

18.

BÖLÜM

KARDİYOMİYOPATİLERDE HAYVAN MODELLERİ

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Kardiyomiyopatiler tanım olarak, obstrüktif koroner arter hastalığı veya anormal yüklenme koşulları ile açıklanamayan ventriküler miyokardın yapısal ve fonksiyonel anormallikleri ile tanımlanır (1). Etiyolojik özellikleri, fenotipi, klinik presentasyonları, ekokardiyografik bulgularına göre birçok kardiyomiyopati türü tanımlanmıştır. Bu kardiyomiyopati türlerinin altında yatan özellikler ve spesifik tedavilerinin tanımlanamamış olması hayvan modellemeleri ile çalışmayı gerekli kılmaktadır.

1.HİPERTROFİK KARDİYOMİYOPATI

Hipertrofik kardiyomiyopati (HKM) en sık görülen birincil kardiyomiyopatidir (prevalans 1:500) ve efor dispnesi, presenkop, atipik göğüs ağrısı, kalp yetmezliği ve ani kardiyak ölüme neden olabilir. Yapısal olarak sol ventrikülde genellikle asimetric şekilde kalınlaşma ile oluşur ve sol ventrikül çıkış yolunda obstrüksiyon, diyastolik fonksiyonların bozulması, oluşan aritmiler kliniğe yansıyan olaylardan sorumludur (2). Kardiyak sarkomerik mutasyonlar, kalıtsal metabolik ve nöromusküler hastalıklar ve genetik sendromlar etiyojide gösterilmiştir (3). İnsandaki HKM hastalığını modellemek için transgenik fareler veya spontan kedi modellemeleri kullanılmaktadır.

A.Transgenik Model

Kardiyak miyozin bağlayıcı protein C'nin (CMyBP-C) homozigot olarak defekte uğratıldığı fare modelleri (cMyBP-C - / -), cMyBP-C'nin normal kardiyak kasılmadaki rolünü ve HCM gelişimini incelemek için kullanılmıştır. Kasılma

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Tablo 1: Kardiyomiyopatilerde en sık kullanılan hayvan modellemesi türleri

| | Transgenik model | İndüklenmiş model | Spontan model |
|----------------|---|---|--|
| HKM | cMyBP-C - / - Tg faresi | | Main Coon |
| Dilate KMP | MLP -/- CSQ fareleri | Pace-maker ile hızlı uyarım Doxorubisin | İrlanda kurt köpeęi Saint Bernards Newfoundlands DobermanPinschers Boxer |
| Restriktif KMP | cTnI193His cTnIK178E HtzD3KO | | Evcil kedi |
| ARVC | | | Boxer |
| Alkolik KMP | | %30 alkollü su | |
| DMD | Distrofin+urotofin faresi DMD / Mdx sıçan | | Golden Retriever |
| Diyabetik KMP | OVE26 fare Akita faresi ob/ob db/db Zucker DM | Streptozosin | |

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