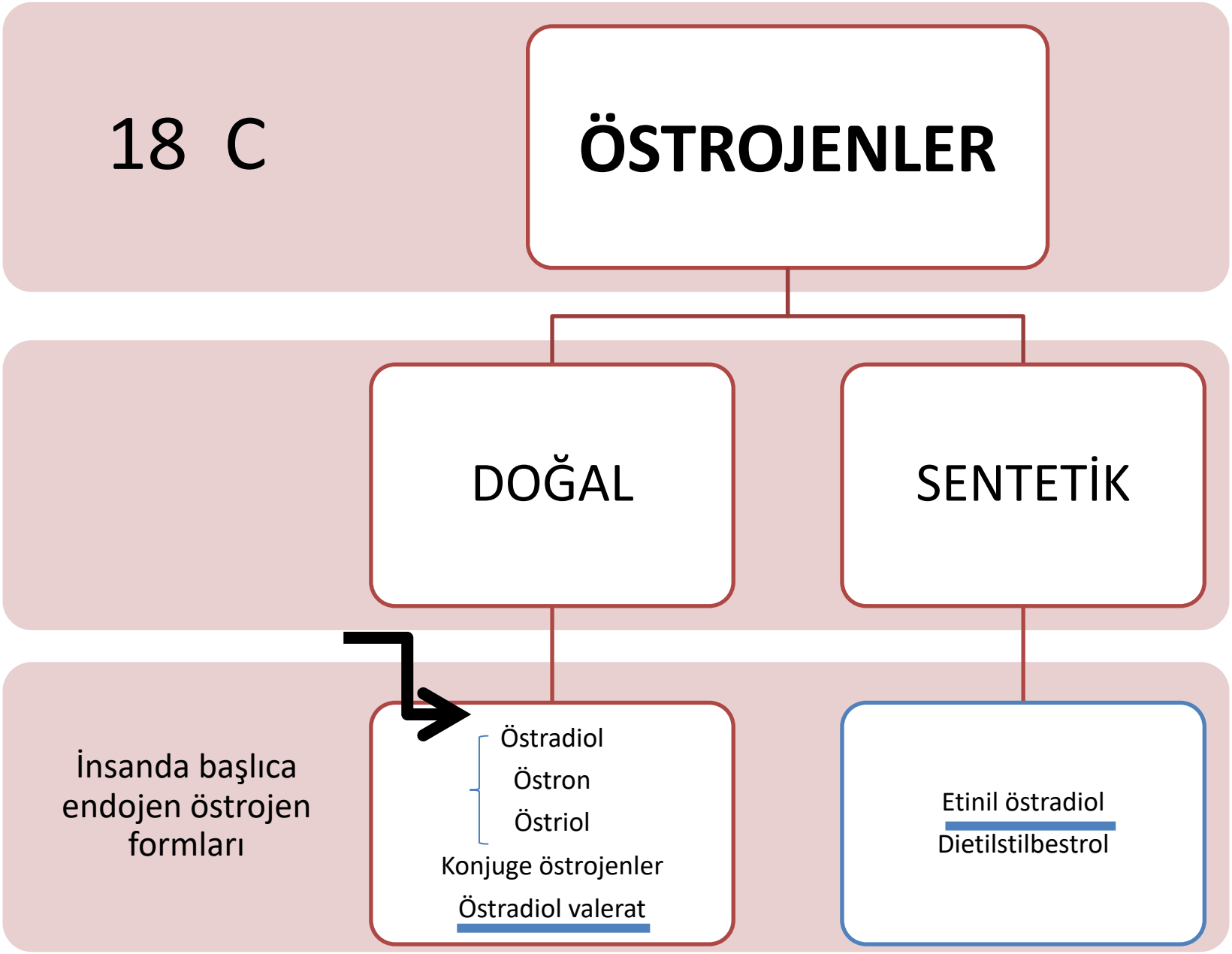

# OLGULARLA KONTRASEPSİYON

Prof. Dr. Yaprak ÜSTÜN


18 C
ÖSTROJENLER
DOĞAL
SENTETİK
İnsanda başlıca endojen östrojen formları
Östradiol
Östron
Östriol
Konjuge östrojenler
Östradiol valerat
Etinil östradiol
Dietilstilbestrol

# EE (17α etinil)-EV

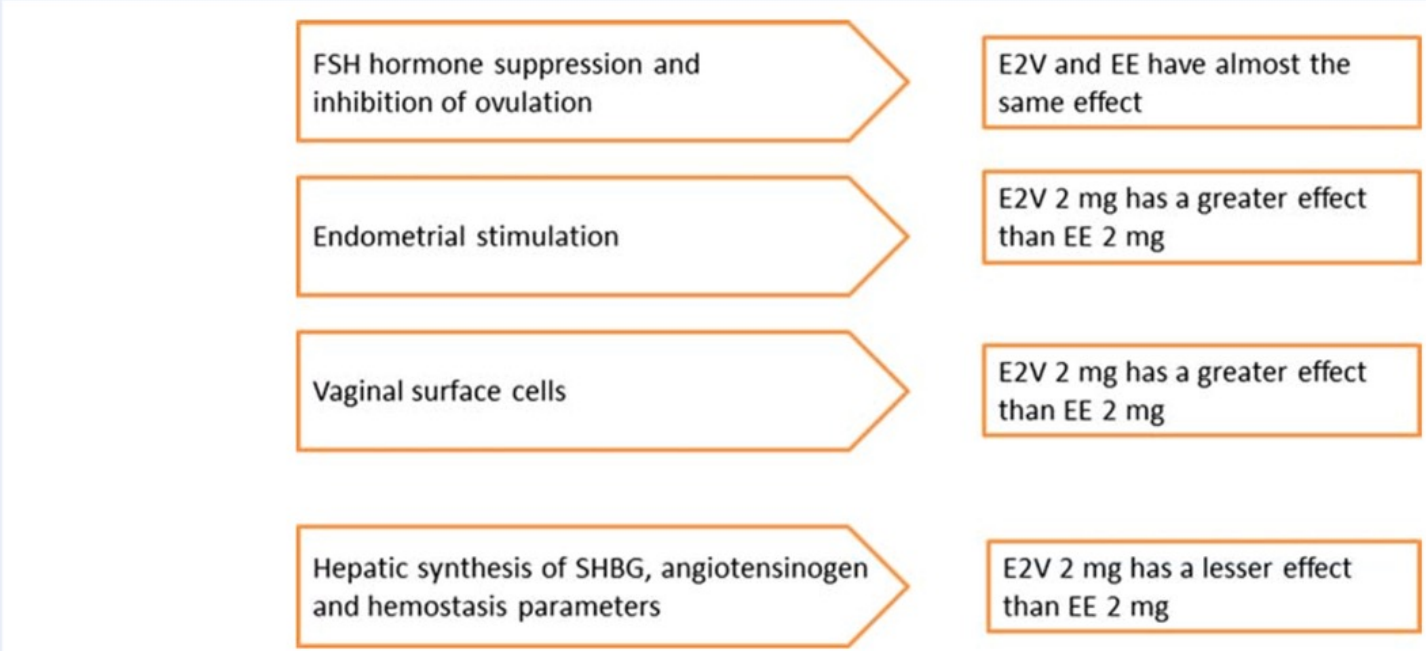
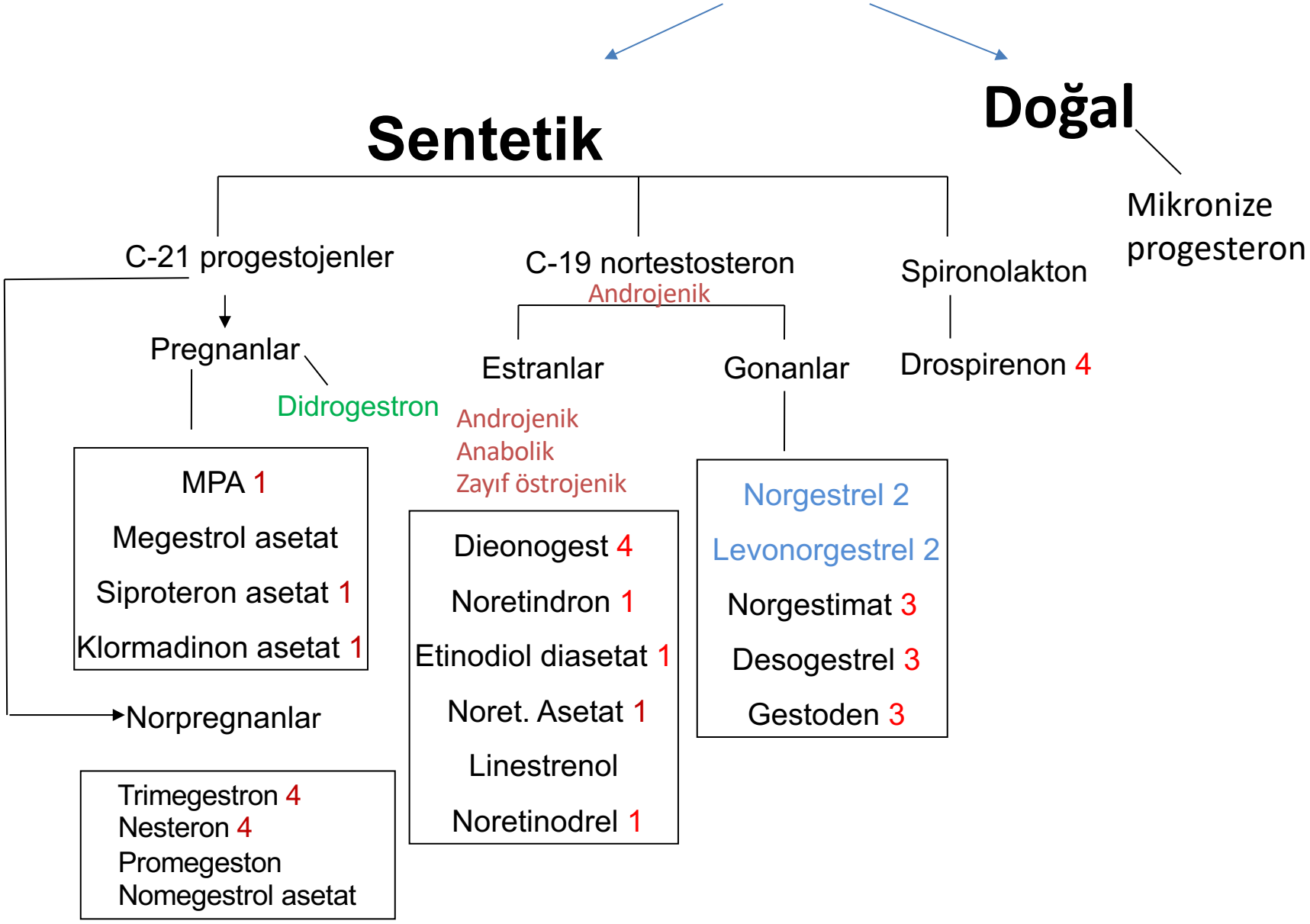
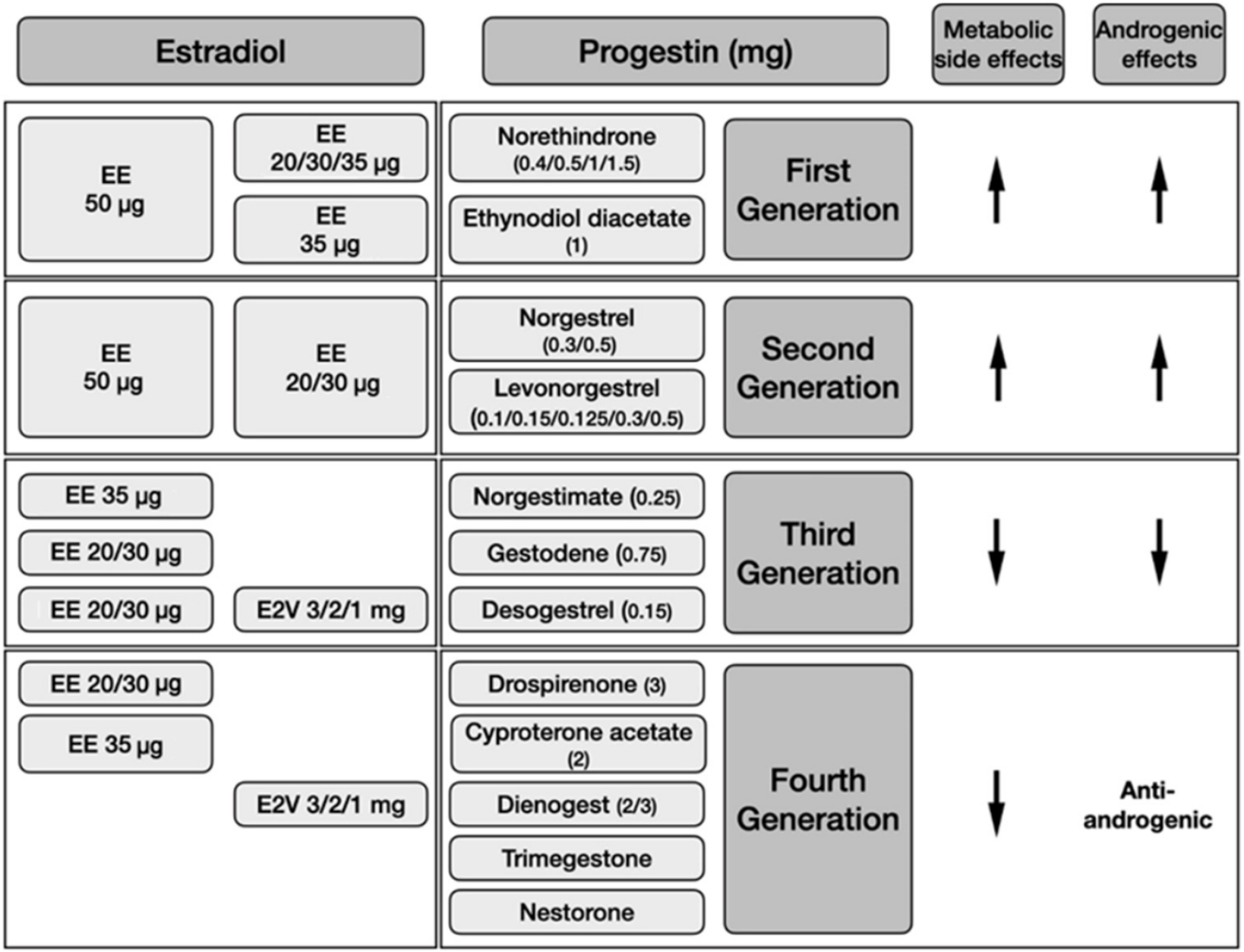



**Figure 1** Comparison of the oral contraceptives (OCs) E2V and EE. SHBG, sex hormone-binding protein; E2V, estradiol valerate; EE, ethinylestradiol.

1 mg EV= 0.76 mg 17 β östradiol


Sentetik
Doğal
Mikronize progesteron
C-21 progestojenler
C-19 nortestosteron
Androjenik
Spironolakton
Pregnanlar
Didrogestron
Estranlar
Gonanlar
Drospirenon 4
Androjenik
Anabolik
Zayıf östrojenik
MPA 1
Megestrol asetat
Siproteron asetat 1
Klormadinon asetat 1
Norpregnanlar
Trimegestron 4
Nesteron 4
Promegeston
Nomegestrol asetat
Dieonogest 4
Noretindron 1
Etinodiol diasetat 1
Noret. Asetat 1
Linestrenol
Noretinodrel 1
Norgestrel 2
Levonorgestrel 2
Norgestimat 3
Desogestrel 3
Gestoden 3




≤35 µg

Gelişim sırası

# OLGU

- BB, 23 yaşında, sağlıklı
- Sigara içmeyen ve tıbbi komplikasyonları olmayan bir kadın.
- KOK  kullanımı için KE yok

Hangi hormonal doğum kontrol yönteminin reçete edileceğine nasıl karar verilir?

- En iyi yönteme karar vermeden önce mevcut ve uygun tüm doğum kontrol biçimlerini tartışın.

- Gebelikten korunma sağlayacak,
- Kontraseptif olmayan faydaları olacak,
- Yan etkileri en aza indirecek, **en düşük dozda** oral kontraseptif kullanın.

# OLGU 1

- 23 y, 0G 0P, VKİ: 24 kg/$m^2$, oligomenore
- FM: FGS:9, USG: PKOS, Lab: N
- Kontraseptif yöntem istiyor

?

# OLGU 1

- 23 y, 0G 0P, VKİ: 24 kg/$m^2$, oligomenore
- FM: FGS:9, USG: PKOS, Lab: N
- Kontraseptif yöntem istiyor
- VTE açısından risk faktörü Ø

Zayıf PKOS + kontrasep.

# Progestagenler

↑antiandrojenik etki

## C-21 progestojenler

### Pregnanlar

- MPA
- Megestrol asetat
- Siproteron asetat
- Klormadinon asetat

### Norpregnanlar

- Trimegeston
- Nesteron

## C-19 nortestosteron

Androjenik

### Estranlar

- Dieonogest 4
- Noretindron 1
- Etinodiol diasetat 1
- Noret. asetat
- Linestrenol
- Noretinodrel 1

### Gonanlar

- Norgestrel 2
- Levonorgestrel 2 → En androjenik
- Norgestimat 3
- Desogestrel 3
- Gestoden 3

Daha az androjenik

## Spironolakton

- Drospirenon 4

3 mg

Jeneras-markete giriş sırası

Yapısal: estran...

**Comparative study of the therapeutic effects of oral contraceptive pills containing desogestrel, cyproterone acetate, and drospirenone in patients with polycystic ovary syndrome**

Sudhindra Mohan Bhattacharya, M.D.,[a] and Ayan Jha, D.P.H.[b]

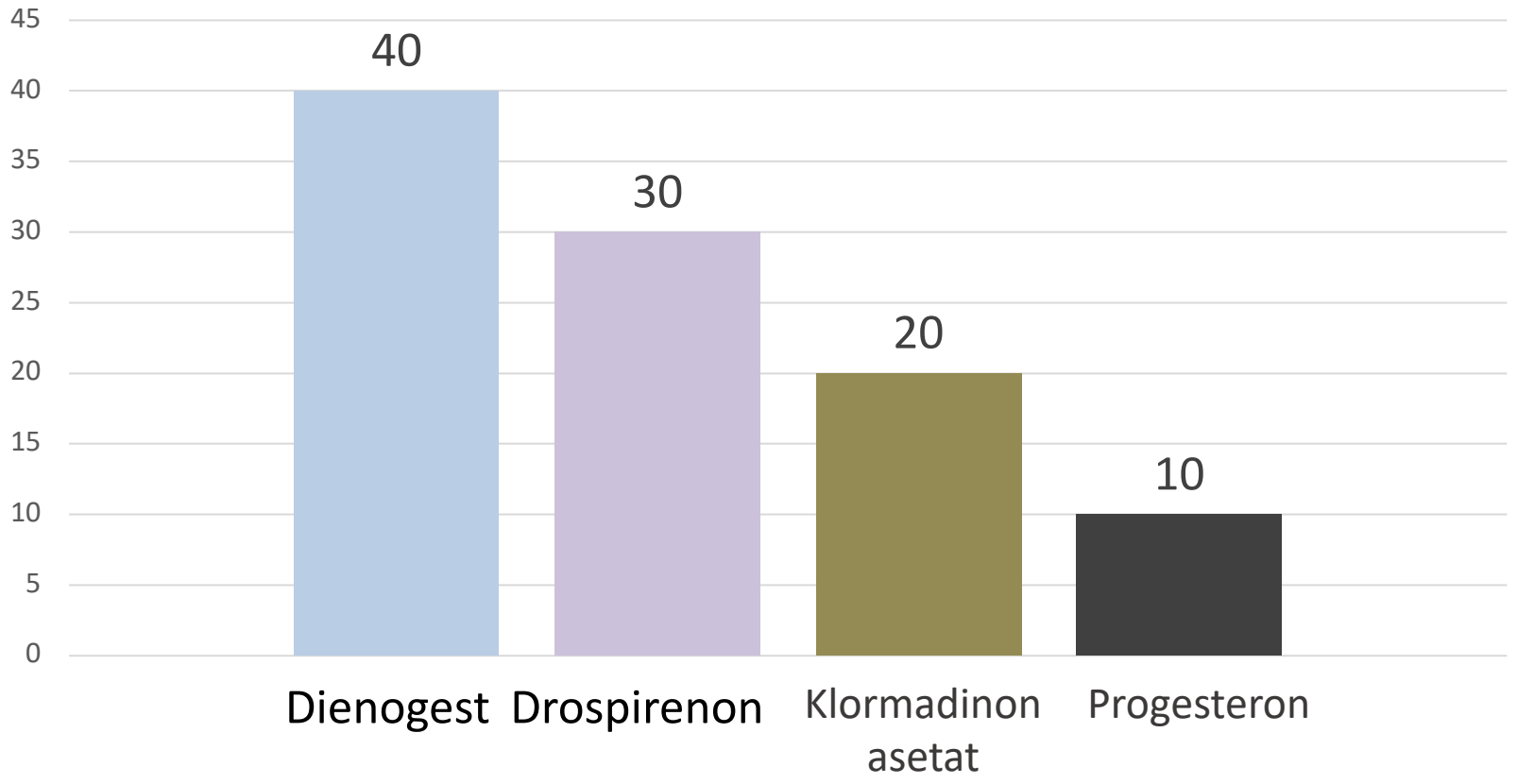
12.ayda

Siproteron asetat >Drospirenon>Desogestrel

| | Change from baseline | | | | | | |
|---|---|---|---|---|---|---|---|
| | Desogestrel (n = 58) | | Cyproterone acetate (n = 56) | | Drospirenone (n = 57) | | *P* value of changes from baseline (ANOVA) |
| rs | Mean | SD | Mean | SD | Mean | SD | |
| | −0.45 | 6.75 | −0.59 | 4.76 | 0.11 | 5.54 | .79 |
| minal circumference | −0.28 | 5.27 | −0.21 | 5.21 | 1.07 | 5.70 | .33 |
| ist–hip ratio | 0.00 | 0.08 | −0.02 | 0.08 | 0.02 | 0.09 | .07 |
| n-FG score | −1.69 | 5.69 | −5.29 | 5.88 | −2.12 | 6.58 | .003[a,b] |

Sitruk Ware, 2006

# Rölatif antiandrojenik aktivite




Siproteron asetat referans moleküldür

Androjen düzeyine etki açısından 20 ve 30 µg arası fark yok

Bhattacharya, 2016

PKOS'ta
PAI-1 aktivitesi ↑

PKOS'ta VTE X 1.5↑
PKOS + KOK - VTE X 2↑

Bird ST, 2013
Gariani, 2020

Etkili en düşük östrojen dozunu kullanmak akılcı

- PKOS'ta VTE nedeniyle **drospirenon ve siproteron asetat** içeren KOK'lar 1. basamak olarak seçilmemelidir

Association between polycystic ovary syndrome and venous thromboembolism: A systematic review and meta-analysis

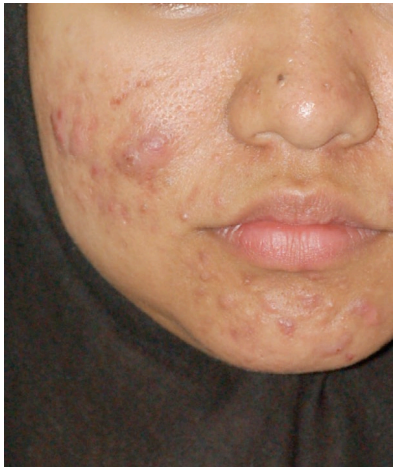
Karim Gariani[a], Justine Hugon-Rodin[b,c], Jacques Philippe[a], Marc Righini[d], Marc Blondon[d,*]

| | EE | Progesteron | Kullanım |
|---|---|---|---|
| *Myralon* | 20 µg | Desogestrel – 150 mg | 21 hap + 7 ara |
| *Desolett* | 30 µg | Desogestrel - 150mg | 21 hap + 7 ara |
| *Belara* | 30 µg | Klormadion asetat – 2mg | 21 hap + 7 ara |
| *Ginera* | 30 µg | Gestoden 150mg | 21 hap + 7 ara |
| *Minulett* | 30 µg | Gestoden 75mg | 21 hap + 7 ara |
| *Mycrogynon/ Leverette* | 30 µg | Levonergestrel 150 mg | 21 hap + 7 ara |
| *Miranova/ Cybelle* | 20 µg | Levonorgestrel 100 mg | 21 hap + 7 ara |
| *Yazz/Drospera* | 20 µg | Drospirenon – 3 mg | 28 hap (24 + 4) |
| *Yasmin/Drosetil* | 30 µg | Drospirenon – 3 mg | 21 hap + 7 ara |
| *Dienille* | 30 µg | Dienogest 2 mg | 21 hap + 7 ara |
| *Qlairista* | 30-20 µg EV | Dienogest 2-3 mg | 28 hap (26 + 2) |

# OLGU 2

- 19 y, 0G, evli, VKİ: 23 kg/$m^2$
- FGS:8, Tedaviye cevap vermeyen, inatçı, püstülokistik - nodülokistik ciddi akne
- USG: N, Lab: N
- Kontrasepsiyon istemi

?



# OLGU 2

- 19 y, 0G, evli, VKİ: 23 kg/$m^2$, mens düzenli
- FGS: 8, Tedaviye cevap vermeyen, inatçı, püstülokistik - nodülokistik ciddi akne
- USG: N, Lab: N
- Kontrasepsiyon istemi

**İdiopatik Hirsutismus + ciddi akne**

# AKNE VULGARİS-KOK

- Cilt hijyeni
- Topikal ajan (retinoid, antibiyotik)
- Sistemik retinoid
- Oral antibiyotik

- < 15 yaş
- Orta-ciddi dirençli püstülokistik ya da nodülokistik
- Konvansiyonel tedaviye cevap vermeyen
- Hiperandrojenizm bulguları
- PMDD bulguları olan
- Kontrasepsiyon isteyen

Östrojen

↓

Androjenlerin pilosebase üniteler üzerindeki uyarıcı etkisini baskılar

↓

Sebum üretimi ve keratinöz materyal birikimi ↓

↓

Yağ bezlerinin boyutu ve işlevi ↓

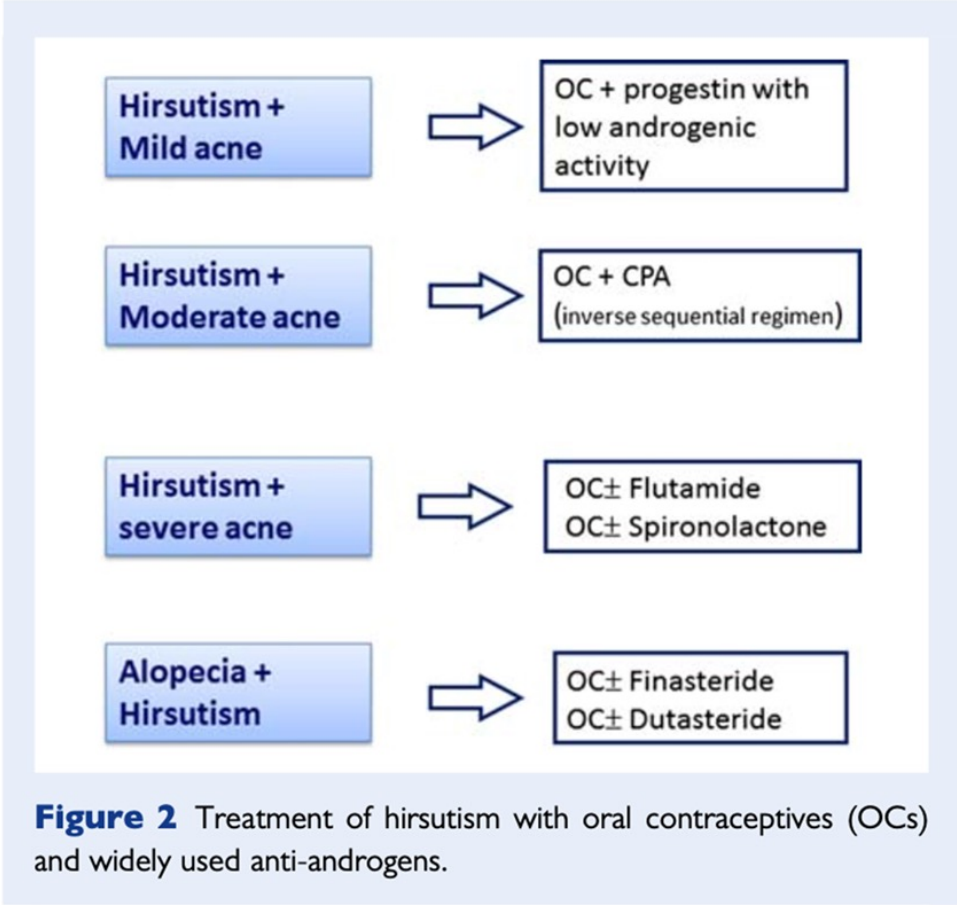



**Figure 2** Treatment of hirsutism with oral contraceptives (OCs) and widely used anti-androgens.

**Dermatology: how to manage acne vulgaris**

Alexander KC Leung[1], Benjamin Barankin[2], Joseph M Lam[3], Kin Fon Leong[4], Kam Lun Hon[5]

# OLGU 3

- 23 y, 0G 0P, VKİ: 31 kg/$m^2$
- FM: FGS:4, USG: N, Lab: N
- Sigara Ø, ek faktör Ø
- Kontraseptif yöntem istiyor

?

# OLGU 3

- 23 y, 0G 0P, VKİ: 31 kg/$m^2$
- FM: FGS:4, USG: N, Lab: N
- Sigara Ø, ek faktör Ø
- Kontraseptif yöntem istiyor

Obez + kontrasep.

## Box 2. Risk Factors for Venous Thromboembolism in Users of Combined Hormonal Contraceptives*

- Smoking and age 35 years or older
- Less than 21 days after giving birth or 21–42 days after giving birth with other risk factors (eg, age 35 years or older, previous venous thromboembolism, thrombophilia, immobility, transfusion at delivery, peripartum cardiomyopathy, body mass index of 30 or greater, postpartum hemorrhage, postcesarean delivery, preeclampsia, or smoking)
- Major surgery with prolonged immobilization
- History of deep vein thrombosis or pulmonary embolism
- Hereditary thrombophilia (including antiphospholipid syndrome)
- Inflammatory bowel disease with active or extensive disease, surgery, immobilization, corticosteroid use, vitamin deficiencies, or fluid depletion
- Systemic lupus erythematosus with positive (or unknown) antiphospholipid antibodies
- Superficial venous thrombosis (acute or history)

HEMOSTASIS AND THROMBOSIS

*Review*

# Hormones and thrombosis: the dark side of the moon

Doris Barcellona[1], Elvira Grandone[2,3,4], Francesco Marongiu[5,6]

- KOK'u obez kadınlara önerirken dikkatli ol
  - VTE için önemli risk faktörü
  - Obez kadında VTE riski 10 x↑
  - Obez + KOK kullanımı vs. zayıf kullanmayan VTE için OR=**23.8**

International Journal of
*Molecular Sciences*

MDPI

*Review*

# A Comprehensive Review of Risk Factors for Venous Thromboembolism: From Epidemiology to Pathophysiology

Daniele Pastori [1,*], Vito Maria Cormaci [1], Silvia Marucci [1], Giovanni Franchino [1], Francesco Del Sole [1],

- OKS hem arteriyel hem de venöz tromboz (↑) için risk faktörüdür
- Risk;
  - Daha yüksek östrojen dozları (**>30** mcg etinil östradiol) ve
  - **Levonorgestrel** olmayan progestin ile artabilir

| Population | Relative Risk | Incidence |
|---|---|---|
| Young women—general population | 1 | 5–10/10,000/year |
| Pregnant women | 12 | 60–120 |
| High-dose oral contraceptives | 6–10 | 30–100 |
| Low-dose oral contraceptives | 2 | 10–20 |
| Leiden mutation carrier | 6–8 | 30–80 |
| Leiden carrier and oral contraceptives | 10–15 | 50–100 |
| Leiden mutation—homozygous | 80 | 400–800 |

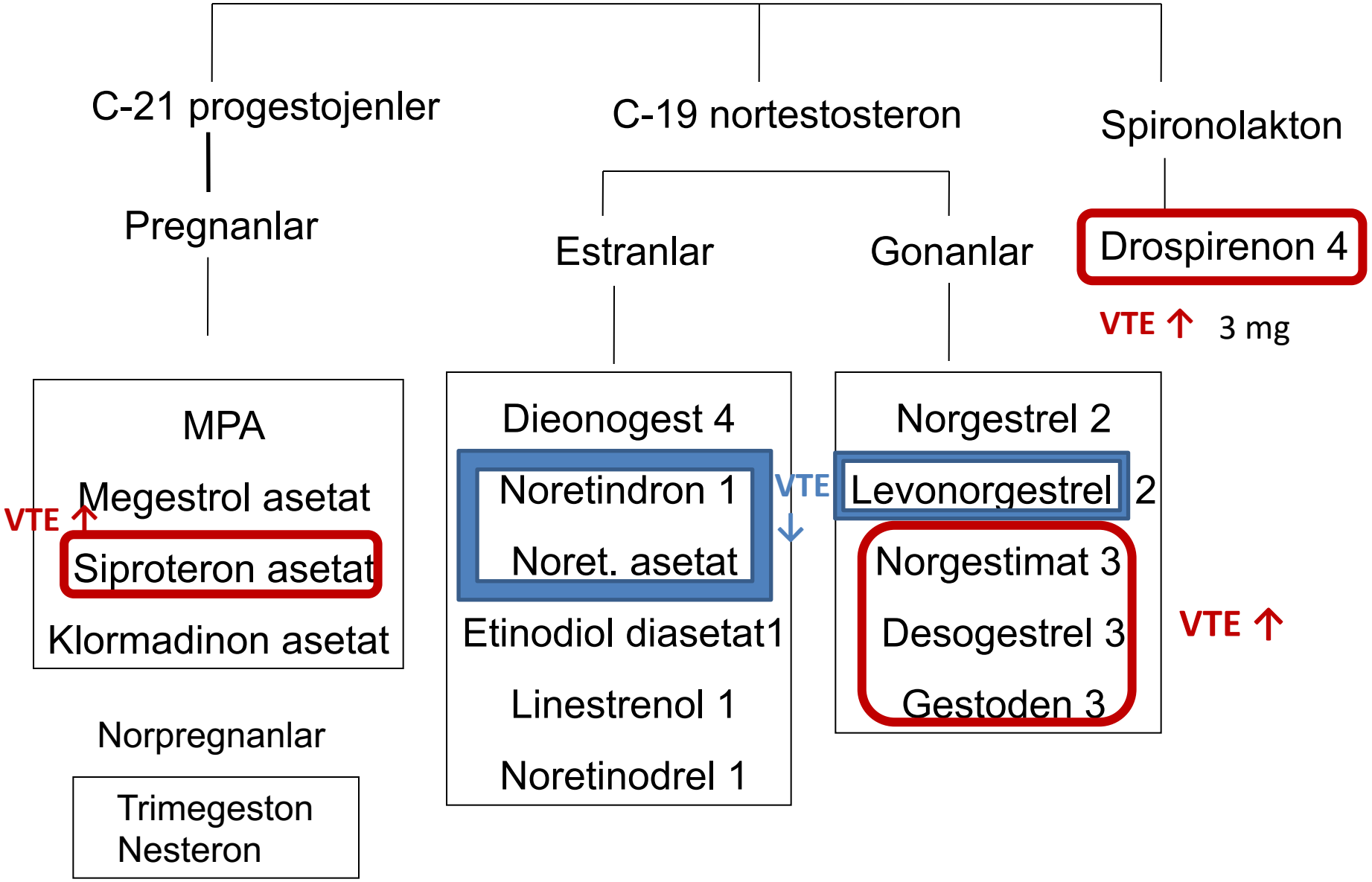
**Trombin oluşumunu artırarak**

Öst. dozuna bağlı rolü MMP'de ↑- intima kollajen ve elastin hasarı, venöz staz, damar geçirgenliğinin artması-venöz tromboz

| | Baseline* | Pregnancy[37] | LNG-IUD | Progestin-only pills |
|---|---|---|---|---|
| VTE risk‡ | 3 | 5–20 | 2 | 2–3 |

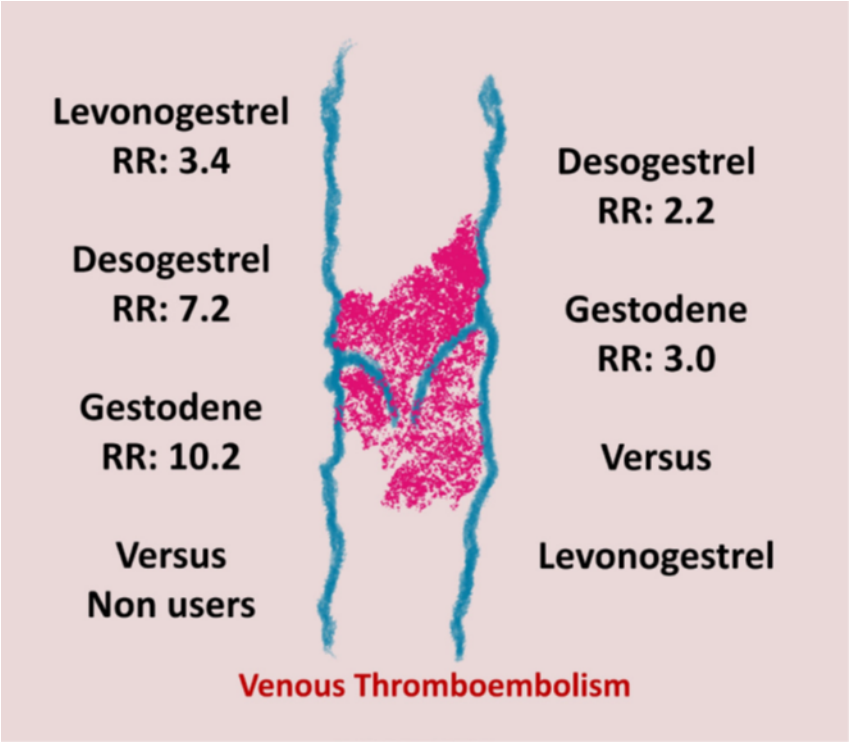
| Second-generation OCs | Fourth-generation OCs | Third-generation OCs | First generation OCs† |
|---|---|---|---|
| 5–7 | 9–12 | 9–12 | 6–12 |

# Progestagenler



# Hormonal contraception and risk of venous thromboembolism: national follow-up study

| PROGESTİN | VTE RİSK |
|---|---|
| Noretisteron | 0.98 (0.71-1.37) |
| Levonorgestrel | 1.00 (referans) |
| Norgestimat | 1.19 (0.96-1.47) |
| Desogestrel | 1.82 (1.49-2.22) |
| Gestoden | 1.86 (1.59-2.18) |
| Drospirenon | 1.64 (1.27-2.10) |
| Siproteron | 1.88 (1.47-2.42) |




Lidegaard, BMJ, 2009

**Table 2.** Risk of Venous Thromboembolism among Combined Oral Contraceptive Users According to the Type of Progestin

| Variable | VTE risk, RR (95% CI) |
|---|---|
| Second-generation | |
| Levonorgestrel | 1 |
| Third-generation | |
| Norgestimate | 1.14 (0.94–1.32)[a] |
| Gestodene | 1.67 (1.32–2.10)[a] |
| | 1.27 (1.15–1.4)[b] |
| Desogestrel | 1.83 (1.55–2.13)[a] |
| | 1.46 (1.33–1.59)[b] |
| Fourth-generation | |
| Drospirenone | 1.58 (1.12–2.14)[a] |
| | 1.40 (1.26–1.56)[b] |
| Cyproterone acetate | 2.04 (1.55–2.49)[a] |
| | 1.29 (1.12–1.49)[b] |
| Dienogest | 1.46 (0.57–5.41)[a] |

VTE, venous thromboembolism; RR, relative risk; CI, confidence interval.

The estimated RR for VTE for 1 year of combined oral contraceptive use was provided from the meta-analyses by [a]Dragoman et al. [42] and [b]Oedingen et al. [48], respectively, in comparison to levonorgestrel. Data on VTE risk were obtained from the general population, and the absolute risk of VTE is low (8–10/10,000 woman-years).

# Venous thrombosis and hormonal contraception: what's new with estradiol-based hormonal contraceptives?

- VTE insidansı
  - EV/dienogest 7.1/10000 kadın yılı
  - EE/levonorgestrel 8.8/10000 kadın yılı

BENZER

Hemostatik faktörlere etki min
D-dimer artışı %39
Koagülasyon aktivasyonu daha ↓

INAS-SCORE
Fruzzetti, 2018

**Table II** **Oral contraceptives and body weight in reproductive life.**

| | Adolescence | Fertile age | Perimenopause |
|---|---|---|---|
|  **Normal weight** **BMI: 18.5-24.9 Kg/m²** | EE 15-20 mcg<br>Neutral Progestin | EE 20-30 mcg<br>Neutral Progestin | EE 15-20 mcg or NE<br>Neutral Progestin<br>Or antiandrogenic |
|  **Overweight** **BMI: >25 Kg/m²** | EE 15-20 mcg or NE<br>Antiandrogenic progestin | EE 15-20 mcg or NE<br>Antiandrogenic progestin | EE 15-20 mcg or NE<br>Antiandrogenic progestin |
|  **Underweight** **BMI: <18.5 Kg/m²** | EE ≥ 30 mcg<br>Neutral progestin or mild antiandrogenic | EE > 30 mcg<br>Neutral progestin or mild antiandrogenic | EE 15-20 mcg or NE<br>Neutral progestin |

In the various phases of female reproductive life, the best combination of oral contraceptive should be chosen on the basis of body weight (EE, ethinylestradiol; NE, natural estradiol). Neutral progestins are deso/etonogestrel, GSD, medroxyprogesterone acetate and norelgestromin. Anti-androgenic progestins are clormadinone, cyprtoterone acetate, DNG and drospirenone.

Diyet öner
Levonorgestrel içeren OKS
Dienogest içeren OKS
İmplant

# OLGU 4

- 40 y, 2G 2P 2Y, VKİ: 24 kg/$m^2$
- PID öyküsü var. VTE öyküsü Ø
- Sigara 10 adet /gün
- Kontraseptif yöntem istiyor

?

# OLGU 4

- 40 y, 2G 2P 2Y, VKİ: 24 kg/$m^2$
- PID öyküsü var. VTE öyküsü Ø
- Sigara 10 adet /gün
- Kontraseptif yöntem istiyor

Yaş > 35 + sigara

## Safety and efficacy of a single-rod etonogestrel implant (Implanon): results from 11 international clinical trials

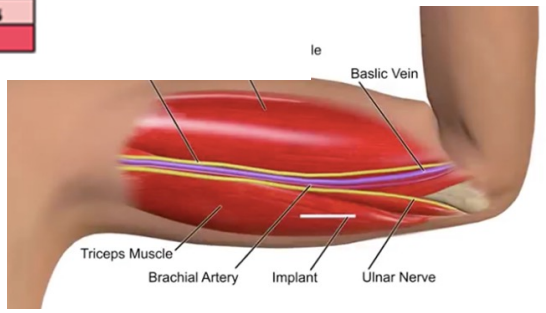
*Philip Darney, M.D.,*[a] *Ashlesha Patel, M.D.,*[b] *Kimberly Rosen, M.D.,*[c] *Lena S. Shapiro, Ph.D.,*[c] *and Andrew M. Kaunitz, M.D.*[d]

- 942 hasta, 2-3 yıl
- DVT Ø, MI Ø

## Summary Chart of U.S. Medical Eligibility Criteria for Contraceptive Use

| Condition | Sub-Condition | Cu-IUD | | LNG-IUD | | Implant | | DMPA | | POP | | CHC | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | I | C | I | C | I | C | I | C | I | C | I | C |
| Deep venous thrombosis (DVT)/Pulmonary embolism (PE) | a) History of DVT/PE, not receiving anticoagulant therapy | | | | | | | | | | | | |
| | i) Higher risk for recurrent DVT/PE | 1 | | 2 | | 2 | | 2 | | 2 | | 4 | |
| | ii) Lower risk for recurrent DVT/PE | 1 | | 2 | | 2 | | 2 | | 2 | | 3 | |
| | b) Acute DVT/PE | 2 | | 2 | | 2 | | 2 | | 2 | | 4 | |
| | c) DVT/PE and established anticoagulant therapy for at least 3 months | | | | | | | | | | | | |
| | i) Higher risk for recurrent DVT/PE | 2 | | 2 | | 2 | | 2 | | 2 | | 4* | |
| | ii) Lower risk for recurrent DVT/PE | 2 | | 2 | | 2 | | 2 | | 2 | | 3* | |
| | d) Family history (*first-degree relatives*) | 1 | | 1 | | 1 | | 1 | | 1 | | 2 | |
| | e) Major surgery | | | | | | | | | | | | |
| | i) With prolonged immobilization | 1 | | 2 | | 2 | | 2 | | 2 | | 4 | |
| | ii) Without prolonged immobilization | 1 | | 1 | | 1 | | 1 | | 1 | | 2 | |
| | f) Minor surgery without immobilization | 1 | | 1 | | 1 | | 1 | | 1 | | 1 | |
| Depressive disorders | | 1* | | 1* | | 1* | | 1* | | 1* | | 1* | |

| Key: | |
|---|---|
| 1 No restriction (method can be used) | 3 Theoretical or proven risks usually outweigh the advantages |
| 2 Advantages generally outweigh theoretical or proven risks | 4 Unacceptable health risk (method not to be used) |



# OLGU 4

- 24 y, 1G 1Y, VKİ: 24 $kg/m^2$
- Siklusun 2. yarısında gerginlik, memede hassasiyet, aşırı yeme, kilo alma, letarji, eklem ağrısı
- VTE risk faktörü yok
- Kontraseptif yöntem istiyor

?

SSRI altın standart

- 20 μg EE + 3 mg Drospirenon

FDA

Management of Premenstrual Dysphoric Disorder: A Scoping Review

Sara V Carlini[1], Teresa Lanza di Scalea[2], Stephanie Trentacoste McNally[3], Janice Lester[4],

# OLGU

- 22 y, bekar, rekürren VTE öyküsü
- Warfarin kullanan hasta INR'de yeterli düzelme olmayınca ilaç değişmiş
- 3 aydır 20 mg/g rivaroxabana (Xarelto) geçmiş
- 8 gündür devam eden HMB
- Hb: 6.5 g/dL

?

# OLGU

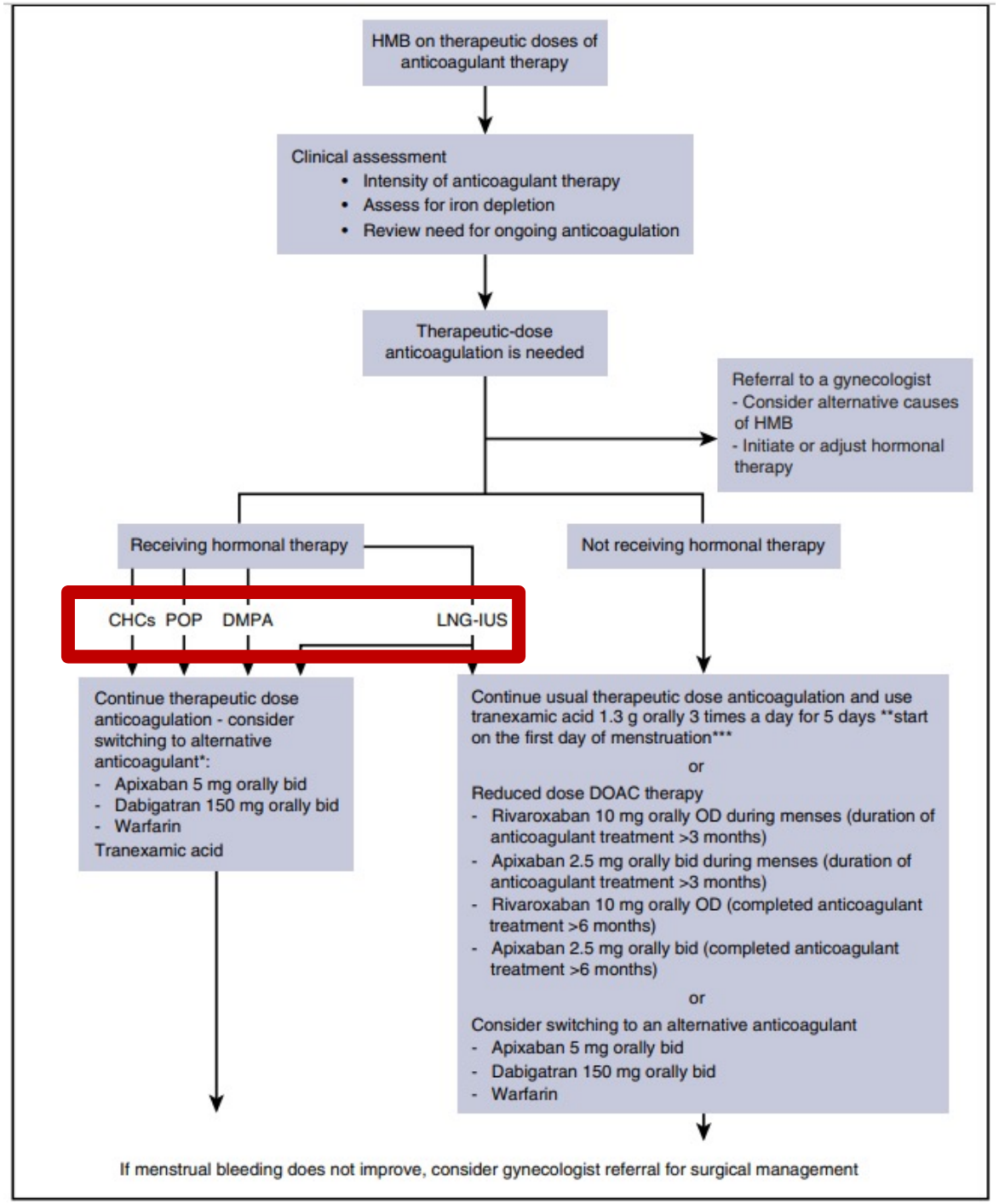
- Tek doz traneksamik asid
- 1 Ü ERT
- Tekrar warfarin ya da doz azaltımı
- LNG-RİA / KOK

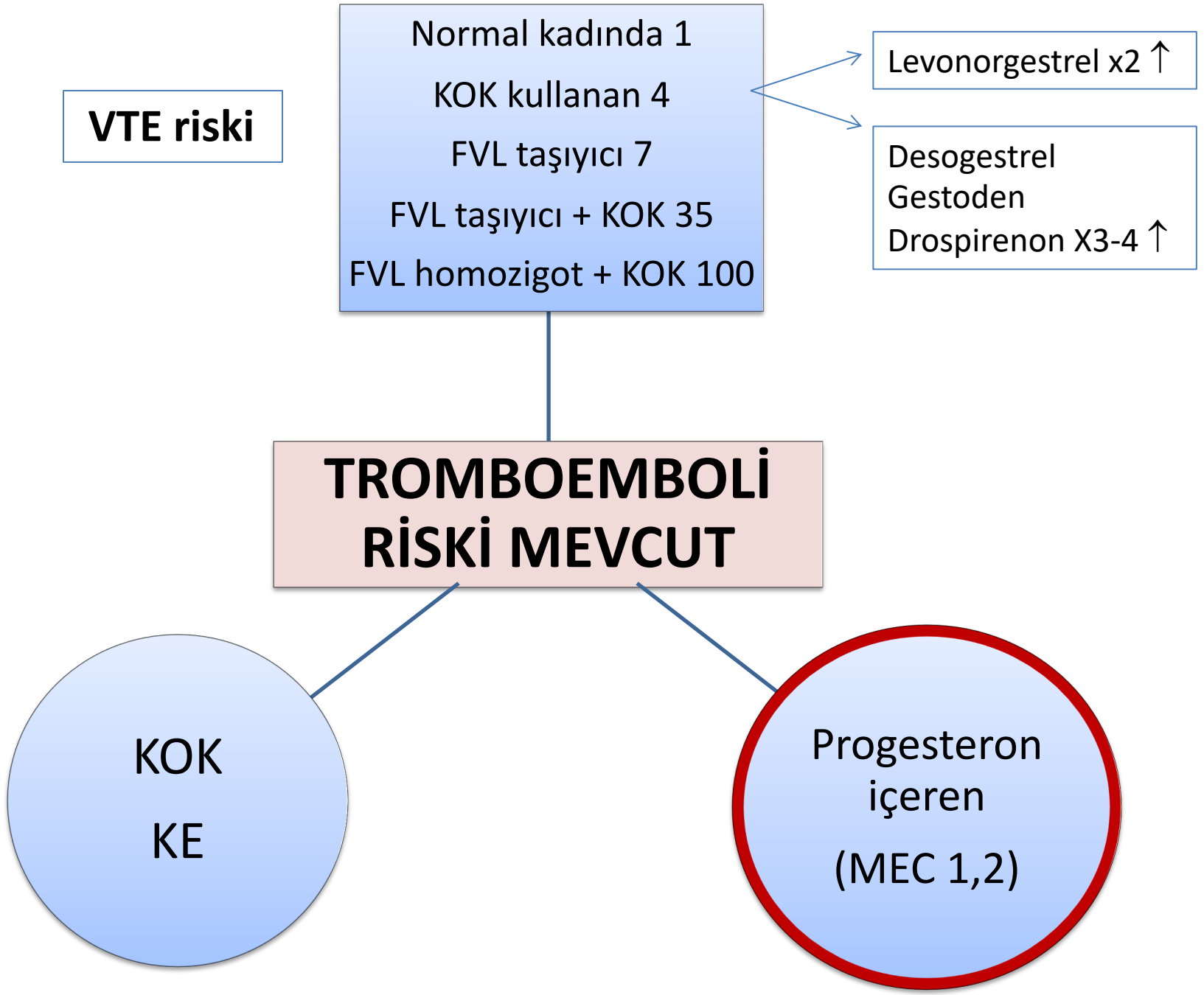
Terapötik dozda antikoagülan kullanımı KOK'un yaratacağı trombotik riskin üstesinden gelir

How I Treat blood

**How I treat heavy menstrual bleeding associated with anticoagulants**

Kochawan Boonyawat,[1,2] Sarah H. O'Brien,[3] and Shannon M. Bates[1,4]


HMB on therapeutic doses of anticoagulant therapy
Clinical assessment
• Intensity of anticoagulant therapy
• Assess for iron depletion
• Review need for ongoing anticoagulation
Therapeutic-dose anticoagulation is needed
Referral to a gynecologist
- Consider alternative causes of HMB
- Initiate or adjust hormonal therapy
Receiving hormonal therapy
Not receiving hormonal therapy
CHCs POP DMPA LNG-IUS
Continue therapeutic dose anticoagulation - consider switching to alternative anticoagulant*:
- Apixaban 5 mg orally bid
- Dabigatran 150 mg orally bid
- Warfarin
Tranexamic acid
Continue usual therapeutic dose anticoagulation and use tranexamic acid 1.3 g orally 3 times a day for 5 days **start on the first day of menstruation***
or
Reduced dose DOAC therapy
- Rivaroxaban 10 mg orally OD during menses (duration of anticoagulant treatment >3 months)
- Apixaban 2.5 mg orally bid during menses (duration of anticoagulant treatment >3 months)
- Rivaroxaban 10 mg orally OD (completed anticoagulant treatment >6 months)
- Apixaban 2.5 mg orally bid (completed anticoagulant treatment >6 months)
or
Consider switching to an alternative anticoagulant
- Apixaban 5 mg orally bid
- Dabigatran 150 mg orally bid
- Warfarin
If menstrual bleeding does not improve, consider gynecologist referral for surgical management

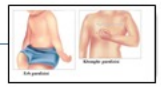

VTE riski
Normal kadında 1
KOK kullanan 4
FVL taşıyıcı 7
FVL taşıyıcı + KOK 35
FVL homozigot + KOK 100
Levonorgestrel x2 ↑
Desogestrel
Gestoden
Drospirenon X3-4 ↑
TROMBOEMBOLİ RİSKİ MEVCUT
KOK
KE
Progesteron içeren
(MEC 1,2)

# Obezite

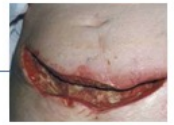
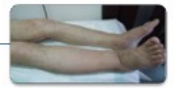
**PRENATAL RİSKLER**

- Düşük — %17 vs %10
- GDM — 1 kg/m²-%1↑
- Gebeliğin indüklediği HT — 5-7 kg/m² x2↑
- Postterm gebelik
- İYE, OSA — %42 ↑

**İNTRAPARTUM RİSKLER**

- Disfonksiyonel eylem
- Eylem indüksiyonu↑
- Sezaryen doğum ↑ — 1kg/m²-%7 ↑
- Başarısız doğum analjezisi
- Omuz distosisi↑ — 

**POSTPARTUM RİSKLER**

- Enfeksiyon riski ↑ — 
- Postpartum hemoraji riski ↑
- Emzirmede başarısızlıklar
- Venöz tromboemboli riski ↑ — 

VTE riski

- KOK 20-30 mcg (MEC 2)
- RİA Progesteron içeren (MEC 1)

# TEŞEKKÜRLER