Assessment of Left Ventricular Systolic Function by Strain Imaging Echocardiography in Various Stages of Feline Hypertrophic Cardiomyopathy

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**Background:** Diastolic dysfunction occurs in many cats with hypertrophic cardiomyopathy (HCM). Less is known about systolic function in various stages of HCM. Myocardial strain analysis by tissue Doppler imaging (TDI) is a noninvasive echocardiographic method to assess systolic function that has not been reported previously in cats.

**Objectives:** To evaluate systolic function in various stages of feline HCM by measurement of myocardial strain.

**Methods:** Cats were classified by echocardiography into one of the following groups: clinically healthy (control) group (n = 160), mild HCM (n = 22), moderate HCM (n = 39), and severe HCM (n = 42). Peak myocardial strain, measured by TDI in the basal and midventricular segment of the interventricular septal wall (IVS) and the left ventricular posterior wall (LVPW), was compared among different HCM and control groups.

**Results:** Whereas conventional echocardiography demonstrated an apparently normal or supernormal contractile state based on percentage of fractional shortening, myocardial strain in all HCM groups was significantly decreased compared with the control group (P < .001). There was a significant correlation between strain values and wall thickness (P < .001). Reproducibility of strain analysis was 6.3% in the IVS and 9.7% in the LVPW.

**Conclusions and Clinical Importance:** Myocardial strain analysis is a new, valuable, and reproducible method in cats. This method allows noninvasive detection of abnormal systolic deformation in cats with HCM despite apparently normal left ventricular systolic function as assessed by conventional echocardiography. The abnormal systolic deformation already was present in mild HCM and increased with progressive left ventricular concentric hypertrophy.

**Key words:** Cardiology; Cats; Myocardial function; Tissue Doppler imaging.

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Feline hypertrophic cardiomyopathy (HCM) is a genetic disorder characterized by left ventricular (LV) concentric hypertrophy, interstitial fibrosis, and myocardial disarray. Autosomal dominant inheritance with a heterogeneous disease outcome has been documented in a family of Maine Coon cats.1,2 The disease is characterized by increased left ventricular concentric hypertrophy which occurs symmetrically or asymmetrically. Papillary muscle hypertrophy is almost always present and can lead to end-systolic obliteration of the left ventricular cavity.3 Concentric hypertrophy results in diastolic dysfunction leading to left-sided congestive heart failure. Sudden cardiac death also is associated with this disease in cats as well as in humans.4 Abnormalities in diastolic function using mitral valve inflow profiles have been well characterized.5,6 However, systolic as well as diastolic function is highly influenced by preload and afterload.7–11 Tissue Doppler imaging (TDI) overcomes some of these problems. It is the method of choice for noninvasive assessment of regional myocardial function in humans.13–17 and is increasingly used in veterinary medicine.18–24 The 1st Doppler method used for the assessment of myocardial function was pulsed wave tissue velocity imaging (TVI) followed by color-coded Doppler TDI to measure myocardial TVI.19,23,25–28 In cats with HCM, indices of diastolic function measured by TVI are different from those of healthy cats and similar to values reported in human beings with HCM and restrictive cardiomyopathy.19,20,23,24,29–32 By color-coded TDI, strain and strain rate (SR) measurements were later introduced into clinical practice to evaluate regional myocardial deformation magnitude and rate, respectively. Doppler-based strain and SR were validated both experimentally with ultrasonic crystals and clinically by tagged magnetic resonance imaging (MRI), and are considered to be less affected by tethering, translational artifacts, and traction than Doppler measurements of myocardial velocities.33–35

The application of TDI in human beings with HCM has shown that in contrast to traditional echocardiographic techniques, which consider diastolic dysfunction as the main abnormality of the disease, systolic...
impairment also is evident, despite the apparently norma-
lar or supernormal contractile state of the LV based on
percentage of fractional shortening (FS) and percentage
of ejection fraction (EF).

Abnormal systolic function also has been found in cats with HCM using TVI me-
asurements, but only as a group, and not in various
disease stages. Noninvasive evaluation of regional systolic function can be performed by measuring myo-
cardial strain.

In humans, strain in particular has been proposed as a sensitive tool to detect early systolic
function abnormalities in patients with HCM. However, longitudinal myocardial strain measurement has
neither been evaluated in healthy cats nor used to assess systolic function in various stages of feline HCM.

The hypothesis of this study was that cats with HCM
would have decreased systolic function assessed by lon-
gitudinal myocardial strain measurement that is
undetected by conventional echocardiography, possibly
even in early stages of HCM. Therefore, the objective of
this prospective study was to evaluate longitudinal myo-
cardial strain to assess systolic function in healthy cats
and in various stages of feline HCM.

Materials and Methods

Animals

A total of 263 cats (male, 151; female, 112) of various breeds were
included in this prospective study. The following breeds were repre-
sented: European short hair (n = 151), Maine Coon (n = 53),
Persian (n = 18), Norwegian Forest Cats (n = 10), and 31 cats of
other breed with <3 cats per group. All cats belonged to owners
living in Germany, Switzerland, or Austria and were patients pre-
tended to the cardiology service of the Clinic of Small Animal
Medicine, or were cats owned by faculty or students.

Examinations

In all cats, clinical examination, echocardiography, and blood pres-
sure measurements were performed. All echocardiographic studies were performed by 1 experienced examiner (G.W.), using an ultra-
sound unit equipped with a 7.0 (3.5/6.9) MHz phased-array
transducer. Ultrasound examinations were performed without seda-
tion in gently restrained cats in lateral recumbency. Standard
echocardiographic views were obtained in right and left lateral recum-
bency. Two-dimensional images were used for LV measurements.
End-diastolic wall thickness of the interventricular septum (IVS) and
the left ventricular posterior wall (LVPW) were measured in the basal
and midventricular segment of the respective myocardial wall using
the right parasternal long-axis view. The left atrium to aorta ratio
(LA/AO) was measured in the short-axis view. At least 3 measure-
ments were performed in each segment of the LVPW and IVS and the
mean value of the measurements was calculated for each segment.
HCM was defined as regional or generalized concentric hypertrophy
with a diastolic wall thickness ≥ 6 mm of the LVPWd or of the IVSd.
The cats were classified according to echocardiographic into one of the following groups: control group (LVPWd and IVSd < 5.5 mm; LA/
AO < 1.5), mild HCM (focal or generalized concentric hypertrophy with LVPWd, IVSd, or both 6.0–6.5 mm and LA/AO < 1.5), moder-
ate HCM (focal or generalized concentric hypertrophy with LVPWd, IVSd, or both 6.5–7.0 mm and LA/AO < 1.8; or LVPWd, IVSd, or both 6.0–6.5 mm and LA/AO 1.5–1.8), and severe HCM (focal or gen-
eralized concentric hypertrophy with LVPWd, IVSd, or both
> 7.0 mm; or LVPWd, IVSd, or both > 6.0 mm and LA/AO > 1.8).

Cats were classified into the HCM groups according to their maximal
wall measurement results, independent if only 1 segment or only 1 wall
was hypertrophied. Color Doppler images of the myocardium were
acquired with a 60°–75° sector size and 180–300 frames per second for
the IVS and LVPW using the left apical 4-chamber view as single wall
images. Complete digital data from 3 heart cycles were stored in cine
loop format and transferred to a computer workstation for subse-
quent myocardial strain analysis8 in the basal and midventricular
segment of the IVS and LVPW using the left apical 4-chamber view.
The mean value of at least 3 peak myocardial strain measurements in
each segment was calculated. To avoid any artifact from aliasing, the
velocity range was adjusted to allow interrogation of the maximal ve-
locity of the myocardium. Wall filters and gain settings also were
optimized for myocardial color saturation for each subject.

Hyperthyroidism and hypertension were excluded as secondary
causes of concentric hypertrophy by measurement of basal T4 and
blood pressure by Doppler technique. Blood pressure was consid-
ered normal if systolic blood pressure was < 150 mmHg. Cats with
evidence of systemic disease or hyperthyroidism were not included
in the study.

Measurement reliability of the echocardiographic examination
was determined for systolic and diastolic LV chamber diameter and
for diastolic wall thickness of the LVPW and IVS as well as for the
strain measurements. Ten digitally stored echocardiograms were
randomly selected to be subjected to 3 repeated analyses within 1
week by 1 investigator (G.W.) to determine intraobserver measure-
ment variability. The investigator was unaware of the results of the
prior echocardiographic analyses.

Statistical Analysis

Data are reported as mean ± SD. All echocardiographic data were
usually inspected and tested for normality by the Kolmogorov-
Smirnov test. A general linear mixed model with Bonferroni adjust-
ment was performed to compare myocardial strain of each segment
(basal and midventricular), in each myocardial wall (IVS and LVPW),
among the HCM groups (mild, moderate, and severe HCM) and with
the control group. Sex, age, concentric hypertrophy presence in the
selected segment (present or absent in regional HCM), and heart rate
were analyzed as covarates in the general linear mixed model with
multivariate analysis and stepwise backward regression analysis. To
determine whether functional regional abnormalities were related to
structural abnormalities, myocardial strain was compared with IVS
and LVPW thickness by linear regression analysis. The intraobserver
coefficients of variations (CV) were calculated by a variance compo-
nent analysis. The CV were obtained by dividing the root of the
variance error by the mean of the repeated measurements multiplied
by 100. A commercially available software program was used for
analysis. Significance was defined as P < .05.

Results

Baseline characteristics of the study population are
shown in Table 1. The majority of cats in the mild HCM
group had a regional, asymmetric HCM form, in which
the concentric hypertrophy was present either in the
LVPW (n = 5) or the IVS (n = 11). In most cats in the
moderate and severe HCM groups, both walls were
hypertrophied. The mean values of the IVSd and
LVPWd are displayed in Table 1. In the HCM groups
the table includes measurements < 6 mm in some cases,
because HCM was present in these cases only regionally
and affected the other myocardial wall (IVS or LVPW,
respectively). As expected, wall thickness of the IVS and
LVPW were significantly different among all groups
(P < .001). The LV diameters in systole and diastole

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1. **Animal Breeds**:
   - European short hair (n = 151)
   - Maine Coon (n = 53)
   - Persian (n = 18)
   - Norwegian Forest Cats (n = 10)
   - Other breeds (31 cats)

2. **Data Analysis**:
   - Stratified by LV wall thickness:
     - Control group (LVPWd and IVSd < 5.5 mm; LA/AO < 1.5)
     - Mild HCM (focal or generalized hypertrophy)
     - Moderate HCM (focal or generalized hypertrophy)
     - Severe HCM (focal or generalized hypertrophy)

3. **Statistical Methods**:
   - General linear mixed model with Bonferroni adjustment
   - Intraobserver measurement variability
   - Multivariate analysis and stepwise backward regression

4. **Clinical Findings**:
   - Baseline characteristics in Table 1
   - IVSd and LVPWd measurements
   - LV diameters in systole and diastole

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**Hypothesis**: Cats with HCM would have decreased systolic function assessed by longitudinal myocardial strain measurement that is undetected by conventional echocardiography, possibly even in early stages of HCM.

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1. **Materials and Methods**:
   - **Animals**: 263 cats (male, 151; female, 112) of various breeds
   - **Examinations**: Clinical examination, echocardiography, blood pressure measurements
   - **Measurements**: Systolic and diastolic LV chamber diameter, strain

2. **Statistical Analysis**:
   - Data are reported as mean ± SD
   - Echocardiographic data were usually inspected and tested for normality
   - General linear mixed model with Bonferroni adjustment
   - Intraobserver measurement variability

3. **Results**:
   - Baseline characteristics in Table 1
   - LV diameters in systole and diastole
were significantly smaller in the HCM groups compared with the control group ($P < .001$). The LA/Ao ratio was significantly higher in the moderate and severe HCM groups compared with the mild HCM and control group and the FS was significantly higher in all HCM groups compared with the control group ($P < .001$). Cats in the control group were significantly ($P < .001$) younger than those in the HCM groups, but this influence was accounted for using the general linear model. Heart rate was not different among the groups ($P = .67$). More than 3,120 strain measurements were performed in 260 cats (4 segments, minimum of 3 strain measurements per segment).

Myocardial strain was significantly lower in all HCM groups compared with the control group ($P < .001$). Median and interquartile ranges for the different groups are shown in Figure 1, separately displayed for each of the myocardial segments. Mean strain in the basal segment of the IVS was $-22.2$ ($\pm 5.7$), $-15.9$ ($\pm 3.9$), $-14.6$ ($\pm 5.3$), and $-11.4$ ($\pm 4.6$) in the control, mild, moderate, and severe groups, respectively. Mean strain in the midventricular segment of the IVS was $-22.2$ ($\pm 5.7$), $-17.0$ ($\pm 5.4$), $-15.6$ ($\pm 6.6$), and $-12.6$ ($\pm 5.1$) in the control, mild, moderate, and severe groups, respectively. In the basal segment of the LVPW, the mean peak systolic strain was $-18.3$ ($\pm 3.8$) in the control group, $-8.9$ ($\pm 4.9$) in the mild HCM group, $-9.0$ ($\pm 4.3$) in the moderate HCM group, and $-6.2$ ($\pm 2.7$) in the severe HCM group. In the midventricular segment of the LVPW, the mean peak systolic strain was $-18.6$ ($\pm 4.3$) in the control group, $-11.5$ ($\pm 7.4$) in the mild HCM group, $-8.4$ ($\pm 4.4$) in the moderate HCM group, and $-7.1$ ($\pm 3.4$) in the severe HCM group. Age, heart rate, sex, breed, and type of concentric hypertrophy (regional or generalized HCM) did not influence the myocardial strain measurements, only disease stage (HCM group) remained significant in the stepwise backward regression analysis using the general linear mixed model in all segments of the IVS and LVPW. The severe HCM group had significantly lower strain values than the moderate HCM group ($P = .017$), mild HCM group ($P = .003$), and control group ($P < .001$). No significant difference in strain values was found between the mild and moderate HCM groups, but results in both HCM groups were significantly lower than in the control group ($P < .001$). A positive strain value was found in 7 cats in the severe HCM group. These values were censored from the analysis, because...
they would have decreased mean strain values (which are negative values) even further. There was a significant correlation ($P < .001$) between strain values and LV wall thickness (Fig 2). The correlation between combined strain values (basal and midventricular) and LV wall thickness was similar in the IVS ($R = 0.59$) and in the LVPW ($R = 0.69$). Results of the echocardiographic repeatability study were acceptable: CV was 3.3% for diastolic LVPW, 2.6% for diastolic IVS, 2.0% for diastolic LV diameter, and 4.2% for systolic LV diameter. CV for the myocardial strain was better in the IVS (6.3%) compared with the LVPW (9.7%).

**Discussion**

The present study is the 1st to evaluate systolic function by TDI strain analysis in various stages of feline HCM. The study shows that strain analysis is a feasible and repeatable method in cats, and that longitudinal systolic myocardial deformation decreased in cats with...
HCM, despite normal echocardiographic indices of global LV systolic function, suggesting the presence of subclinical systolic dysfunction that is not detectable by conventional echocardiographic methods. Recently, new echocardiographic techniques such as TVI and strain imaging have become clinically available. Strain and SR in particular provide direct quantitative information on regional systolic and diastolic myocardial function without using geometrical assumptions. Strain imaging has been shown to be a sensitive method to quantify regional systolic myocardial function in a variety of cardiac diseases. It enables the evaluation of regional myocardial deformation in different myocardial segments in the radial, longitudinal, or circumferential directions and therefore is ideal to characterize heterogeneity in myocardial function in cardiomyopathies. Myocardial strain analysis assessed by color TDI is a sensitive tool to detect early systolic function abnormalities in human patients with HCM. The present study shows that strain analysis can be used in cats and that the repeatability of strain measurements is good in both LV myocardial walls. The CV was better in the IVS, possibly because it is more difficult to align the LVPW with the ultrasound beam (compared with the IVS).

The present study demonstrates that systolic myocardial strain is already decreased in mild forms of HCM and decreases more in more severe HCM stages. Decreased systolic myocardial tissue velocity previously has been demonstrated in cats with HCM, but not in various stages of HCM and not using myocardial strain. From a clinical perspective, HCM is considered to be predominantly a diastolic disorder with relaxation abnormalities in the early stages that can progress toward a more restrictive physiology later in the disease process. In patients with HCM, diastolic dysfunction is thought to precede systolic dysfunction. A recent study in humans by TDI showed that left ventricular diastolic dysfunction is thought to precede systolic dysfunction. A recent study in human carriers of HCM mutations that have normal LV wall thickness, peak systolic strain was deceased. Similarly, magnetic resonance tagging data suggest that myocardial shortening and thickening are heterogeneously decreased and inversely correlated with end-diastolic wall thickness in HCM patients. An MRI tagging study to evaluate regional myocardial function found a marked reduction in longitudinal deformation in all myocardial segments, which was more pronounced in the more hypertrophied septum. There are discrepancies between measures of regional and global myocardial function assessed by conventional echocardiography (FS or EF) and myocardial strain analysis for several reasons. First, endocardial indices of LV function such as FS and EF are known to overestimate systolic function in the presence of LV concentric hypertrophy. Normally, endocardial wall thickening is higher than epicardial wall thickening and this difference becomes more pronounced with greater degrees of concentric hypertrophy. For this reason, one should be cautious when using endocardial indices in the setting of increased wall thickness. Secondly, patients with HCM have smaller end-diastolic diameter and increased wall thickness, resulting in decreased ventricular afterload. The load dependency of both FS and EF is a well-known shortcoming of these indices. In the presence of substantial concentric hypertrophy, higher values of FS and EF are seen, despite decreased wall thickening. Therefore, the commonly used echocardiographic measures of systolic function (ie, EF and FS) might not reliably reflect intrinsic myocardial contractile function in the presence of remodeled hearts such as that occurring in HCM. Studies in humans with HCM have identified decreased longitudinal and circumferential strain by TDI and MRI, respectively. Interestingly, the present study showed decreased strain in both hypertrophied and nonhypertrophied regions, a finding in accordance with studies in humans.

Hence, strain analysis appears to be a more sensitive index of myocardial function than standard LV function assessment, emphasizing the diffuse nature of the disease. The reduction in systolic strain correlates with the degree of concentric hypertrophy in a linear fashion. Different factors explain this relationship. HCM is a disorder characterized by LV concentric hypertrophy, interstitial fibrosis, and myocardial disarray. Myocardial structural abnormalities with more pronounced fiber disarray are present in the more severely hypertrophied myocardial segments. When fibers are not geometrically arranged in a coherent direction but are randomly structured, contraction of these fibers will not result in an organized deformation pattern. Fibrosis and wall thickness were both multivariate predictors of lower segmental longitudinal strain in a human HCM study. Myocardial fibrosis was associated with impaired longitudinal strain in patients with HCM. Additionally, changes in passive mechanical characteristics caused by fibrosis and altered collagen deposition also affect deformation when active force is developed within a myocardial segment. Finally, increased concentric hypertrophy can cause an imbalance between oxygen demand and delivery exceeding regional coronary flow reserve, potentially resulting in regional ischemia.

A recent study showed that left ventricular diastolic dysfunction, systolic dysfunction, or both at follow-up are relatively frequent in HCM and are associated with a poor prognosis. Thus, myocardial strain measurements in cats might be useful to detect early or progressive systolic dysfunction at follow-up examinations. The use of positive inotropic drugs in humans or cats with HCM has not been evaluated and studies on that subject are necessary before such drugs can be recommended. A limitation of the present study was the noninvasive study design. The study was carried out on pet animals.
of feline HCM, but challenge the concept that diastolic
provide not only new insights into the pathophysiology
nature of the disease. The results of the present study
standard LV function assessment, emphasizing the diffuse
sensitive index of global myocardial function than stan-
mild HCM and increased with progressive LV concentric
tractile state of the LV based on percentage of FS. The
HCM, despite an apparent normal or supernormal con-
ysis is a feasible and repeatable method to assess systolic
In summary, this study demonstrates that strain anal-
ical new echocardio-graphic method and provides useful additional
information in cats with HCM. The present study shows
that systolic TDI strain measurement allows noninvasive
detection of abnormal systolic deformation in cats with
HCM, despite an apparent normal or supernormal con-
tractile state of the LV based on percentage of FS. The
abnormal systolic deformation already was present in
mild HCM and increased with progressive LV concentric
hypertrophy. Hence, strain analysis appears to be a more
sensitive index of global myocardial function than stan-
dard LV function assessment, emphasizing the diffuse
nature of the disease. The results of the present study
provide not only new insights into the pathophysiology
of feline HCM, but challenge the concept that diastolic
dysfunction precedes systolic dysfunction.

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