2.
BÖLÜM

AKUT DERİN VEN TROMBOZU HAYVAN MODELLERİ

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Akut derin ven trombozu (DVT), hastalığın doğal seyri ve komplikasyonları nedeni ile önemli bir halk sağlığı problemidir (1). Sadece Amerika Birleşik Devletlerinde (ABD) yılda 1 milyon yeni akut DVT tanısı konulmaktadır. Aynı ülkede her yıl doğrudan veya dolaylı pulmoner tromboemboliye bağlı 50.000-200.000 arası ölüm olayı gerçekleşmektedir. Ülkemizin de dâhil olduğu Kafkas ırkında akut DVT insidansı ise 50-124/100.000 olarak bildirilmiştir (2). Akut DVT'nin etiyolojisinde bilinen birçok faktör vardır. Bunlar; kanser, postoperatif uzun süreli yatak bağımlılığı, ileri yaş, obezite, tütün kullanımı, organ yetmezliği, nörolojik hastalıklar, kalıtsal nedenler ve artmış kırmızı kan hücresi dağılım genişliğidir (RDW) (3).

Aslında sayılan risk faktörlerinin esası Alman patolog Rudolf Virchow tarafından 1856 yılında; staz, endotel hasarı ve hiperkoagülobilite olarak tanımlanmıştır (4). DVT'nin altında yatan patofizyoloji bilindiği için oluşturulacak deney modellerinde kullanılacak mekanizmalarda az çok belli olacaktır. Ancak çalışmanın neyi hedeflediği kullanılacak hayvan modellerinde ister istemez değişiklik yapacaktır. Nitekim tıbbi cihazlar üzerine yapılacak çalışmalarda orta-büyük hayvan modellerini seçmek daha uygun iken, ilaç veya etiyoloji yöntemleri çalışmalarında daha küçük hayvan modelleri daha kullanışlı olacaktır.

İster akut olsun ister kronik, ister arteriyal olsun ister venöz bütün modellemeler intravasküler trombüs oluşturma esasına dayanır. Ancak oluşum süreci, yeri ve süresi yapılacak çalışmalarda modellemelerin esasını oluşturmaktadır. İntravasküler trombüs oluşturmaya yönelik mekanizmalar 4 ana başlık altında aşağıda incelenmiştir.

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mA elektrik akımının 30 dakika damar içine uygulanması tromboz oluşturma için yeterli bulunmuştur (90). Daha kompleks kombine modellemelere Wakefield ve arkadaşlarının yaptığı modelleme örnek gösterilebilir. Bu modellemede protein C inhibisyonu, venöz staz ve venöz injury eş zamanlı olarak uygulanmış ve mükemmel bir sonuç elde etmişlerdir (91).

Bazende artmış derin ven trombozu riski bulunan hastalıkların kesişim kümesinde bir modelleme gereksinimi olabilir. Nitekim kanser ve derin ven trombozu arasındaki ilişki bilinen bir gerçektir. Böyle bir ihtiyaç için Mege ve arkadaşları mikropartikül aracılı kanser ve derin ven trombozu modellerini bir araya getirmiştir (66). Rouleau ve Guertin ise spinal kord yaralanması ve derin ven trombozu modellemeleri bir araya getirmiştir (67). Özellikle tıbbi cihaz, stent ve endovasküler materyal çalışmalarında çalışılan materyalle ilgili kendine has tromboz modelleri de oluşturulabilir (70-72, 99). Lin ve arkadaşları venöz stent hayvan çalışmasında stentin ortasına parsiyel oklüzyona ve venöz akım yavaşlamasına neden olan huni benzeri bir PTFE greft ile tromboz modeli geliştirmişlerdir (73).

Yukarda sayılmayan ancak kombine olmayan yöntemlerden birisi de damar içine sklerozan madde enjeksiyonudur. Boersma ve arkadaşlarının oluşturduğu keçi modelinde bu model kullanılmıştır (92). Bir diğer yöntem de intravasküler kollajen veya epinefrin enjeksiyonudur. Bu yöntem daha çok farelerde kullanılmaktadır (97).

Derin ven trombozu için in-vivo modellemelerin dışında ex-vivo modellemelerde oluşturulmuştur. Karpiouk ve arkadaşları bir hazneye kan ilave ederek lazer yardımı ile trombüs oluşumunu tetiklemişlerdir (68). Ancak bu tür modellemeler daha çok görüntüleme yöntemleri çalışmalarında tercih edilebilir özelliktedir.

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