4. Atriyal Fibrilasyon Zirvesi 2015
10 - 11 Nisan 2015
Cornelia Hotel, Antalya

ANİ ÖLÜMLE İLİŞKİLİ YAPISAL KALP HASTALIKLARIN TEDAVİSİNDE SON GELİŞMELER

HİPERTROFİK KARDİYOMİYOPATİ

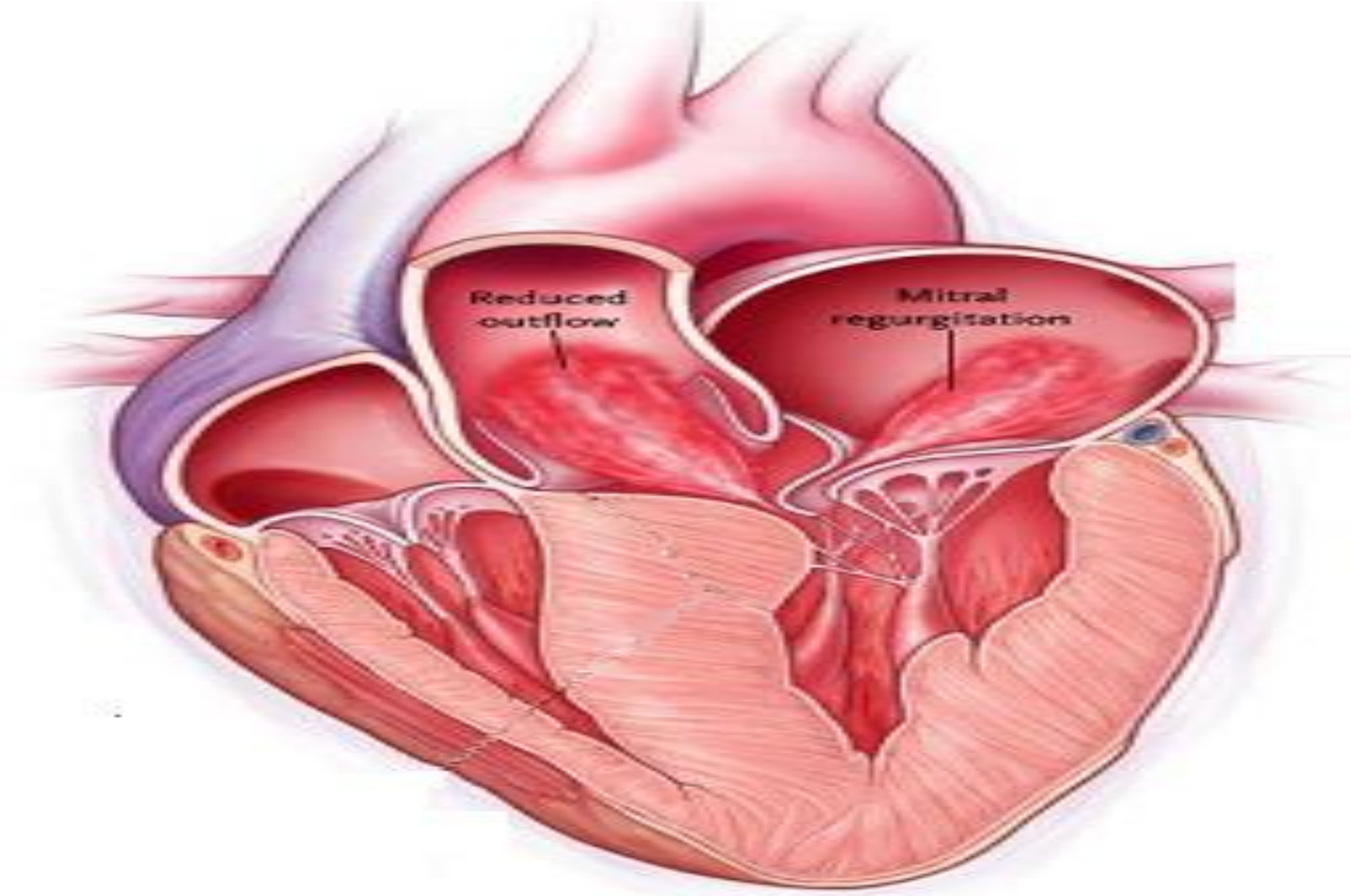
Dr. Murat Sucu

Gaziantep Üniversitesi Tıp Fakültesi Kardiyoloji AD.

Tanım

- Eko, MR veya CT ile
  - Herhangi bir sol ventrikül segmentinde açıklanamamış >15 duvar kalınlığı
- Birinci derece akrabalarında sol ventrikül kalınlığı için eşik değer 13 mm.
- Prevalansı %0.05-0.2 civarındadır.
  - **Cinsiyet:** Erkek> Kadın (genç, daha semptomatik)
  - **Yaş:**
    - Sıklıkla 30-40 yaşlarında

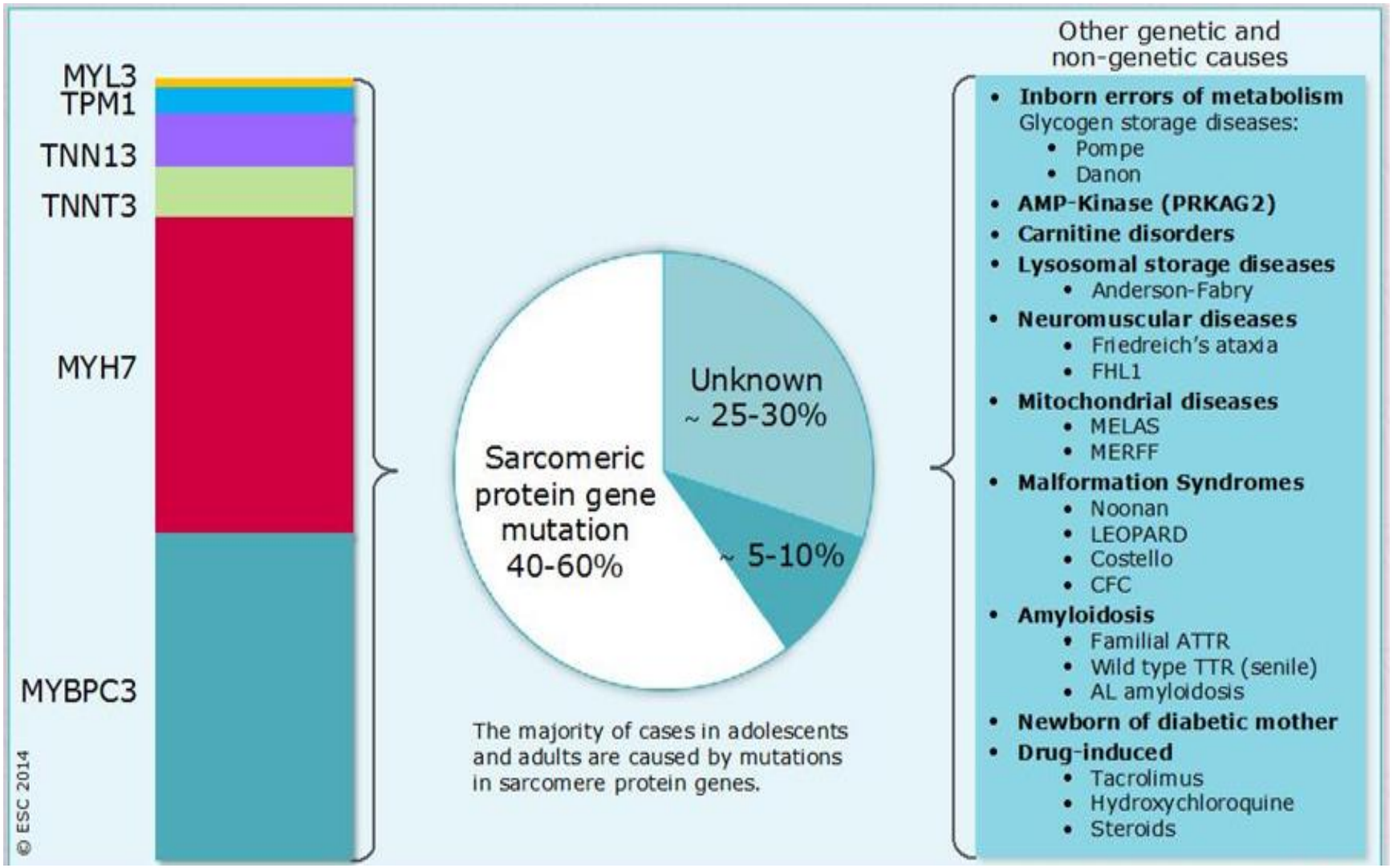
Klinik Seyir ve Hikaye



Sol Ventriküler Midkaviter Obstrüksiyon

- Midkaviter obstrüksiyon %10 görülüyor.
- Bunların ¼’ inde apikal anevrizma görülmektedir.
- Bu anevrizmalar yüksek oranda ventriküler taşikardi riski taşımaktadır.
- Diğer risk faktörleri yoksa ICD implantasyonu önerilmemektedir.

Genetik ve Aile Taraması



Tanı

Symptom/sign	Diagnosis
Learning difficulties, mental retardation	• Mitochondrial diseases • Noonan/LEOPARD/Costello syndrome • Danon disease
Sensorineural deafness	• Mitochondrial diseases (particularly with diabetes) • Anderson-Fabry disease • LEOPARD syndrome
Visual impairment	• Mitochondrial diseases (retinal disease, optic nerve atrophy) • TTR-related amyloidosis (cotton wool type vitreous opacities) • Danon disease (retinitis pigmentosa) • Anderson-Fabry disease (cataracts, corneal opacities)

Tanı

Symptom/sign	Diagnosis
Gait disturbance	• Friedreich's ataxia
Paraesthesia/sensory abnormalities/neuropathic pain	• Amyloidosis • Anderson-Fabry disease
Carpal tunnel syndrome	• TTR-related amyloidosis (especially when bilateral and in male patients)
Muscle weakness	• Mitochondrial diseases • Glycogen storage disorders • FHL1 mutations • Friedreich's ataxia
Palpebral ptosis	• Mitochondrial diseases • Noonan/LEOPARD syndrome • Myotonic dystrophy
Lentigines/café au lait spots	• LEOPARD/Noonan syndrome
Angiokeratomata, hypohidrosis	• Anderson-Fabry disease

Ekokardiyografik Ayırıcı Tanı

Echocardiographic features that suggest specific aetiologies[a]	
Finding	**Specific diseases to be considered**
Increased interatrial septum thickness	Amyloidosis
Increased AV valve thickness	Amyloidosis; Anderson-Fabry disease
Increased RV free wall thickness	Amyloidosis, myocarditis, Anderson-Fabry disease, Noonan syndrome and related disorders
Mild to moderate pericardial effusion	Amyloidosis, myocarditis
Ground-glass appearance of ventricular myocardium on 2-D echocardiography	Amyloidosis
Concentric LVH	Glycogen storage disease, Anderson-Fabry disease, PRKAG2 mutations
Extreme concentric LVH (wall thickness ≥30 mm)	Danon disease, Pompe disease
Global LV hypokinesia (with or without LV dilatation)	Mitochondrial disease, TTR-related amyloidosis, PRKAG2 mutations, Danon disease, myocarditis, advanced sarcomeric HCM, Anderson-Fabry disease
Right ventricular outflow tract obstruction	Noonan syndrome and associated disorders

İskemi ve HKMP

- ⇧ Miyokardiyal kas kitlesi
- ⇧ Miyokardiyal oksijen İhtiyacı(⇧ duvar stresi)
- ⇧ Diastolik doluş basıncı
- ⇩ Koroner kapiller yogunluk
- ⇩ Vazodilatötör yanıt
- Anormal intramural koroner arterler
- ⇧ Koroner arterlere sistolik basınç

HKMP ve Koroner Arter Hastalığı

- Tedavi stratejisini değiştirebileceği için göğüs ağrısı yada ventriküler taşikardinin KAH'a bağlı olabileceği düşünülen hastalarda anjiyografi planlanmalıdır.
- 40 yaşın üzerindeki hastalarda septal alkol ablasyon kararı verilen hastalarda CT anjiyo yada invaziv anjiografi yapılması önerilmekte.

LVOT Obstrüksiyon

⇧ İntraventriküler basınç

⇧ Ventriküler gevşeme

⇧ Miyokardiyal duvar stresi

⇧ Oksijen ihtiyacı

⇩ Kardiyak output

LVOT Obstrüksiyon

- Uzun süreli LV outflow obstrüksiyon kalp yetmezliği semptomları ve ani ölüm için major determinanttır.
- SAM subaortik outflow obstriksiyona neden olur
- Arteriyel ve venöz dilatötörler,alkol,dehidratasyon, fosfodiesteraz tip 5 inhibitörleri,kontrolsüz AF den kaçınılmalıdır.

Semptomatik Nonobstruktif LVOT

- Semptomatik normal Ef olan hastalarda istirahatte ve egzersiz ile LVOTO artış yok ise kalp hızını yavaşlatarak LV doluşunu artırmak için ß-blokerler, verapamil veya diltiazem dikkatli kullanım ile diüretikler
- Permanant yada paroksismal AF de sinüs ritmi sağlanmalı
- EF düşük ve kalp yetmezliği semptomları var ise ß-blokerler diüretikler, ACE inhibitörleri ARB'ler ve mineralokortikoid reseptör blokerleri kontrollü bir şekilde verilebilir.

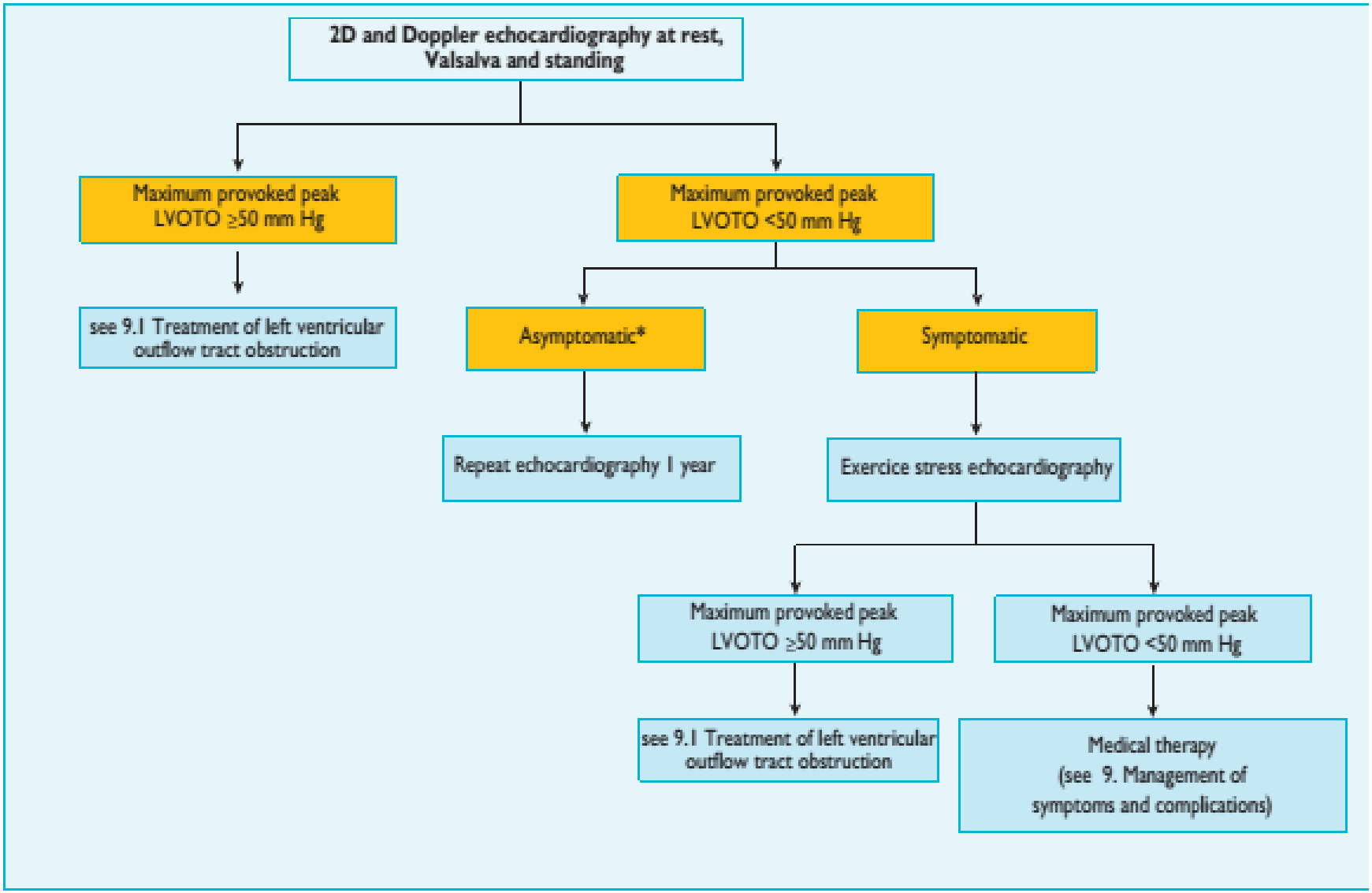
İlaçlar

- Beta-Blokerler: (Metoprolol, Propranolol, Atenolol, Sotalol)
- Kalsiyum Kanal Blokerleri: (Verapamil,Diltiazem)
- Antiaritmik: Amiodaron ve Disopiramid
- Antitussif ajanlar

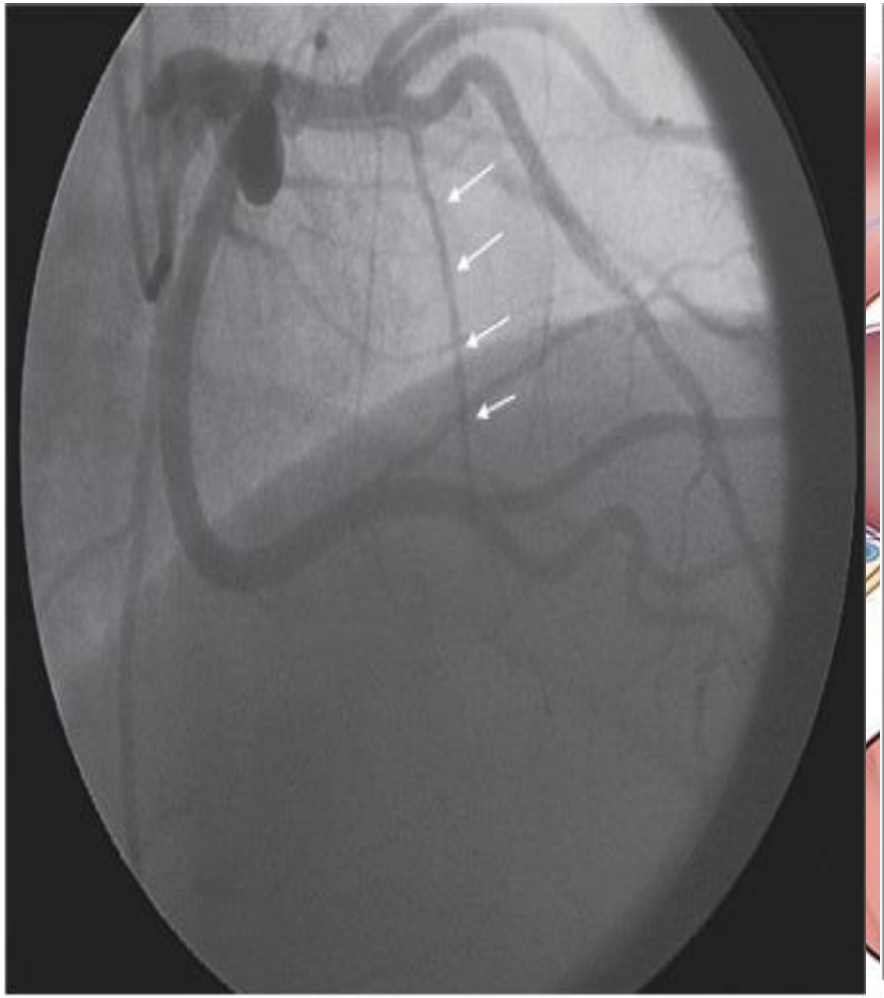
Kontrendike İlaçlar

- İnotropik Ajanlar
- Sempatomimetikler
- Nitratlar
    - KAH olanlar hariç
- Digoksin
    - Kontrolsüz AF hariç
- Diüretikler
    - ⇩ Preload ve ventriküler volüm
    - ⇧ Outflow gradient

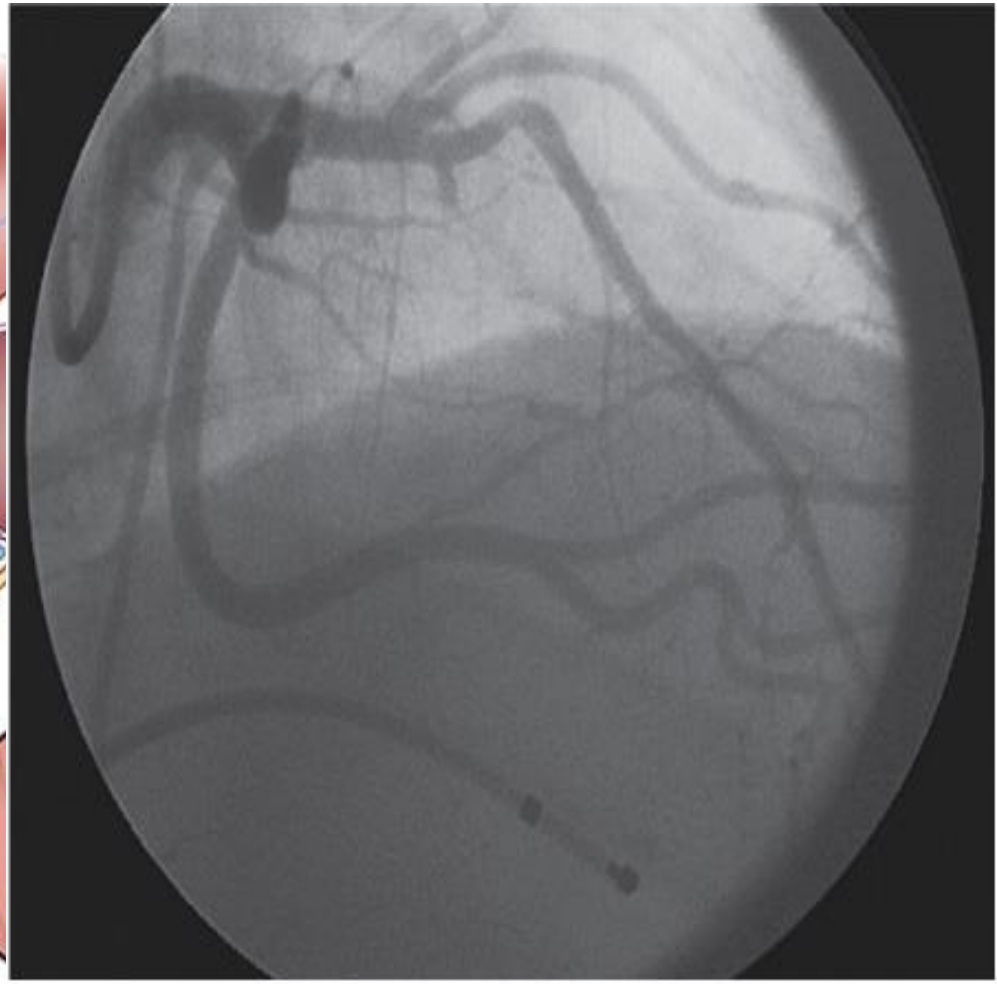
İnvaziv Tedavi(ESC 2014)



Cerrahi Miyemektomi ve Alkol Ablasyon



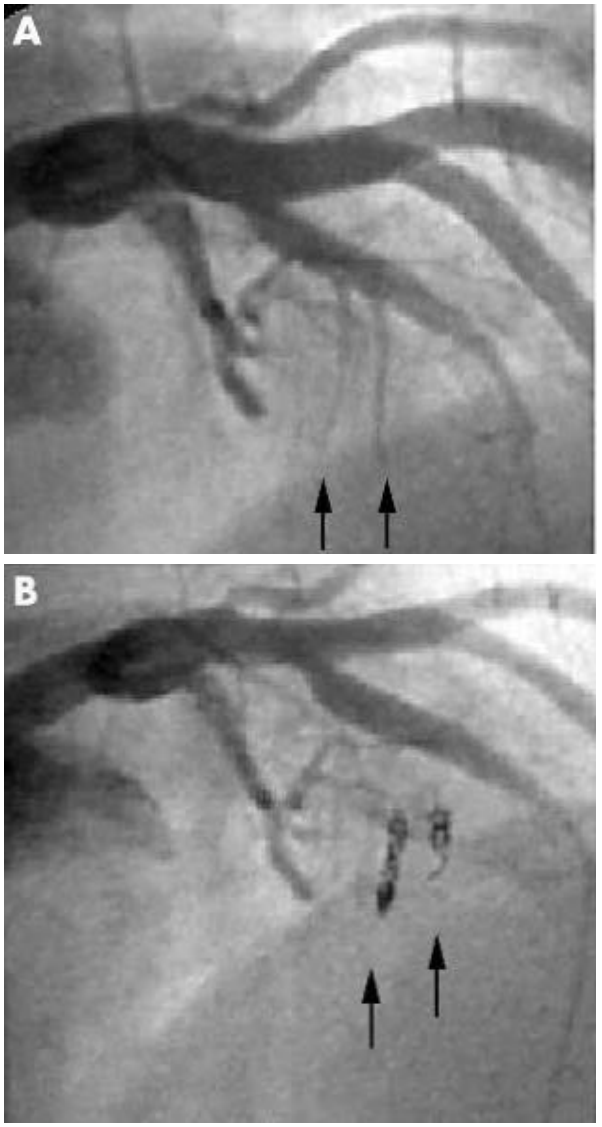
Source: Fuster V, O'Rourke RA, Walsh RA, Poole-Wilson
P: *Hurst's The Heart*, 12th Edition: http://www.accessmedicine.com



Source: Fuster V, O'Rourke RA, Walsh RA, Poole-Wilson
P: *Hurst's The Heart*, 12th Edition: http://www.accessmedicine.com

Coil Embolizasyon

- İlaca refrakter 20 olgu HKMP
- Septal perforator dallar.
- NYHA ve pik oksijen tüketimi artmış.
- Ekoda azalmış septum kalınlığı.



European Heart Journal 2008;29:350.

Recommendations on septal reduction therapy	Class[a]	Level[b]
It is recommended that septal reduction therapies be performed by experienced operators, working as part of a multidisciplinary team expert in the management of HCM.	I	C
Septal reduction therapy to improve symptoms is recommended in patients with a resting or maximum provoked LVOT gradient of ≥50 mmHg, who are in NYHA functional Class III–IV despite maximum tolerated medical therapy.	I	B
Septal reduction therapy should be considered in patients with recurrent exertional syncope caused by a resting or maximum provoked LVOTO gradient ≥50 mmHg despite optimal medical therapy.	IIa	C
Septal myectomy, rather than SAA, is recommended in patients with an indication for septal reduction therapy and other lesions requiring surgical intervention (e.g. mitral valve repair/replacement, papillary muscle intervention).	I	C
Mitral valve repair or replacement should be considered in symptomatic patients with a resting or maximum provoked LVOTO gradient ≥50 mmHg and moderate-to-severe mitral regurgitation not caused by SAM of the mitral valve alone.	IIa	C
Mitral valve repair or replacement may be considered in patients with a resting or maximum provoked LVOTO gradient ≥50 mmHg and a maximum septal thickness ≤16 mm at the point of the mitral leaflet–septal contact or when there is moderate-to-severe mitral regurgitation following isolated myectomy.	IIb	C

Dual Chamber Pacing

- Sadece miyektomi veya septal alkol ablasyonuna uygun olmayan ve maksimal tıbbi tedaviye dirençli ciddi LVOTO olan HKMP'li olgularda (Sınıf IIb)
- Ventriküler depolarizasyon ve kontraksiyon apeksten başladığı için outflow gradient ve semptomlar azalabilir.
- Randomize çalışma sonuçları tartışmalı
- Cerrahi tedaviyi tolere edemeyen hastalarda düşünülebilir.

Cihazlar

Cardiac resynchronization therapy

Recommendations	Class	Level
Cardiac resynchronization therapy to improve symptoms may be considered in patients with HCM, maximum LVOTG <30 mmHg, drug refractory symptoms, NYHA functional Class II–IV, LVEF<50% and LBBB with a QRS duration >120 ms.	IIb	C

Left ventricular assist devices

Recommendations	Class	Level
Continuous axial flow LVAD therapy may be considered in selected patients with end-stage HF despite optimal pharmacological and device treatment, who are otherwise suitable for heart transplantation, to improve symptoms, and reduce the risk of HF hospitalization from worsening HF and premature death while awaiting a transplant.	IIb	C

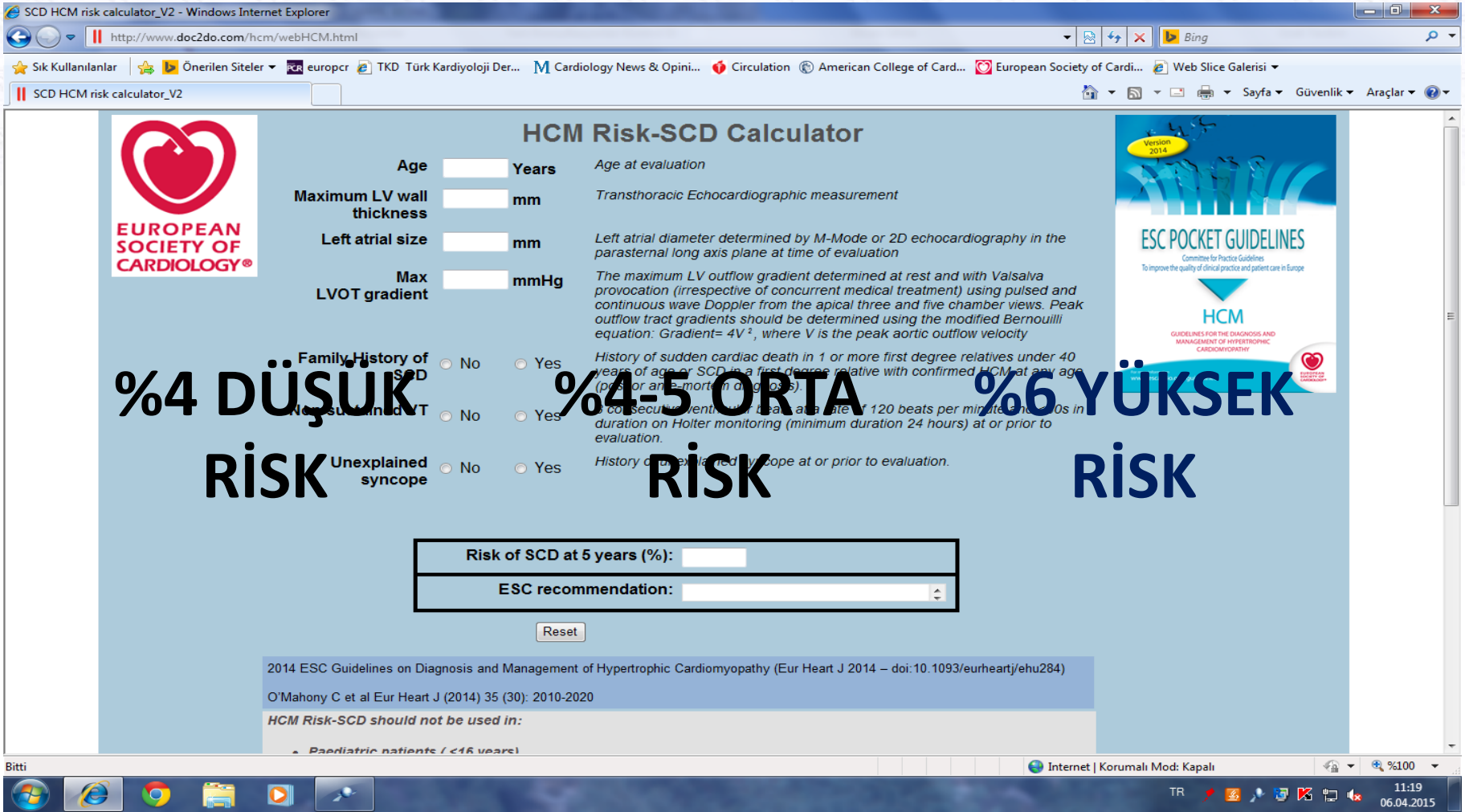
Ani Kardiyak Ölüm Risk Faktörleri

- YAŞ: Genç hastalarda yaşla ilişkili olarak AKÖ riski artmıştır.
- AİLEDE <40 YAŞ ALTINDA AKÖ HİKAYESİ(HKMP var/yok)
- LV ÇIKIŞ YOLU OBSTÜRÜKSİYONU
- AÇIKLANAMAYAN SENKOP
- NONSUSTAİNED VT ATAGI(120 vuru/dk üzerinde ambulatory (Holter) EKG de dökümente VT atağı saptanması)
- MAKSİMAL LV DUVAR KALINLIĞI(≥30 mm)
- SOL ATRİYUM ÇAPI
- EGZERSİZ İLE KAN BASINCI YANITI (en az 20 mmHg artış olmaması yada 20 mm Hg dan daha fazla düşüş görülmesi)
- Ventriküler fibrilasyon hikayesi, sustained VT, yada AKÖ hikayesi

5-year risk of SCD using the HCM Risk-SCD model

Probability $_{\text{SCD at 5 years}} = 1 - 0.998^{\exp(\text{Progostic index})}$

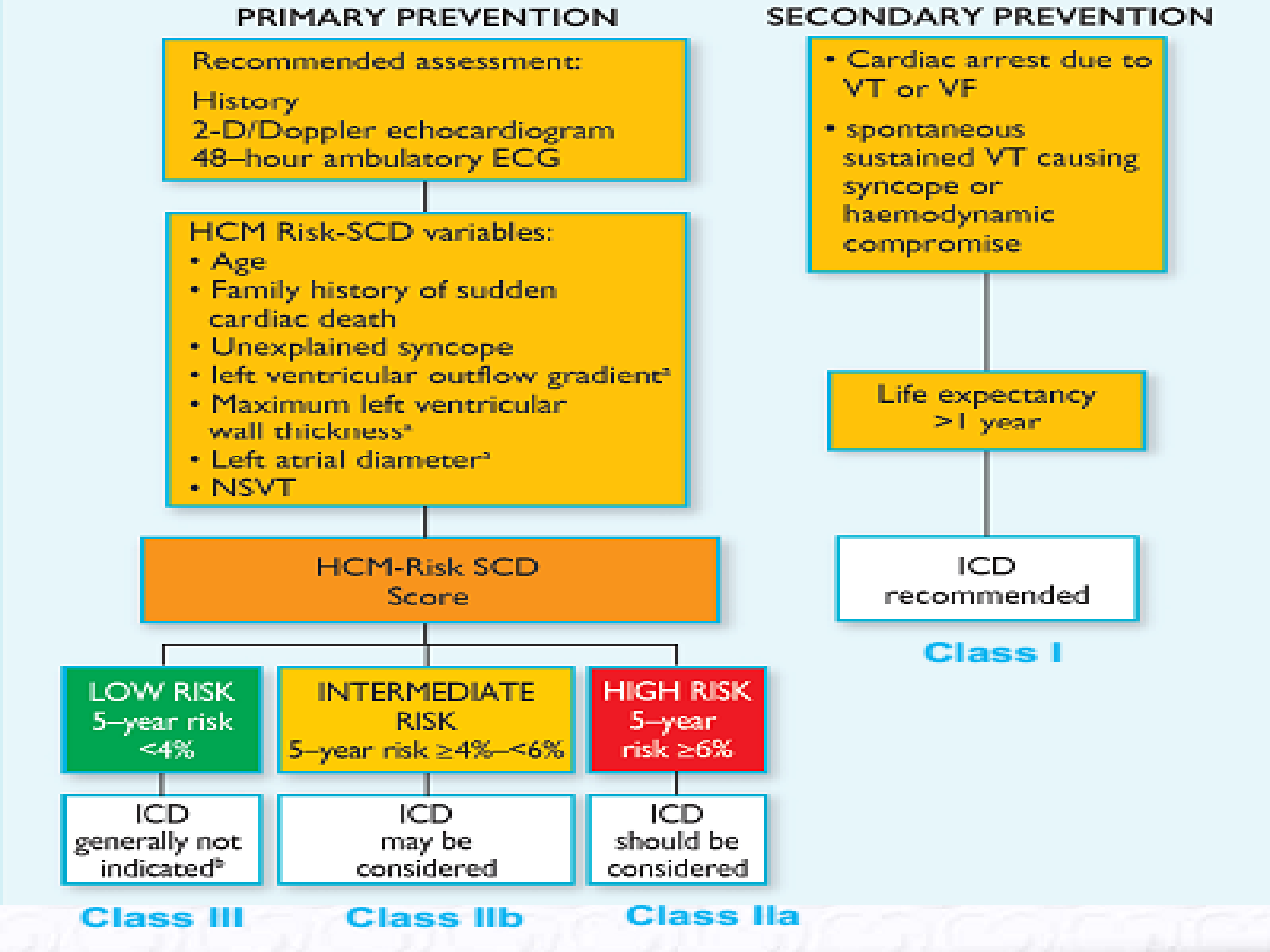
where Prognostic index = [0.15939858 x maximal wall thickness (mm)] − [0.00294271 x maximal wall thickness^2 (mm^2)] + [0.0259082 x left atrial diameter (mm)] + [0.00446131 x maximal (rest/Valsalva) left ventricular outflow tract gradient (mm Hg)] + [0.4583082 x family history SCD] + [0.82639195 x NSVT] + [0.71650361 x unexplained syncope] − [0.01799934 x age at clinical evaluation (years)].



AKÖ Risk Modeli

- 16 yaş altı olgular
- Elit atletler
- Metabolik/infiltratif bozukluklar
- Egzersizle sol ventrikül çıkış yolunda basınç farkı olanlar
- Önceden miyektomi ve/veya septal alkol ablasyonu işlemi geçirmiş olanlar
- Maksimum sol ventrikül kalınlığı 35 mm üzerinde olanlarda

Kullanılması Önerilmiyor


PRIMARY PREVENTION
SECONDARY PREVENTION
Recommended assessment:
History
2-D/Doppler echocardiogram
48–hour ambulatory ECG
HCM Risk-SCD variables:
• Age
• Family history of sudden cardiac death
• Unexplained syncope
• left ventricular outflow gradient[a]
• Maximum left ventricular wall thickness[a]
• Left atrial diameter[a]
• NSVT
HCM-Risk SCD Score
LOW RISK 5–year risk <4%
INTERMEDIATE RISK 5–year risk ≥4%–<6%
HIGH RISK 5–year risk ≥6%
ICD generally not indicated[b]
ICD may be considered
ICD should be considered
Class III
Class IIb
Class IIa
• Cardiac arrest due to VT or VF
• spontaneous sustained VT causing syncope or haemodynamic compromise
Life expectancy >1 year
ICD recommended
Class I

Prevention of sudden cardiac death

Recommendations	Class	Level
Avoidance of competitive sports is recommended in patients with HCM.	I	C
ICD implantation is recommended in patients who have survived a cardiac arrest due to VT or VF, or who have spontaneous sustained VT causing syncope or haemodynamic compromise, and have a life expectancy of >1 year.	I	B
HCM Risk-SCD is recommended as a method of estimating risk of sudden death at 5 years in patients aged ≥16 years without a history of resuscitated VT/VF or spontaneous sustained VT causing syncope or haemodynamic compromise.	I	B
It is recommended that the 5-year risk of SCD be assessed at first evaluation and re-evaluated at 1–2 yearly intervals or whenever there is a change in clinical status.	I	B
ICD implantation should be considered in patients with an estimated 5-year risk of sudden death of ≥6% and a life expectancy of >1 year, following detailed clinical assessment that takes into account the lifelong risk of complications and the impact of an ICD on lifestyle, socio-economic status and psychological health.	IIa	B

Kalp Transplantasyonu

- Maksimal farmakolojik ve nonfarmakolojik tedaviye rağmen semptomatik hastalar

Cardiac transplantation

Recommendations	Class	Level
Orthotopic cardiac transplantation should be considered in eligible patients who have an LVEF <50% and NYHA functional Class III–IV symptoms despite optimal medical therapy or intractable ventricular arrhythmia.	IIa	B
Orthotopic cardiac transplantation may be considered in eligible patients with normal LVEF (≥50%) and severe drug refractory symptoms (NYHA functional Class III–IV) caused by diastolic dysfunction.	IIb	B

Atriyal Fibrilasyon

- Mümkün ise en kısa sürede sinüs ritmi sağlanmalı.
- Sol atriyum çapı 45 mm ve üzerinde ise 6-12 ayda bir 48-saatlik Holter ile AF taranması sınıf IIa olarak öneriliyor. Saptanması halinde, HKMP'de herhangi bir tromboemboli risk skorlamasından bağımsız olarak doğrudan hayat boyu OAK tedavi (varfarin) endikasyonu oluşturuyor.(CHA2DS2-VASc bağımsız).
- Varfarin kullanılamayan hastalarda Dabigatran, Rivoraksaban vb. YOAK ajanlar kullanılabilir.
- Aspirin + klopidogrel sadece herhangi bir oral antikoagülanı alamayan veya almak istemeyen olgularda (Sınıf IIa)
- Sol atriyumu genişlememiş ve ilaçlara dirençli hastalarda AF ablasyon
- Hastalar sinüs ritmine dönse bile ömür boyu antikoagülan tedavi önerilmeli.

Gebelik

- Ciddi semptomlar, LVOTO veya ciddi sol ventrikül sistolik fonksiyon bozukluğu varsa gebelik önerilmiyor.
- HKMP'nin tıbbi tedavisinde kullanılan tüm ilaçlar gebelikte de kullanılabilir.
- Doğumun Uyarılması:
  - Prostaglandin $\Rightarrow$ vazodilatatör etkisi var
  - Oxytosin $\Rightarrow$ iyi tolare
- Tokolitik ajanlar
  - β-agonist $\Uparrow$ LVOT obstriksiyon
  - $MgSO_4$ tercih
- Kaçınılması gereken durumlar
  - Kan kaybı
  - Vazodilatatörler
  - Sempatik uyarılar

Komplikasyon ve Prognoz

- Birçok HKMP hastası asemptomatik.
  - Kalp yetmezliği
  - Ventriküler aritmi
  - Supraventriküler aritmi
  - İnfektif mitral endokardit
  - Atriyal fibrilasyon
  - Ani kardiyak ölüm
- Genç hastalarda mortalite hızı daha yüksek
  Yıllık mortalite:%1-3 ve %6 olarak bildirilmiş.

Klinik Öneriler

- Dehidratasyonun önlenmesi
- Aşırı alkol alımının engellenmesi,
- Yarışmalı sporlardan uzak durulması,
- Kuvvetli vazodilatör ve
- Pozitif inotropik ilaçlardan kaçınılması
- Genetik Tarama

Recommendations on genetic counselling	Class[a]	Level[b]
Genetic counselling is recommended for all patients with HCM when their disease cannot be explained solely by a non-genetic cause, whether or not clinical or genetic testing will be used to screen family members.	I	B
Genetic counselling should be performed by professionals trained for this specific task working within a multidisciplinary specialist team.	IIa	C

Klinik Öneriler

Topic	General guidance
Exercise	• Patients with HCM should avoid competitive sports activities, but should maintain a healthy lifestyle • Advice on recreational activities should be tailored to symptoms and the risk of disease-related complications including sudden cardiac death
Diet, alcohol and weight	• Patients should be encouraged to maintain a healthy body mass index • Large meals can precipitate chest pain, particularly in patients with LVOTO. Smaller, more frequent meals may be helpful • Avoid dehydration and excess alcohol, particularly in patients with LVOTO • Constipation is a frequent side-effect of verapamil/disopyramide and should be managed with diet and if necessary aperients
Smoking	• There are no data that show an interaction between tobacco smoking and HCM, but patients should be provided with general advice on the health risks associated with smoking and, when available, information on smoking cessation
Sexual activity	• Patients should be given the opportunity to discuss their concerns about sexual activity. Anxiety and depression following a diagnosis are frequent and some patients may express guilt or fear about their genetic diagnosis and the risk of transmission to offspring • Patients should be counselled on the potential effect of their medication on sexual performance • In general, patients should avoid PDE_5 inhibitors, particularly when they have LVOTO
Medication	• Patients should be provided with information about their medication, including potential side-effects and interactions with prescribed medications, over-the-counter remedies and other complementary therapies • Where possible, peripheral vasodilators should be avoided in patients, particularly when they have LVOTO
Vaccination	• In the absence of contraindications, symptomatic patients should be advised to have yearly influenza vaccination
Driving	• Most patients should be eligible for an ordinary driving licence and can continue driving unless they experience distracting or disabling symptoms • Advice on driving licences for heavy goods or passenger-carrying vehicles should be in line with local legislation • For further advice on driving with ICD see EHRA guidance[324] and local rules
Occupation	• Most people with HCM will be able to continue in their normal job. The implications of heavy manual jobs that involve strenuous activity should be discussed with the appropriate specialist • For some occupations such as pilots, and military and emergency services, there are strict guidelines on eligibility • The social and financial implications of a diagnosis of HCM should be included in the counselling of relatives *before* clinical or genetic screening
Holidays and travel insurance	• Most asymptomatic or mildly symptomatic patients can fly safely. For further advice see *Fitness to fly for passengers with cardiovascular disease*[325] • Insurance companies may charge more for travel insurance. In some countries, patient support organizations can provide further advice about obtaining reasonable insurance
Life insurance	• The diagnosis of HCM will result in difficulty obtaining life insurance or mortgages. Advice on the rules that apply in different countries should be provided to patients at diagnosis
Pregnancy and childbirth	• See Reproduction and contraception (section 11)
Education/schooling	• Teachers and other carers should be provided with advice and written information relevant to the care of children with HCM • In the absence of symptoms and risk factors, children should be allowed to perform low to moderate level aerobic physical activity, in accordance with advice from their cardiologist • Provision should be made for children with learning difficulties and other special needs