, a complete review was performed in all other cases of KD in the database in which a coronary artery abnormality had been identified.**

Results. **There were 203 patients diagnosed during the study period who had 2 or more echocardiograms performed, and 67 had the requisite studies in the subacute period and later follow-up. The median age at onset of KD was 3.0 years (range: 0.2–16), the median duration of follow-up was 12.5 months (range: 1.7–100), and the median number of echocardiograms performed was 3 (range: 2–8). Intravenous immunoglobulin was given in 62 cases, and high-dose aspirin was given in 63. There were 35 children with no echocardiographic abnormalities at any point, and 15 other children had early abnormalities (including coronary ectasia, perivascular brightness, pericardial effusion, and ventricular dysfunction) but had a normal echocardiogram between 2 weeks and 2 months. Of these 50 children, none were noted to have abnormalities on later studies. Three children had effusion and/or perivascular brightness after 2 weeks; follow-up studies were normal in each. Six children had coronary ectasia after 2 weeks; it persisted on follow-up in 1 child and had resolved in 5 children. Eight children had coronary aneurysms on studies after 2 weeks; in 3 children, the aneurysm resolved on later follow-up. No coronary abnormalities were demonstrated on a late follow-up echocardiogram in any child with normal coronaries between 2 weeks and 2 months.**

Conclusions. **All children with KD should have an echocardiogram at the time of diagnosis with a follow-up study 4 to 6 weeks after the onset of fever. In the current environment of cost-containment, additional echocardiographic studies are justified only if abnormalities are present at 4 to 6 weeks.** *Pediatrics* **1999;104(5). URL: http://www.pediatrics.org/cgi/content/full/104/5/e57;** ***Kawasaki disease, coronary artery aneurysm, echocardiography, coronary ectasia.***

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ABBREVIATIONS. KD, Kawasaki disease; IVIG, intravenous immunoglobulin.

Kawasaki disease is an acute inflammatory disease with potential for serious morbidity and mortality attributable to coronary artery aneurysms. First described in Japan in 1967, it is characterized by fever, adenopathy, conjunctivitis, skin rash, and laboratory signs of systemic inflammation.[1] There is often an associated vasculitis that most notably affects the coronary arteries. Coronary artery dilation may be seen toward the end of the first week of illness, reaching peak incidence and severity by 4 to 6 weeks after onset. In untreated patients, ~30% develop coronary involvement, with giant coronary aneurysms (>8 mm) in 2% to 5%.[2] Aneurysms may lead to obstruction from acute thrombosis or chronic narrowing, resulting in myocardial ischemia, myocardial infarction, and even sudden death. Recent studies also have shown that coronary blood flow reserve may be decreased, even in patients who did not have echocardiograph evidence of coronary involvement.[3]

Echocardiography has been shown to be a very sensitive detector of proximal aneurysms[4] and, therefore, is used to monitor patients diagnosed with KD. Current American Heart Association recommendations are for echocardiograph evaluation in the acute phase with follow-up 4 to 6 weeks after onset and again at 6 to 12 months after onset.[5] Although echocardiography is noninvasive, because it can be a costly procedure and even can require sedation, we sought to determine whether the third study identified any additional cases of coronary pathology when earlier studies were normal. We hypothesized that no patient who had normal coronary arteries during the 4- to 6-week study would later develop ectasia, aneurysms, or other pathology.

METHODS

This was a retrospective chart review. Cases were identified by a search of the database in the Cardiology Division of Children's Hospital of Pittsburgh. A complete record review was performed on all patients diagnosed with KD from June of 1988 through December of 1996 who had at least two echocardiograms, includ-

ing one between 2 weeks and 2 months from the onset of the illness and one in subsequent follow-up.

Two dimensional echocardiography views of the proximal coronary arteries were obtained using standard Hewlett-Packard or Acuson echocardiogram equipment with 3.5- to 7.0-MHz transducers. Adequate visualization of the proximal coronaries was assumed unless otherwise stated in the report.

We accepted the diagnosis of aneurysm in the echocardiogram report as documentation of aneurysm. We classified a patient as having ectasia when the study report described the coronary as larger than normal for age, but without discrete aneurysm. We used the first day of fever in the illness diagnosed as KD as the date of onset. We noted whether the patient had received intravenous immunoglobulin (IVIG) or aspirin therapy and recorded the date that this therapy was initiated.

In the event of conflicting information (such as a report indicating no change from previous study but reaching a different diagnosis), videotape of the echocardiograms in question were reviewed. We analyzed our data using McNemar's test for discordant pairs. A value of $P < .05$ was considered significant.

Additionally, a complete chart review was performed on all other cases with KD in the database who were noted to have a coronary artery abnormality but who did not meet the entry criteria for this study.

RESULTS

There were 203 patients diagnosed with KD during the study period (June 1988 through December 1996), and 67 had the requisite echocardiograph studies at 2 weeks to 2 months after onset and another in follow-up. Of these selected patients, the median age at diagnosis of KD was 3.0 years with a range of 0.2 to 16 years. The median period of follow-up was 12.5 months (range: 1.7–100 months). In 13 patients, the latest study was performed <6 months after the onset of illness. The median number of echocardiograms performed was 3 (range: 2–8). There was documentation of IVIG administration in 62 patients, and the use of high-dose aspirin was documented in 63. The mean interval between the onset of illness and administration of IVIG was 7.5 days (range: 2–31). The majority (35 patients) had a single infusion of 2 g per kilogram of body weight, and 27 received 500 mg/kg/day for 4 days. All 8 patients who developed aneurysms received IVIG, which was administered after the 10th day of illness in 5 cases.

There were 35 patients whose echocardiograms were normal each time they were obtained. In 27 of these patients, an early (<2 weeks into the illness) study was obtained and was normal; all had normal studies between 2 weeks to 2 months after onset. Another 15 patients had one or more abnormalities <2 weeks from onset but had normal follow-up echocardiograms between 2 weeks and 2 months from onset. The early abnormalities included coronary ectasia (6), pericardial effusion (6), perivascular brightness (6), and ventricular dysfunction (3), (several patients had more than one of these abnormalities). Of these 50 patients with normal echocardiograms between 2 weeks and 2 months from onset, all had normal studies on subsequent follow-up.

Eight patients had coronary aneurysms seen on echocardiograms between 2 weeks and 2 months after the onset of KD. The shortest interval between the onset of illness and documentation of aneurysm was 12 days, and the earliest documented resolution of an aneurysm was 79 days. Of these 8 patients, 6 had echocardiograms before 2 weeks from onset, and this study was normal in 1. Early abnormal findings in the other 5 patients included pericardial effusion (1), coronary ectasia (2), perivascular brightness (1), and aneurysm (1). Of the 8 patients, 3 had resolution of the aneurysm on follow-up studies. Of the 8 patients, 6 had cardiac catheterization, with confirmation of a persistent aneurysm in 2 patients, coronary ectasia in 2, and normal coronaries in 2.

Six patients had coronary ectasia that persisted beyond 2 weeks from the onset of KD, and 1 of these also had pericardial effusion 21 days after onset. Of these 6 patients, 4 had an echocardiogram before 2 weeks from onset, and this study was abnormal in each. Of these 6 patients, 5 had resolution of the ectasia on subsequent follow-up. In 1 patient, ectasia was still present at 131 days; based on other clinical data, this patient was suspected of having a recurrent case of KD. Of these patients with persistent ectasia, 2 had cardiac catheterizations, confirming resolution of the enlargement in both.

Three patients had perivascular brightness (1), pericardial effusion (1), or both (1), on a study conducted >two weeks after the onset of illness. The earlier study (performed <2 weeks after the onset of illness) was also abnormal in the 2 patients who had had one. These abnormalities resolved on later studies in all 3 patients.

To summarize, of the 67 patients included in the study, 50 had normal echocardiograms performed between 2 weeks and 2 months from the onset of KD, and all 50 remained normal on any later follow-up echocardiogram. Of the 17 with abnormal studies after 2 weeks, 11 resolved on subsequent follow-up, and 6 remained abnormal (see Fig 1). In this analysis, McNemar's test for discordant pairs yields a χ^2 value of >33, corresponding to a P value of <.0001.

There were a total of 20 patients in the study group with coronary artery lesions (coronary ectasia or aneurysm). Three additional patients had coronary artery lesions but were not included attributable to the lack of an echocardiogram between 2 weeks and 2 months from onset. Therefore, the incidence among all patients diagnosed with KD and studied with at least two echocardiograms during the study period was 11% (23/203). In all cases, the pathology involved one or both proximal coronary arteries. Of the 23 patients, 11 had a catheterization during the study period, with confirmation of echocardiograph diagnoses in each case.

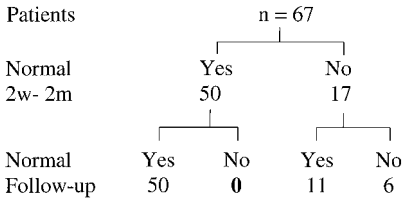

Fig 1. Echocardiographic results. The diagram illustrates the number of patients with normal and abnormal coronary arteries on echocardiography at each stage of evaluation. McNemar's test for discordant pairs yields a χ^2 value of >33, corresponding to a P value of <.0001.

DISCUSSION

The pathophysiology of KD consists of a vasculitis which begins to affect the coronary arteries at the same time as other acute symptoms manifest. In cases in which coronary pathology occurs, echocardiograph evidence almost always is seen by 2 weeks after onset. Aneurysm formation occurs in the subacute period and may develop in patients with normal initial studies. All of the patients with KD diagnosed at our institution since June of 1988 with documentation of coronary artery abnormalities and all who had echocardiograms between 2 weeks and 2 months with later follow-up were reviewed in this study. None developed coronary abnormalities not seen on echocardiograms in the subacute period.

The 67 patients reviewed here are not representative of all patients with KD; the selection criteria of echocardiograms at specific points has skewed this population toward an increased incidence of pathology. In fact, 20 (30%) of the 67 had coronary lesions at some point, compared with only 3 (2%) of the 136 who were excluded for insufficient echocardiograms. Furthermore, statistics relating to the efficacy of IVIG could not be determined because data were not obtained on all patients receiving this therapy.

Adequate quality imaging, with multiple views of the coronary arteries, should be emphasized, especially if no additional routine imaging will be performed, as we would recommend. Because proper visualization of the coronary arteries is difficult and because pathology can be missed on an inadequate study, sedation or follow-up studies are indicated in patients who cooperate poorly. This should be accomplished by 2 months after the onset of KD, because aneurysms can form and resolve within this time. The proximal coronary arteries can be imaged well in most patients from parasternal views. The distal portions of the coronary arteries are more difficult to visualize, but distal coronary aneurysms in the presence of normal proximal vessels have not been seen at our institution on this or previous studies.[6]

The long-term ramifications of coronary artery involvement in patients with KD remain primarily unknown. There is increasing evidence that patients with minimal echocardiograph evidence of coronary involvement may have impaired coronary function. Follow-up, including exercise testing, is warranted in patients found to have coronary pathology and may be useful in all patients with KD. However, routine echocardiography is not likely to show any abnormalities not seen in the subacute period. Our study shows that a third echocardiogram, performed between 6 and 12 months after illness in a patient with KD as recommended by the American Heart Association, is unlikely to demonstrate new abnormalities in patients with previously normal studies. Indeed, in our institution the yield was zero.

The estimated incidence of KD is ~5000 cases per year in the United States.[2] If the same proportion of cases have normal echocardiograms after 2 weeks as seen in our study (50 of 67), then 3700 extra studies would be performed by following the American Heart Association guidelines. Given the very low yield demonstrated by our study, the extra expense for these studies is not cost-effective.

CONCLUSION

In summary, we agree that echocardiography is important at the time of diagnosis of KD and that a repeat study should be performed between 4 and 6 weeks after onset to rule out coronary involvement. However, additional studies are indicated only if abnormalities are present, new symptoms develop, or the follow-up study is inadequate. In the current environment of cost-containment, additional routine echocardiography is not justified.

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