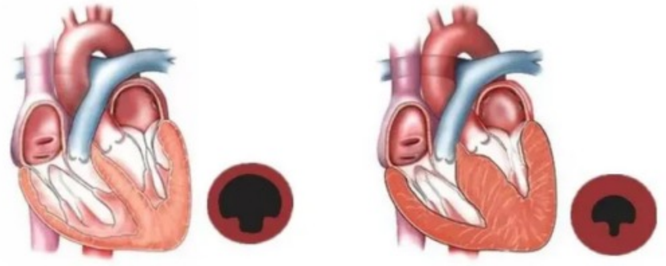
04

HYPERTROPHIC CARDIOMYOPATHY

4.1 About hypertrophic cardiomyopathy, HCM

Hypertrophic cardiomyopathy (HCM) is an inherited disease of the heart muscle character_x0002_ized by otherwise unexplained thickening of the left ventricle. Left ventricular outflow tract (LVOT) obstruction is present in approximately two-thirds of patients and substantially increases the risk of disease complications. Invasive treatment with septal myectomy or alcohol septal ablation can improve symptoms and functional status, but currently available drugs for reducing obstruction have pleiotropic effects and variable therapeutic responses.

New medical treatments with more targeted pharmacology are needed, but the lack of pre_x0002_clinical animal models for HCM with LVOT obstruction has limited their development. HCM is a common cause of heart failure in cats, and a subset exhibit systolic anterior motion of the mitral valve leading to LVOT obstruction.



Healthy Cat's Heart

Cat's Heart with HCM

4.2 What is Capromo?

Capromo (MYK461) is used for obstructive hypertrophic cardiomyopathy (HCM) to improve shortness of breath and the ability to be active. Capromo works by allowing your heart muscle to relax, which reduces the obstruction and improves overall heart function. Obstructive hypertrophic cardiomyopathy (HCM) occurs when the walls of the heart become excessively thickened, leading to an obstruction in the outflow of the left ventricle which reduces the heart's ability to pump blood effectively.

Capromo is an allosteric and reversible inhibitor selective for cardiac myosin. Myosin is a protein in the heart muscle that is involved in making the heart muscle contract and relax. When Capromo binds to myosin, the heart muscle relaxes more, so the heart fills with blood and is able to pump more effectively.

4.3 About Capromo

Capromo® Indications

Capromo® is a reversible allosteric inhibitor of cardiac myosin, used to treat adult animals with obstructive hypertrophic cardiomyopathy (HCM) of New York Heart Association (NYHA) Class II-III (B-C), to improve function and symptoms.

Primarily used for hypertrophic cardiomyopathy caused by ventricular wall thickening leading to left ventricular outflow tract (LVOT) obstruction. Best effects are seen in Class B heart failure classification. For Class C heart failure classification, Refer to the "Dosage" section in the instruction manual for medication instructions. In severe heart failure cases, such as pulmonary edema, pleural effusion, or breathing difficulties, stabilize the condition with conventional treatment before oral medication. Discontinue medication immediately if orthopnea (indicative of breathing difficulty, possibly due to myocardial contraction weakness) is observed and visit the hospital for blood pressure and echocardiography checks. Medication is permissible when left ventricular ejection fraction (LVEF/EF) at rest is >60%. Discontinue medication if EF drops below 50% during treatment. After EF recovery, continue medication at a reduced dose. Switch to a lower maintenance dose when interventricular septal diameter (IVSD) is less than 6. The low-dose medication period is over 6 months.

For cats, after discontinuation of medication, check the heart once in the first half-year every 1-3 months. If multiple heart checks are normal, then check every 3-6 months. Decide whether to resume medication based on changes. If cardiac indicators remain normal, medication is not necessary. On recheck, if interventricular septum is greater than 7 or other indicators increase, meeting the criteria for medication, resume medication or follow doctor's advice.

1-3 months

check the heart once

3-6 months

multiple heart checks are normal

Normal

medication is not necessary

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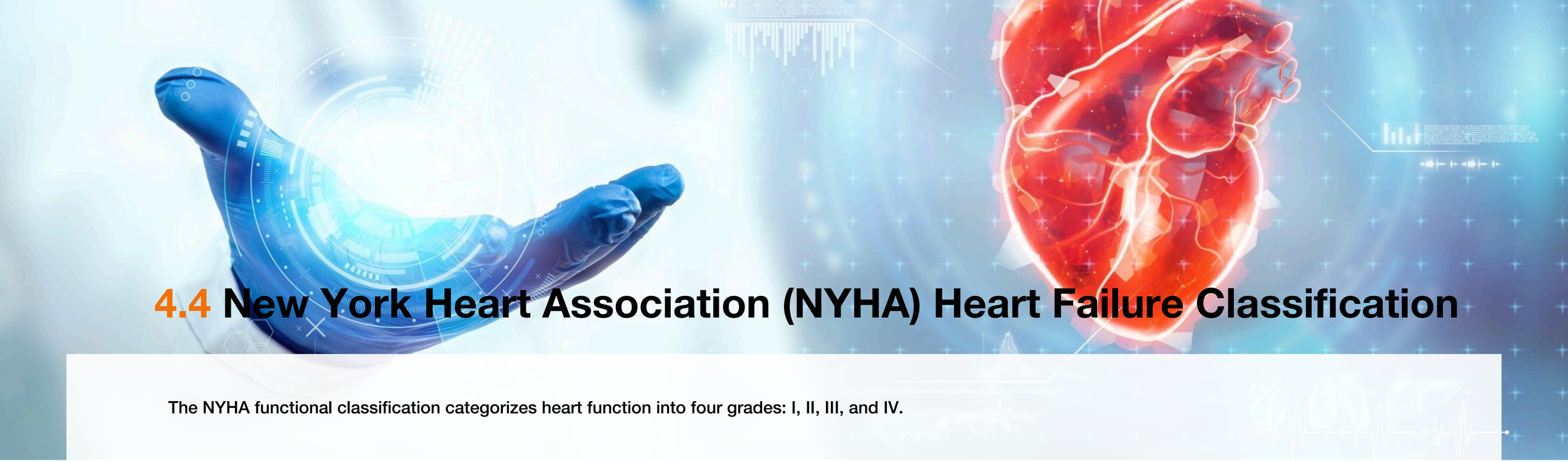

4.4 New York Heart Association (NYHA) Heart Failure Classification

The NYHA functional classification categorizes heart function into four grades: I, II, III, and IV.

Class I

Patients in NYHA Class I have heart disease but are not limited in their physical activity.
They do not experience symptoms such as undue fatigue, palpitations, dyspnea (shortness of breath), or angina (chest pain) during ordinary physical activity.

Class II

NYHA Class II patients have mild limitations during physical activity. They are comfortable at rest, but ordinary physical activity results in symptoms such as undue fatigue, palpitations, dyspnea, or angina.

Class III

Patients in NYHA Class III have marked limitations during physical activity. They are comfortable at rest, but less than ordinary activity causes symptoms.

Class IV

NYHA Class IV patients are unable to carry on any physical activity without discomfort.
Symptoms of heart failure are present even at rest. If any physical activity is undertaken, discomfort increases.

4.5 Left Ventricular Outflow Tract Obstruction (LVOTO)

Diagnostic Criteria

Currently, LVOTO is primarily assessed using Doppler echocardiography and is defined as an instantaneous peak pressure gradient across the left ventricular outflow tract (LVOT) of ≥30 mmHg (1 mmHg = 0.133 kPa).

LVOTO Mechanisms of LVOTO

Currently, two main mechanisms are believed to contribute to LVOTO: a. Asymmetric Septal Hypertrophy (ASH), particularly thickening at the basal part of the interventricular septum and structural changes in the mitral valve (including leaflet elongation and anterior displacement of papillary muscles), leading to mechanical obstruction of LVOT. b. Systolic Anterior Motion (SAM) of the mitral valve anterior leaflet exacerbating dynamic obstruction of LVOT.

Influencing Factors

LVOTO in HCM patients is dynamic and sensitive to changes in ventricular load and contractility. Enhanced myocardial contractility or reduced cardiac preload and afterload (e.g., using inotropes, assuming an upright posture, performing a Valsalva maneuver, nitroglycerin administration, or vasodilators) can worsen LVOTO. Conversely, weakened myocardial contractility or increased cardiac preload and afterload (e.g., using beta-blockers, assuming a squatting position, leg lifting) can alleviate LVOTO.

Provocative Testing

In HCM patients without resting LVOTO, provocative testing combined with echocardiography is required to assess for latent LVOTO. Provocative tests can include the Valsalva maneuver or bedside maneuvers like repetitive lying-to-standing or squatting-to-standing, upright exercise bicycle testing, or semi-recumbent bicycle testing. Due to lack of specificity, drug stress testing with dobutamine is no longer recommended in current guidelines.

Prognostic Impact

LVOTO increases left ventricular systolic pressure and exacerbates myocardial ischemia, which is a major contributor to symptoms in obstructive HCM patients. Studies have shown that LVOTO significantly increases the risk of adverse events in HCM patients, including sudden cardiac death (SCD), progression to moderate-to-severe heart failure (heart failure), stroke, and death.

[Description]

Capromo® is a reversible allosteric inhibitor of cardiac myosin, used to treat adult animals with obstructive hypertrophic cardiomyopathy (HCM) of New York Heart Association (NYHA) Class II-III (B-C), to improve function and symptoms. It contains 0.5 mg Mavacamten(MYK 461) active ingredients,accompanied by inactive components such as Microcry-stalline cellulose, Polyvinylpolypyrrolidone cross-linked, Magnesiumstearate.

[Specification]

0.5mg/tablet*28

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