Endometrioziste Tanı: Yeni ne var?

Doç.Dr. Mehmet B. Çetinkaya
Ondokuz Mayıs Üniversitesi, Tıp Fakültesi
Kadın Hastalıkları ve Doğum Ad.

Endometriozis Sempozyumu 23 Ocak 2011-Ankara

Non invaziv veya semi invaziv, rutinde kullanılan, tanı değeri yüksek test olmadığı için semptomların başlaması ile cerrahi olarak onaylanan tanı arasında geçen süre Amerika ve İngiltere'de 8 yıla kadar uzamaktadır.

- Hadfield et al., Human Reproduction, Vol.24, No.12 pp. 3025–3032, 2009
- (Ballard et al., 2006).

Diagnostic delay according to the revised ASRM stage

	rAFS stage				
	Stage I (n = 30)	Stage II (n = 23)	Stage III (n = 15)	Stage IV (n = 12)	Advanced stage IV (n = 15)
Diagnostic delay (years)	3.5 ± 3.4	6.7 ± 5.8	5.5 ± 5.0	6.3 ± 4.6	14.4 ± 5.7[a]

Note: Stage IV defined as revised ASRM score ≤70 and advanced stage IV as revised ASRM score >70. All data are expressed as mean ± SD (years).

[a] $P<.0001$ versus stage I, $P<.003$ versus stage II, $P<.003$ versus stage III, $P<.005$ versus stage IV.

Matsuzaki. Diagnostic delay of endometriosis. Fertil Steril 2006.

- Her evredeki bekleme süresi farklı
- Ortalama 18 ay aile hekimine gitmeye karar verme
- Aile hekiminin jinekoloğa refere etmesi için geçen süre 3 yıl
- Tanının kesinleşmesi için geçen süre 9 ay
- 7025 endometriozisli kadında yapılan anket sonucu (European Endometriosis Alliance, 2006) ilk tanının %65 oranında yanlış, %46 kadının doğru tanı öncesinde, 5 veya daha fazla doktoru gördüğü bildirilmiştir.

Tanı yöntemlerinin performansı

	Hastalık (+)	Hastalık (-)
Test (+)	**GP**	**YP**
Test (-)	**YN**	**GN**

Duyarlılık: Duyarlılık = GP / (GP + YN), Spesifite: Özgüllük = GN / (GN + YP)
YP= Yanlış pozitiflik, YN = Yanlış negatiflik, GN = Gerçek negatiflik

- Duyarlılık (*Sensitivity*): Testin, gerçek hastaları ayırma yeteneğidir.

A / (A+C) = GP / (GP + YN)

- Özgüllük (*Specificity*) testin, gerçek sağlamları ayırma yeteneğidir.

D / (D + B) = GN / (GN + YP)

- Yanlış negatiflik oranı: Gerçek hastalar içinden testin hatalı olarak sağlam dediği olgulardır.

1-Duyarlılık = C /(A + C) = YN/ (YN + GP)

- Yanlış pozitiflik oranı: Gerçek sağlamlar içinden testin hasta dediği olgular.

YP = 1-Özgüllük = B /(B+D) = YP / (YP+GN)

- Pozitif olabilirlik oranı (LHR+): Testin, hastalığa var dediği zaman doğruyu bildirmesinin, yanılmasına oranıdır.
- Tanı koymanın doğruluk oranıdır. Bu oran ne kadar yüksek olursa, gerçek hastalar o derecede iyi ayrımlanmaktadır

LHR+ ; Duyarlılık/(1-Özgüllük) = A (B+D) / B (A+C) = GP (YP+GN) / YP (GP+YN)

- Negatif olabilirlik oranı (LHR -): Hastalık yok tanısının doğruluk oranıdır. Bu oran ne kadar küçük olursa, gerçek sağlamlar o kadar iyi ayrımlanabilmektedir

LHR- ; (1-Duyarlılık) / Özgüllük = C(B+D) / D (A+C) = YN (YP+GN) / GN (GP+YN)

- Doğruluk (Accuracy): Gerçekte testin hasta ve sağlam olarak toplam doğru tanı oranına "doğruluk" denir. Diğer oranlardan farklı olarak doğruluk, aynı duyarlılık-özgüllük için bile hastalık sıklığına bağlı olarak değişebilir.

Doğruluk; (A+D)/(A+B+C+D) = (GP+GN) / (GP+YP+YN+GN)

- Pozitif sonucun kestirim değeri (PKD): Tanı testi hasta yargısı verdiğinde, gerçekten hasta olma olasılığıdır.

PKD; P(H+/T+) = A /(A+B) = GP / (GP+YP)

- Negatif sonucun kestirim değeri (NKD): Tanı Testi sağlam dediğinde gerçekten sağlam olma olasılığıdır.

NKD; P(H-/T+) = D / (D+C) = GN / (GN+YN)

QUADAS

(Quality Assessment of Diagnostic Studies)

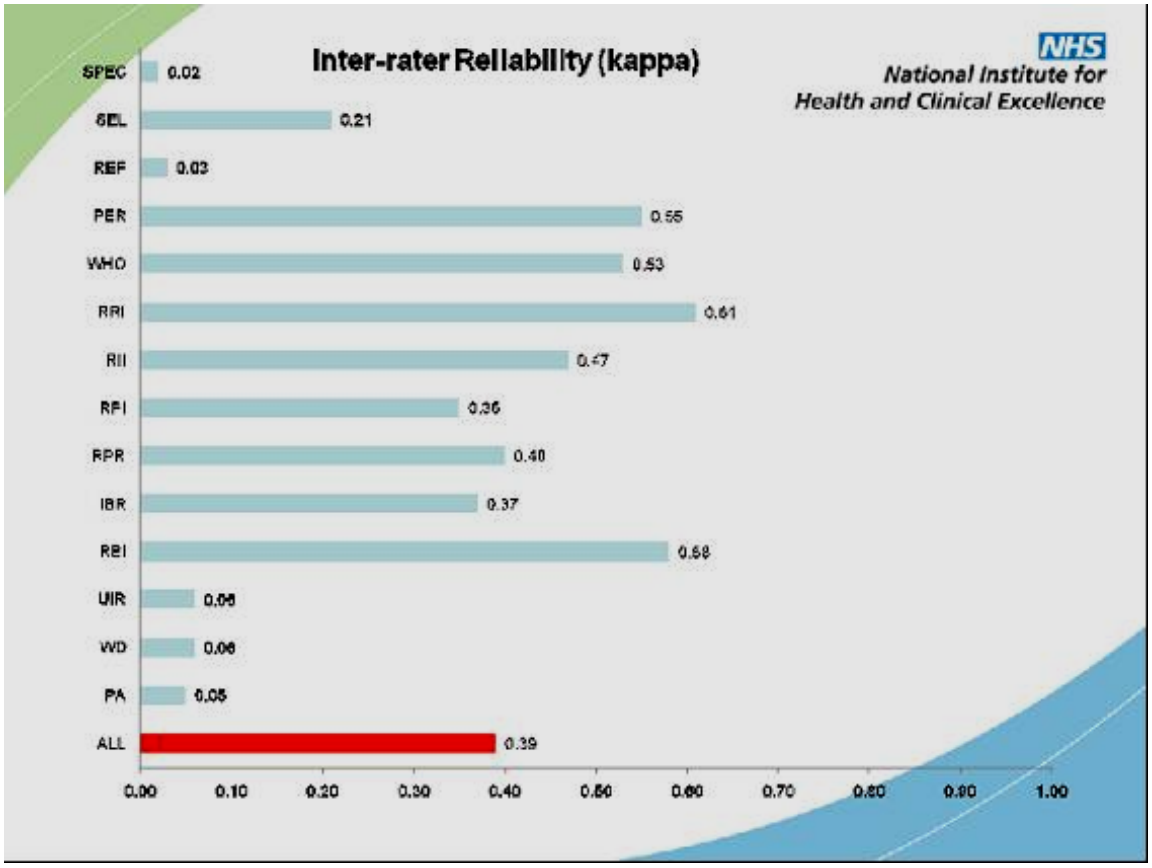
The QUADAS tool

Item		Yes	No	Unclear
1.	Was the spectrum of patients representative of the patients who will receive the test in practice?	( )	( )	( )
2.	Were selection criteria clearly described?	( )	( )	( )
3.	Is the reference standard likely to correctly classify the target condition?	( )	( )	( )
4.	Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?	( )	( )	( )
5.	Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?	( )	( )	( )
6.	Did patients receive the same reference standard regardless of the index test result?	( )	( )	( )
7.	Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?	( )	( )	( )
8.	Was the execution of the index test described in sufficient detail to permit replication of the test?	( )	( )	( )
9.	Was the execution of the reference standard described in sufficient detail to permit its replication?	( )	( )	( )
10.	Were the index test results interpreted without knowledge of the results of the reference standard?	( )	( )	( )
11.	Were the reference standard results interpreted without knowledge of the results of the index test?	( )	( )	( )
12.	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?	( )	( )	( )
13.	Were uninterpretable/ intermediate test results reported?	( )	( )	( )
14.	Were withdrawals from the study explained?	( )	( )	( )

Whiting *et al. BMC Medical Research Methodology* 2003 **3**:25 doi:10.1186/1471-2288-3-25

QUADAS

(Quality Assessment of Diagnostic Studies)



QUADAS

(quality assessment of diagnostic studies)

< 0.2	**(poor)**
0.21 to 0.40	**(fair)**
0.41 to 0.60	**(moderate)**
0.61 to 0.80	**(good)**
0.81 to 1.00	**(very good).**

Endometrioziste tanı yöntemleri

- Non İnvaziv
  - Öykü ve fizik muayene
  - Periferik biyo-markerler
    - Serum
    - İntra-peritoneal
    - İdrar
  - Görüntüleme yöntemleri
    - Ultrasonografi
      - » Konvansiyonel (Transvajinal USG, Transrektal USG)
      - » 3D USG
    - Magnetik Rezonans Görüntüleme (MRI)
    - Komputerize tomografi
- Semi-invaziv
  - Endometrial biyopsi
- İnvaziv
  - Laparoskopi/Laparatomi

- Bazı olgularda laparoskopi ve görsel tanı yeterlidir, eğer şüphe varsa histolojik onaylama önerilmektedir.
- Ancak pozitif histoloji bütün hastalarda tanı için mutlak gerekli değildir.

    - European Society of Human Reproduction and Embryology guideline (2005),
    - American College of Obstetricians and Gynecologists Practice Bulletin (2000)
    - American College of Obstetricians and Gynecologists Committee Opinion (2005)

- Rutin histolojik tanı gerekliliği tartışmalı
    - Royal Collage of Obstetrics and Gynaecologists (RCOG) 2006 guidelines,
    - Stegmann B. , A logistic model for the prediction of endometriosis. Fertility and Sterility, Vol. 91, 2009

- Endometriozisi bulunan kadınların %20'sinde irritabl barsak sendromu, interstisyel sistit, ağrılı mesane, fibromyalji ve migren olmak üzere kronik ağrı bulunmaktadır.
- Endometrioziste, bu diğer tanılar dışlanmalı ve multidisipliner yaklaşım gerekebilmektedir.
    - Hsu AL. Invasive and Noninvasive Methods for the Diagnosis of Endometriosis .Clinical Obstetrics and gynecology ,2010;Vol 53(2), 413–419

Hangi evrede tanı optimal?

- Semptomu olan evre I ve II endometriozis olguları laparoskopik tanı ve tedaviden yararlanabilmektedir.

- Ancak benzer semptomlara sahip hasta grubunda yanlış tanı laparoskopinin morbiditesini artıracaktır.

- Yüzeyel peritoneal lezyonlar,
- Ovarian endometrioma,
- Derin infiltratif endometriozis (Deep infiltrating endometriosis; DIE)

Endometriozisin yeri

Sık görülen	Daha az sıklıkta	Nadir görülen yerler
Over ve fossa ovarika	Çekum	Meme
Anterior ve posterior cul-de-sac	Servix	KC, Safra kesesi
Posterior broad ligament	Vagina ve Rektovaginal septum	Pankreas
Utero-sakral ligament	İleum	Böbrek, üretra
Tubalar	İnguinal kanal	Ekstremiteler
Sigmoid kolon	Abdominal veya perineal skar	Kemik Vertebra
Appendix	Umbilicus	Akciğer, Diafram
Round ligament	Üreter ve mesane	SSS, Beyin Periferik sinirler

Giudice and Kao. *Lancet. 2004^ Mounsey et al. Am Fam Physician. 2006*

Belirtiler

- Şiddetli dismenore;
- Disparoni
- Kronik pelvik ağrı
- Anormal uterin kanama
- İnfertilite
- Kronik yorgunlukla birlikte veya tek başına, siklik veya perimenstrual semptomlar (barsak veya mesane ile ilişkili)

Human Reproduction Vol.20, No.10 pp. 2698–2704, 2005
Advance Access publication June 24, 2005.
doi:10.1093/humre

ESHRE guideline for the diagnosis and treatment of endometriosis

Stephen Kennedy[1,10], Agneta Bergqvist[2], Charles Chapron[3], Thomas D'Hooghe[4], Gerard Dunselman[5], Robert Greb[6], Lone Hummelshoj[7], Andrew Prentice[8] and Ertan Saridogan[9] on behalf of the ESHRE Special Interest Group for Endometriosis and Endometrium Guideline Development Group*

Table I. Hierarchy of evidence

Level	Evidence
1a	Systematic review and meta-analysis of randomized controlled trials (RCT)
1b	At least one RCT
2a	At least one well-designed controlled study without randomization
2b	At least one other type of well-designed quasi-experimental study
3	Well-designed, non-experimental, descriptive studies, such as comparative studies, correlation studies or case studies
4	Expert committee reports or opinions and/or clinical experience of respected authorities

Table II. Strength of evidence corresponding to each level of recommendation

Grade	Strength of evidence
A	Directly based on level 1 evidence
B	Directly based on level 2 evidence or extrapolated recommendation from level 1 evidence
C	Directly based on level 3 evidence or extrapolated recommendation from either level 1 or level 2 evidence
D	Directly based on level 4 evidence or extrapolated recommendation from either level 1, 2 or 3 evidence
GPP	Good practice point based upon the views of the Guideline Development Group

C	Deeply infiltrating nodules are most reliably detected when clinical examination is performed during menstruation (Koninckx *et al.*, 1996).	Evidence level 3

Diagnosis

C	For a definitive diagnosis of endometriosis, visual inspection of the pelvis at laparoscopy is the 'gold standard' investigation, unless disease is visible in the vagina or elsewhere.	Evidence level 3

Histology

GPP	Positive histology confirms the diagnosis of endometriosis; negative histology does not exclude it. Whether histology should be obtained if peritoneal disease alone is present is controversial: visual inspection is usually adequate but histological confirmation of at least one lesion is ideal. In cases of ovarian endometrioma (>3 cm in diameter), and in deeply infiltrating disease, histology **should be obtained** to identify endometriosis and to exclude rare instances of malignancy.

GPP	If the patient wants pain symptoms suggestive of endometriosis to be treated without a definitive diagnosis, then a therapeutic trial of a hormonal drug to reduce menstrual flow is appropriate (see 'Empirical treatment' section).

GPP	The management of severe/deeply infiltrating endometriosis is complex. Therefore, if disease of such severity is suspected or diagnosed, referral to a centre with the necessary expertise to offer all available treatments in a multi-disciplinary context, including advanced laparoscopic surgery and laparotomy, is strongly recommended.

Investigations

Ultrasound

A	Compared to laparoscopy, transvaginal ultrasound (TVS) has no value in diagnosing peritoneal endometriosis, but it is a useful tool both to make and to exclude the diagnosis of an ovarian endometrioma (Moore *et al.*, 2002). TVS may have a role in the diagnosis of disease involving the bladder or rectum.	Systematic review of diagnostic tests

Magnetic resonance imaging

A	Compared to laparoscopy, magnetic resonance imaging (MRI) has limited value as a diagnostic tool for endometriosis (Ang *et al.*, submitted).	Systematic review of diagnostic tests

Blood tests

A	Serum CA-125 levels may be elevated in endometriosis. However, compared to laparoscopy, measuring serum CA-125 levels has no value as a diagnostic tool (Mol *et al.*, 1998).	Systematic review of diagnostic tests

Investigations to assess disease extent

GPP	If there is clinical evidence of deeply infiltrating endometriosis, ureteral, bladder and bowel involvement should be assessed. Consideration should be given to performing MRI or ultrasound (transrectal and/or transvaginal and/or renal), with or without intravesical pressure (IVP) and barium enema studies depending upon the individual circumstances, to map the extent of disease present, which may be multi-focal.

Endometriozis düşündüren fizik muayene bulguları
Posterior fornikste palpasyonda hassasiyet
culde-sac veya utero-sakral ligamentlerde lokalize gerginlik
Cul-de-sac, uterosakral ligmentler, veya rektovaginal septumda gergin palpabl nodüller
Bimanuel muayenede pelvik gerginlik ve rahatsızlık, uterus ve serviks hareketlerinde ağrı
Gergin ve ağrılı normalden büyük adneksler
Uterusun mobilitesinde azalma, adnekslerin fikse oluşu veya retrovert uterus
Vaginal muayenede serviksin stenotik veya lateralize görünümde olması
Derin infiltratif endometrioziste vagina veya servikste lezyonlar izlenebilir
Bimanuel ve spekulum gibi ağrısız muayenelerde tolerans azalması, hiperaljezi
Bimanuel vajinal USG ?
Mounsey et al. *Am Farn Physician. 2006; Practice Committee* of the American Society for Reproductive

- Pelvik muayene zayıf negatif prediktif değere sahip
- Cerrahi olarak saptanan ve kronik pelvik ağrı semptomu bulunan 91 hastanın %47'sinde bimanuel muayene normal olarak bulunmuştur.

    - Nezhat C. Comparison of transvaginal sonography and bimanual pelvic examination in patients with laparoscopically confirmed endometriosis. J Am Assoc Gynecol Laparosc. 1994;1:127–130.6

- Tek başına düşük sensitivite spesifite ve prediktif değerine rağmen, endometriozisin tanısında cerrahi öncesi görüntüleme yöntemine karar vermede ve yöntemin başarısını artırmada önemlidir.

    - Holland TK, Yazbek J, Cutner A, Sarıdoğan E,. Hoo WL, Jurkovic D. Value of transvaginal ultrasound in assessing severity of pelvic endometriosis Ultrasound Obstet Gynecol 2010; 36: 241–248
    - Hudelist G, Oberwinkler KH, Singer CF, Tuttlies F, Rauter G, Ritter O, Keckstein J. Combination of transvaginal sonography and clinical examination for preoperative diagnosis of pelvic endometriosis. Hum Reprod 2009; 24: 1018–1024.

Biyokimyasal Belirteçler

Endometriozisle ilşkili biyokimyasal marker olarak, 100 veya daha fazla faktör çalışıldı, ancak bugüne kadar tek başına hiçbiri spesifik olarak endometriozis tanısında optimal sonucu veremedi. Mevcut markerler başka patolojilerde de artmaktadır.

- Sitokinler
- İmmunolojik
- Glikoproteinler
- Hücre adezyon molekülleri
- Büyüme faktörleri
- Proteomics
- Hormonlar
- Angiogenetik faktörler
- Apoptozis

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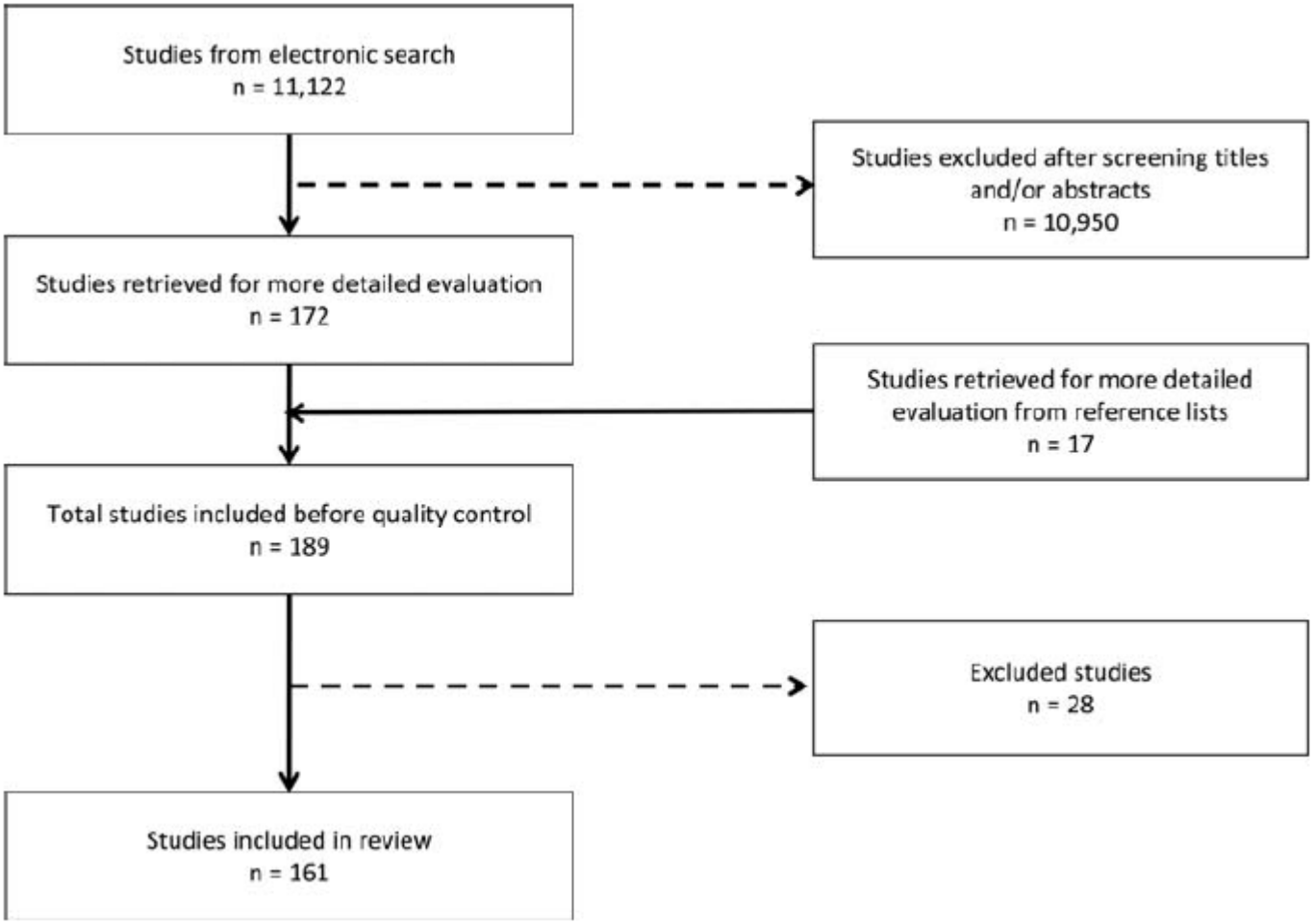
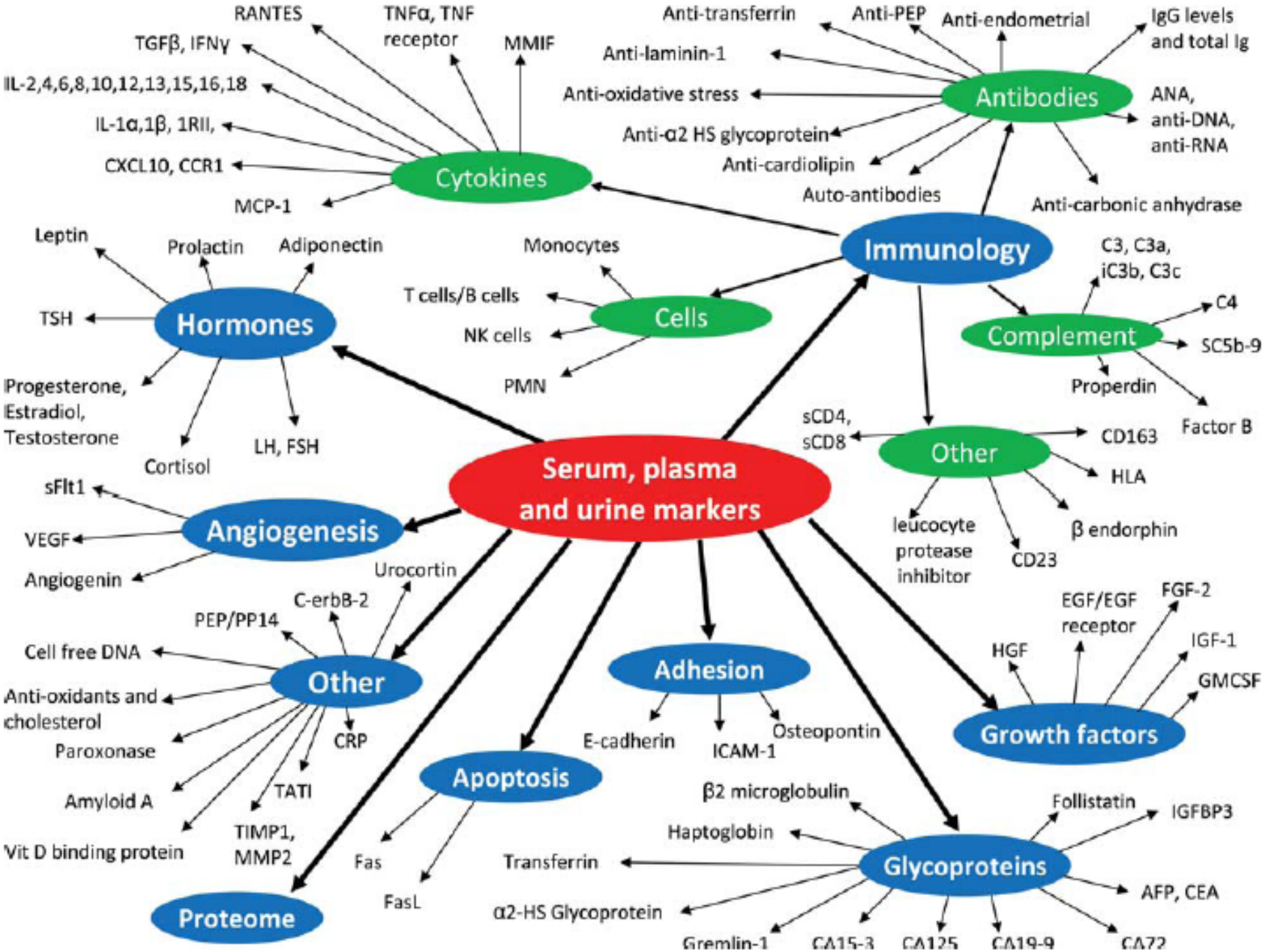
doi:10.1093/humupd/dmq009

human reproduction update

Peripheral biomarkers of endometriosis: a systematic review

K.E. May[1,†], S.A. Conduit-Hulbert[1,2,†], J. Villar[1], S. Kirtley[1], S.H. Kennedy[1], and C.M. Becker[1,*]




Serum, plasma and urine markers
Cytokines
RANTES
TNFα, TNF receptor
MMIF
TGFβ, IFNγ
IL-2,4,6,8,10,12,13,15,16,18
IL-1α,1β, 1RII,
CXCL10, CCR1
MCP-1
Antibodies
Anti-transferrin
Anti-PEP
Anti-endometrial
IgG levels and total Ig
Anti-laminin-1
Anti-oxidative stress
ANA, anti-DNA, anti-RNA
Anti-α2 HS glycoprotein
Anti-cardiolipin
Auto-antibodies
Anti-carbonic anhydrase
Immunology
Hormones
Leptin
Prolactin
Adiponectin
TSH
Progesterone, Estradiol, Testosterone
Cortisol
LH, FSH
Cells
Monocytes
T cells/B cells
NK cells
PMN
Complement
C3, C3a, iC3b, C3c
C4
SC5b-9
Properdin
Factor B
Other
sCD4, sCD8
CD163
HLA
β endorphin
CD23
leucocyte protease inhibitor
Angiogenesis
sFlt1
VEGF
Angiogenin
Other
Urocortin
C-erbB-2
PEP/PP14
Cell free DNA
Anti-oxidants and cholesterol
Paroxonase
Amyloid A
CRP
TATI
TIMP1, MMP2
Vit D binding protein
Adhesion
E-cadherin
ICAM-1
Osteopontin
Growth factors
EGF/EGF receptor
FGF-2
IGF-1
HGF
GMCSF
Apoptosis
Fas
FasL
Proteome
Glycoproteins
β2 microglobulin
Follistatin
IGFBP3
Haptoglobin
Transferrin
AFP, CEA
α2-HS Glycoprotein
Gremlin-1
CA15-3
CA125
CA19-9
CA72

- Endometriosis ve adenomyoziste, Cognate chemokine reseptör(CCR1)/HPRT mRNA periferik kanda artmış
- Serum MCP-1 ve CA125 düzeyleri ile birlikte kombine edildiğinde endometiozis tanısı için sensitivitesi %92.2, spesifisitesi %81.6, NPV %83.3, PPV %92.3, +LHR 5.017 ve (-) LHR 0.096
    - Admir A. Combination of CCR1 mRNA, MCP1, and CA125 Measurements in Peripheral Blood as a Diagnostic Test for Endometriosis. Reproductive Sciences 2008; 15(9), 906-11.

Table 1. Sensitivity, Specificity, Positive Predictive Values (PPV), and Negative Predictive Values (NPV) of the Test in Different Stages of Endometriosis (Eo)

	Eo-I	Eo-II	Eo-III	Eo-IV
Sensitivity (%)	86.96	92.86	94.12	93.55
Specificity (%)	81.63	81.63	81.63	81.63
PPV (%)	68.96	59.09	78.05	76.32
NPV (%)	93.02	97.56	95.24	95.24

Human Reproduction, Vol.25, No.3 pp. 654–664, 2010
Advanced Access publication on December 9, 2009 doi:10.1093/humrep/dep425

human reproduction ORIGINAL ARTICLE *Gynaecology*

Non-invasive diagnosis of endometriosis based on a combined analysis of six plasma biomarkers

A. Mihalyi[1,2], O. Gevaert[3], C. M. Kyama[1,2,4], P. Simsa[1,2,5], N. Pochet[3,6,7], F. De Smet[3,8], B. De Moor[3], C. Meuleman[1], J. Billen[9], N. Blanckaert[9], A. Vodolazkaia[1,2], V. Fulop[5], and T. M. D'Hooghe[1,4,10]

- Endometriozisle ilgili olduğu düşünülen plazma belirteçleri çalışılmış

- Ancak hasta grubu homojen değil (infertilite ve ağrı)

- İnterlökin (IL)-6, IL-8, Tümör nekroz faktör-alfa (TNF-a), CA-125, CA-19-9 ve yüksek sensitiv C-reaktif protein (hsCRP),
  - Mihalyi et al., 2005; Kyama et al., 2006; Debrock et al., 2006; Kyama et al., 2008).(

Kontrol grubuna göre endometrioizis Evre I ve II artmış IL-8 ($P < 0.0003$), IL-6 ($P < 0.001$) ve azalmış TNF-a ($P < 0.0001$), Evre III ve IV endometrioziste ise artmış plazma IL-6 ($P < 0.001$), IL-8 ($P < 0.0003$), hsCRP ($P < 0.001$) ve CA-125 (P , 0.0001) ve azalmış TNF-a ($P < 0.0001$) düzeyleri saptanmış

Evre I-II ile III-IV karşılaştırıldığında ileri evre grubunda, artmış hsCRP ($P <0.001$) ve CA-125 ($P < 0.0001$) düzeyi saptanmış.

Table II Logistic regression model performance: AUC, sensitivity, specificity, accuracy, PPV and NPV for logistic regression models according to cycle phase and disease stage

Cycle phase	Stage	Selected proteins	AUC	Sensitivity*	Specificity*	Accuracy	PPV	NPV	LR+	LR−
All	Ctrl versus All	IL-8, CA-125	0.790	71.3	71.0	71.2	84.2	53.2	2.46	0.40
All	Ctrl versus I, II	IL-8, CA-125	0.736	95.5	39.8	72.6	69.4	86.0	1.59	0.11
All	Ctrl versus III, IV	IL-6, TNF-α, CA-125	0.934	91.3	86.0	88.3	82.9	93.0	6.52	0.10
Menstrual	Ctrl versus All	CA-125	0.817	80.5	73.7	78.3	86.8	63.6	3.06	0.26
Menstrual	Ctrl versus I, II	IL-6, TNF-α	0.814	88.5	63.2	77.8	76.7	80.0	2.40	0.18
Menstrual	Ctrl versus III, IV	CA-125	0.951	100.0	73.7	85.3	75.0	100.0	3.80	0.00
Proliferative	Ctrl versus All	CA-125	0.731	65.1	72.2	67.2	84.4	47.3	2.34	0.48
Proliferative	Ctrl versus I, II	CA-125	0.679	58.3	72.2	63.5	77.8	51.0	2.10	0.58
Proliferative	Ctrl versus III, IV	CA-125	0.867	82.6	72.2	76.3	65.5	86.7	2.97	0.24
Secretory	Ctrl versus All	IL-8, TNF-α, CA-125	0.852	89.7	71.1	83.6	86.4	77.1	3.10	0.14
Secretory	Ctrl versus I, II	IL-6, TNF-α	0.845	87.2	71.1	80.0	78.8	81.8	3.02	0.18
Secretory	Ctrl versus III, IV	IL-6, TNF-α, CA-125	0.966	100.0	84.2	91.3	83.8	100.0	6.33	0.00

AUC, area under the ROC curve; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR−, negative likelihood ratio.
*The operating point on the ROC was chosen by maximizing the sum of the sensitivity and specificity with the following constraints: sensitivity >90% or specificity >60%.

British Journal of Cancer (2009) 100, 1315 – 1319

www.bjcancer.com

Serum HE4 concentration differentiates malignant ovarian tumours from ovarian endometriotic cysts

K Huhtinen[1,2], P Suvitie[2], J Hiissa[3], J Junnila[1], J Huvila[2], H Kujari[4], M Setälä[5], P Härkki[6], J Jalkanen[6], J Fraser[7], J Mäkinen[2], A Auranen[2], M Poutanen[1,8] and A Perheentupa*[,1,2]

Adneksiyel kitlelerin ayırıcı tanısında Human epididymal secretory protein 4 (HE4) çalışılmış ve CA-125 düzeyi ile karşılaştırılmıştır.

Table 3 Tumour marker accuracy and sensitivity at 95% specificity for ovarian cancer and ovarian endometriosis

Markers	Accuracy (%)	ROC-AUC (%)	Sensitivity (%)
OvCa vs OvEndo			
CA125+HE4	94.0	91.3	78.6
CA125	92.8	77.0	64.3
HE4	91.6	91.9	71.4
OvCa vs ctrl			
CA125+HE4	96.3	91.1	92.9
CA125	96.3	91.7	78.6
HE4	93.8	95.5	78.6
OvEndo vs ctrl			
CA125+HE4	82.2	86.8	62.3
CA125	83.0	87.7	60.9
HE4	60.7	60.5	5.8
OvCa vs OvEndo vs ctrl			
CA125+HE4	81.9		
CA125	81.2		
HE4	59.7		

OvCa = ovarian cancer; OvEndo = ovarian endometriosis.

Görüntüleme

Görüntülemenin erken evre endometrioziste tanı değeri kısıtlıdır özellikle süperfisyel peritoneal implant ve adezyonların gösterilmesinde yeterli değildir.

- Ultrason (Ucuz, kolay, ancak kullanıcıya göre değişken)

- Endometrioma tanısında transvaginal USG'nin sensitivitesi ve spesifisitesi %84–100 ve 90–%100, olarak bildirilmiştir.
    - Abrao , 2007; Bazot, 2007, 2009; Piketty, 2009; Garcia-Velasco Somigliana, 2009; Savelli, 2009.

Adneksiyel kitlelerde tanı (ACOG)

Modality	Sensitivite (%)	Spesifisite (%)	+ LH	- LH
Doppler USG	0.86	0.91	9.6	0.15
MRI	0.91	0.88	7.6	0.10
CT	0.90	0.75	3.6	0.13
CA 125	0.78	0.78	3.5	0.28
Gray-scale TV-USG	0.82 to 0.91	0.68 to 0.81	3.3	0.19
PET	0.67	0.79	3.2	0.42

Trans-rektal ultrason

- Derin infiltre endometrioziste rektal tutulum
- Posterior mesane duvarı lezyonları için
    - Bazot M. Accuracy of transvaginal sonography and rectal endoscopic sonography in the diagnosis of deep infiltrating endometriosis. Ultrasound Obstet Gynecol. 2007;30:994–1001.

Table IV Sensitivity, specificity, positive and negative predictive value of TVUS and TRUS in the diagnosis of rectal involvement for patients presenting with DIE (n = 134)

	TVUS		TRUV	
	% (n)	95% CI	% (n)	95% CI
Sensitivity	90.7% (68/75)	0.84/0.97	96.0% (72/75)	0.92/1.00
Specificity	96.5% (56/58)	0.92/1.01	100% (59/59)	1.00/1.00
PPV	97.1% (68/70)	0.93/1.01	100% (72/72)	1.00/1.00
NPV	88.9% (56/63)	0.81/0.97	95.2% (59/62)	0.90/1.01

PPV, positive predictive value; NPV, negative predictive value.

- Ancak uterosakral ligament, vagina ve rektovaginal alandaki endometrioziste MRI daha anlamlı
    - Bazot 2004.

- TV-USG rektal endometriozis tanısında rektal USG kadar etkili
    - Bazot, 2007.

- TV-USG; derin infiltratif endometrioziste (DIE) tanı değeri var mı?
- TV USG rektum ve mesanedeki derin endometriotik infiltrasyonu doğru predikte etmekte
- Bimanuel muayene TV-USG ve MRI 104 olguda karşılaştırılmış
    - Abrao et al. (2007)

Table III Sensitivity, specificity, PPV, NPV, accuracy and positive and negative LHR and corresponding CI for preoperative detection of endometriosis of the rectum and depth of endometriotic infiltration by TVS in 195 patients with suspected endometriosis

Localization	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	+ve LHR	−ve LHR
M	98 (40/41)	99 (153/154)	98 (40/41)	99 (153/154)	99 (193/195)	150.24	0.02
CI	93–100	98–100	93–100	98–100	–	21.3–1060.5	0.00–0.17
MUC	62 (8/13)	96 (175/182)	53 (8/15)	97 (175/180)	94 (183/195)	16	0.4
CI	35–88	93–99	28–79	95–100	–	6.9–37.2	0.2–0.8

DIE of the rectum was finally diagnosed by laparoscopy, radical resection and histological confirmation of endometriosis in 43 out of 195 patients. PPV, positive predictive value; NPV, negative predictive value; +ve LHR, positive likelihood ratio; −ve LHR, negative likelihood ratio.

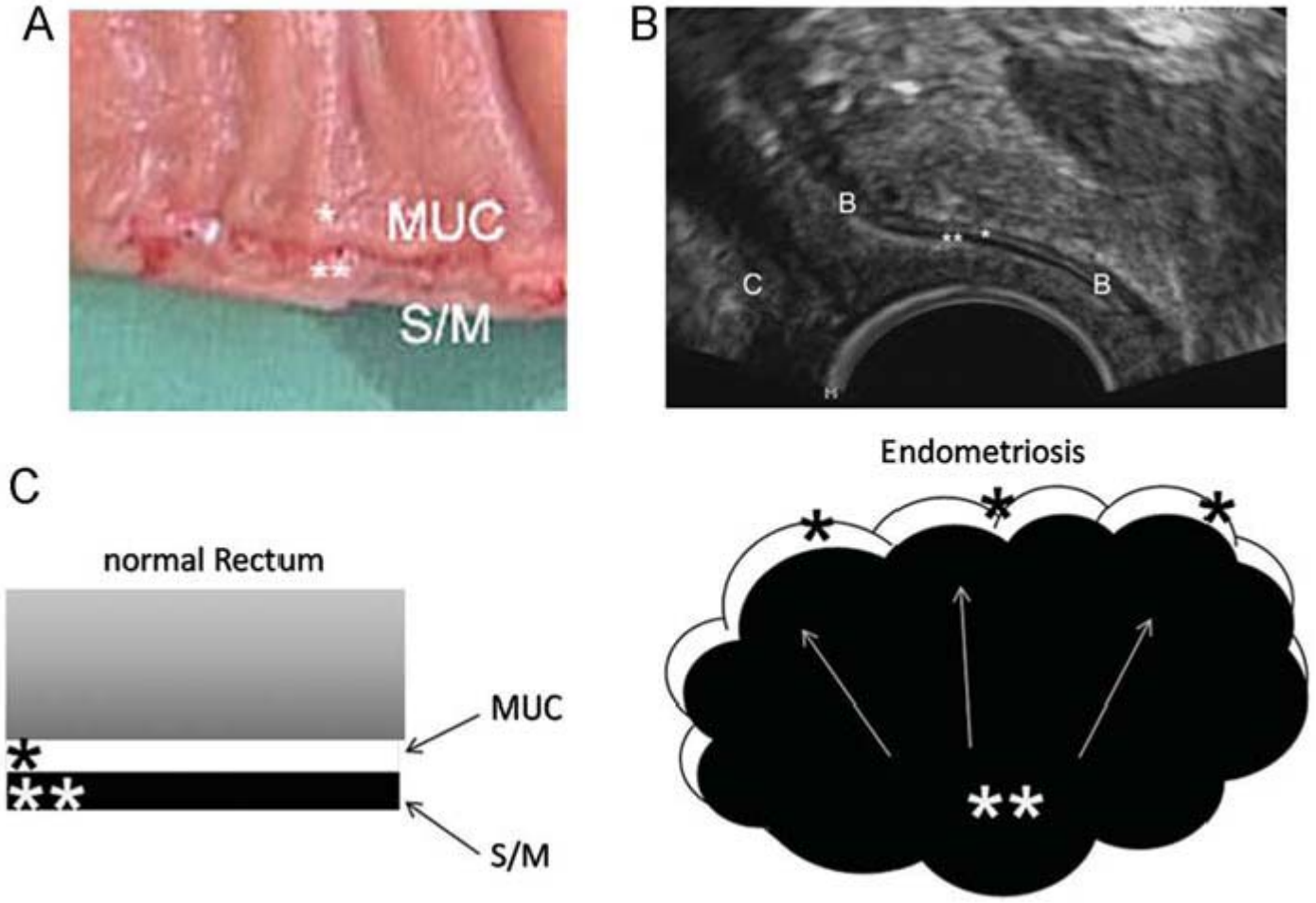
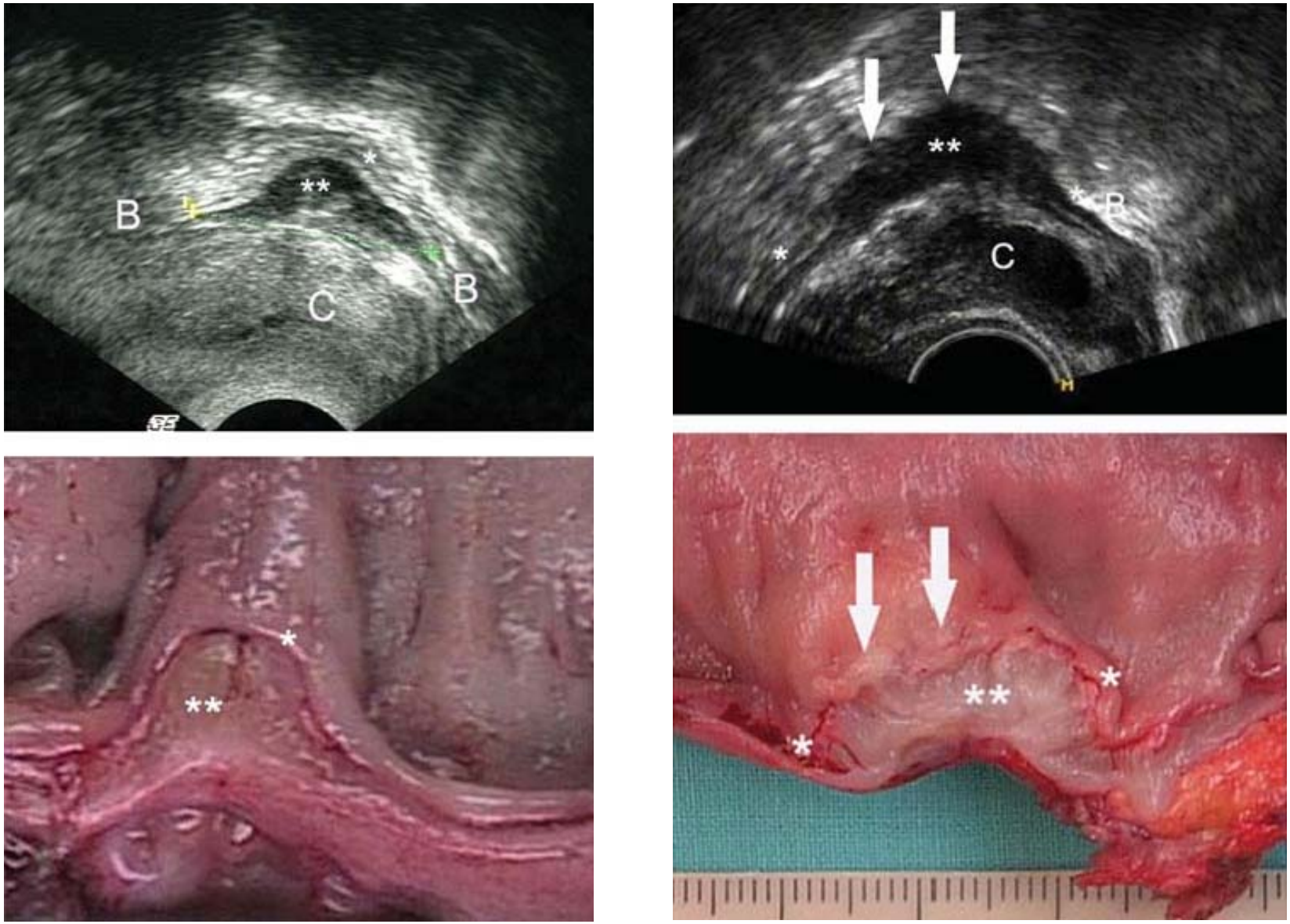


Figure I (**A**) Macroscopic appearance of rectal wall layers (**rectal smooth muscle layer, S/M; *rectal submucosa/mucosa, MUC). (**B**) Sonographic appearance of normal rectal wall layers on TVS: the rectal serosa and smooth muscle layer appear as a thin, hypoechogenic line (**) covered by the rectal submucosa and mucosa (*) which can be visualized as a hyperechogenic rim covering the rectal smooth muscle layer (C, cervix; B, anterior rectal wall). (**C**) Schematic TVS appearance of the normal rectal wall layers (**rectal S/M layer, *rectal MUC) and sonomorphological changes causes by infiltration of endometriotic tissue confined to the rectal smooth muscle layer (**), which is associated with thickening and hypertrophy of the smooth muscle layer covered by an intact MUC layer (*).

G. Hudelist. Can transvaginal sonography predict infiltration depth in patients with deep infiltrating endometriosis of the rectum?. Human Reproduction, Vol.24, No.5 pp. 1012–1017, 2009



G. Hudelist. Can transvaginal sonography predict infiltration depth in patients with deep infiltrating endometriosis of the rectum?. Human Reproduction, Vol.24, No.5 pp. 1012–1017, 2009

Hudelist	Yıl	Tanı kriteri	Olgu/ Recto-sigmoid endometriosis	Test yöntemi	Referans tanı	QADAS
Bazot	2003	Muscularis propriada kalınlaşma (>3mm),	30; 22	TVS, RES	histoloji	orta
Bazot	2004	Muscularis propriada kalınlaşma (>3mm),	142; 47	TVS	histoloji	orta
Carbognin	2006	belirtilmemiş	32; 17	TVS, MRI	laparoskopik görünüm	zayıf
Abrao	2007	Nodüler, solid, İntestinal loopa yapışık hipoekojenikl ezyon	104; 54	TVS, MRI, PV	histoloji	orta
Valenzano	2008	Rectovaginal hipoekoik kitle Muskularis mukozada kalınlaşma İntestianal duvara yapışıklık/penetrasyon	90; 23	TVS, TVS,RWC	histoloji	iyi
Guerriero	2008	Kitle merkezinden kaynaklanan İnce bant şeklinde eko görünümü	88; 39	TVS	histoloji	iyi
Piketty	2009	Hipoekoik kitle ile birlikte hipo/hiperekoik odaklı, kolonun muskuler tutulumu	134; 115	TVS	histology	iyi
Bazot	2009	Yukarıdaki gibi	92; 63	TVS, MRI, PV, RES	histoloji	iyi
Hudelist	2009	Yukarıdaki gibi	200; 48	TVS&PV	histoloji	orta
Goncalves	2010	İntestinal yapışıklık hipoekoik uzun nodüler, solid, lezyon	194; 81	TVS	histoloji	iyi

Hudelist	Yıl	prevalans	Sensitivite (%)	Spesifisite (%)	PPV/NPV (%)	Tanı Uyumu (%)	(+) LHR (%95 CI)	(-) LHR (%95 CI)
Bazot	2003	22/30 73.3%	21/22 95%	8/8 100%	100%,89%	97%	-	0.05 (0.01-0.31)
Bazot	2004	47/142 33%	41/47 87%	92/95 97%	93%,94%	94%	27.62 (9.02 -84.58)	0.13 (0.06-0.28)
Carbognin	2006	17/32 53.1%	12/17 71%	15/15 100%	100%,75%	84%	4.8 (1.26 -18.31)	0.29 (0.14-0.61)
Abrao	2007	54/104 51.9%	53/54 98%	50/50 100%	100%,98%	99%	-	0.02 (0.00-0.13)
Valenzano	2008	23/90 25.5%	22/23 96%	67/67 100%	100%,99%	99%	-	0.04 (0.01-0.3)
Guerriero	2008	39/88 44.3%	26/39 66%	45/49 92%	87%,78%	81%	8.17 (3.11 -21.44)	0.36 (0.23-0.57)
Piketty	2009	75/134 60%	68/75 91%	56/58 97%	97%,89%	93%	26.29 (6.72-102.83)	0.10 (0.05-0.20)
Bazot	2009	63/92 68.5%	59/63 94%	29/29 100%	100%,88%	96%	-	0.06 (0.02-0.16)
Hudelist	2009	48/200 24%	46/48 96%	149/152 98%	94%,99%	98%	48.56 (15.81-149.10)	0.04 0.01-0.17)
Goncalves	2010	81/194 41.7%	79/81 98%	113/113 100%	100%,98%	99%	-	0.02 (0.01-0.10)

Abdominal Imaging

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Diagnosis of deep infiltrating endometriosis: accuracy of magnetic resonance imaging and transvaginal 3D ultrasonography

Rosario Francesco Grasso,[1] Vincenza Di Giacomo,[1] Pietro Sedati,[1] Ornella Sizzi,[2] Giuseppe Florio,[2] Eliodoro Faiella,[1] Alfonso Rossetti,[2] Riccardo Del Vescovo,[1] Bruno Beomonte Zobel[1]

3D TV-USG ve MR, preoperatif derin infiltratif endometriozisi göstermesi bakımından çift kör yöntemle karşılaştırılmış

3d TV-USG

Table 2. Sensitivity, specificity, positive and negative predictive value and accuracy of TVUS for diagnosis of deep pelvic endometriosis

Location of pelvic endometriosis	Sensitivity 3DTVUS (%)	Specificity 3DTVUS (%)	PPV 3DTVUS (%)	NPV 3DTVUS (%)	Accuracy 3DTVUS (%)
Deep infiltrating endometriosis	78.9	70	86.6	44.4	77.7

MRI

Table 4. Sensitivity, specificity, positive and negative predictive value and accuracy of MR for diagnosis of deep pelvic endometriosis

Location of pelvic endometriosis	Sensitivity MR (%)	Specificity MR (%)	PPV MR (%)	NPV MR (%)	Accuracy MR (%)
Deep infiltrating endometriosis	96.1	85.7	96.1	85.7	93.9

Grasso RF. Abdom Imaging (2010) 35:716–725

3d TV-USG

Table 3. Results of TVUS

Location of deep pelvic endometriosis	Sensitivity 3DTVUS (%)	Specificity 3DTVUS (%)	PPV 3DTVUS (%)	NPV 3DTVUS (%)	Accuracy 3DTVUS (%)
USL	50	94.7	71,4	87.8	85.4
Posterior vaginal fornix	84	80	70	83	83
Rectovaginal septum	76.9	100	100	78.5	87.5
Sigmoid colon	33.3	100	100	91.3	91.6
Ureters	NA	NA	NA	NA	NA
Bladder	25	100	100	86.9	87.5

MRI

Table 5. Results of MR

Location of deep infiltrating endometriosis	Sensitivity MR (%)	Specificity MR (%)	PPV MR (%)	NPV MR (%)	Accuracy MR (%)
USL	69.2	94.3	75	92.5	89.3
Posterior vaginal fornix	83.3	88.8	62.5	96	87.8
Rectovaginal septum	76.4	100	100	80	87.8
Sigmoid colon	75	100	100	96.6	96.9
Ureters	66.6	100	100	98.3	98.4
Bladder	83.3	100	100	96.4	96.9

Grasso RF. Abdom Imaging (2010) 35:716–725

Ultrasound Obstet Gynecol 2010; 36: 241–248
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Value of transvaginal ultrasound in assessing severity of pelvic endometriosis

T. K. HOLLAND*, J. YAZBEK*, A. CUTNER†, E. SARIDOGAN†, W. L. HOO† and D. JURKOVIC†

Bu çalışmanın farkı, transvaginal ultrasonografinin mevcut patolojideki morfolojik özelliklerden çok , tanının ASRM skorlamasındaki evrelere göre uyumluluğunu araştırması

Table 1 Comparison of ultrasound and laparoscopic assessment of severity of pelvic endometriosis using the American Society for Reproductive Medicine classification

	Laparoscopy					
Ultrasound	*Absent*	*Minimal*	*Mild*	*Moderate*	*Severe*	*Total*
Absent	59	29	27	3	2	120 (59.7)
Minimal	0	1	0	0	0	1 (0.5)
Mild	1	1	4	2	1	9 (4.5)
Moderate	2	1	0	20	4	27 (13.4)
Severe	0	1	0	2	41	44 (21.9)
Total (%)	62 (30.8)	33 (16.4)	31 (15.4)	27 (13.4)	48 (23.9)	201 (100)

Data are expressed as *n* or as *n* (%).

Erken evrede adezyon varlığı özellikle bimanuel muyenedeki gibi abdominal ve vaginal manuplasyonlarla saptanabilir
Pelvik adezyonları göstermesi bakımından, MRI daki sabit görüntülemeye göre daha dinamik ve fonksiyonel .

Yönlendirilmiş USG ileri evre endometioziste MRI göre üstün, tanı uyumu yüksek bir test olarak görünmektedir.

Table 2 Accuracy of ultrasound in diagnosing different stages of pelvic endometriosis using laparoscopy as the gold standard

	Sensitivity (n (%, 95% CI))	*Specificity* (n (%, 95% CI))	*LR+* (95% CI)	*LR−* (95% CI)
Absent vs. present	78/139 (56.1, 47.8–64.1)	59/62 (95.2, 86.7–98.3)	11.60 (3.81–35.32)	0.461 (0.379–0.561)
Absent to mild vs. moderate to severe	67/75 (89.3, 80.3–94.5)	122/126 (96.8, 92.1–98.8)	28.14 (10.69–74.0)	0.11 (0.057–0.212)
Absent to moderate vs. severe	41/48 (85.4, 72.8–92.8)	150/153 (98.0, 94.4–99.3)	43.5 (14.12–134.39)	0.149 (0.075–0.295)

LR+, positive likelihood ratio; LR−, negative likelihood ratio.

Holland TK, Yazbek J, Cutner A, Sarıdoğan E,. Hoo WL, Jurkovic D. Value of transvaginal ultrasound in assessing severity of pelvic endometriosis Ultrasound Obstet Gynecol 2010; 36: 241–248

Farklı operatörlerin USG ile tanı uyumu karşılaştırılmış
İkisi arasında fark bulunamamış.

Table 3 Comparison of performance of Examiners A and B at diagnosing severe pelvic endometriosis using ultrasound, with laparoscopy as the gold standard

	Examiner A	*Examiner B*
Sensitivity (%)	81.8 (47.7–96.8)	93.3 (78.7–98.2)
Specificity (%)	98.9 (93.3–99.9)	97.4 (86.5–99.5)
LR+	76.1 (10.6–545)	33.4 (4.82–231)
LR–	0.184 (0.0524–0.644)	0.099 (0.0339–0.292)
PPV (%)	89.8	96.6
NPV (%)	97.8	94.9
Accuracy (AUC)*	0.904	0.938

Data shown in parenthesis are 95% CI. *Comparison of area under receiver–operating characteristics curves (AUC), $P = 0.627$. LR+, positive likelihood ratio; LR–, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

Holland TK, Yazbek J, Cutner A, Sarıdoğan E,. Hoo WL, Jurkovic D. Value of transvaginal ultrasound in assessing severity of pelvic endometriosis Ultrasound Obstet Gynecol 2010; 36: 241–248

- MRI ileri evre endometrioziste daha yakın kestirime sahip, ancak pahalı ve kolay uygulanabilir değil

- MRI rektosigmoid bileşke ve mesanedeki endometriozis lezyonlarını göstermede ultrasonografiye göre üstün
    - Ballyguier C. Comparison of magnetic resonance imaging and transvaginal ultrasonography in diagnosing bladder endometriosis. J Am Assoc Gynecol Laparosc. 2002;9: 15–23.

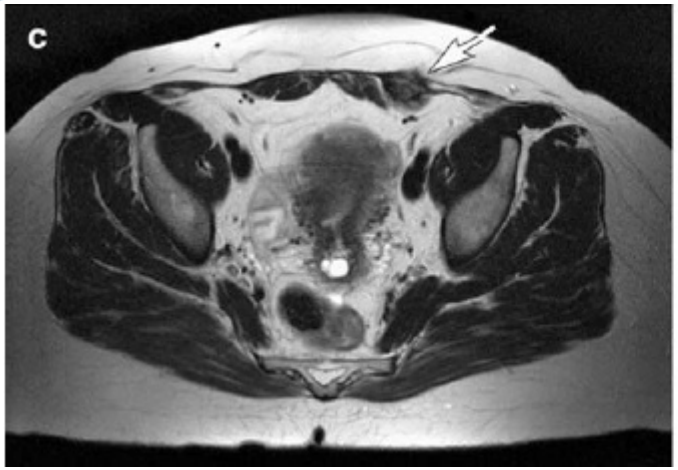
- Tomografi (pelvik organ görüntülemesi iyi değil, ancak kontrastlı tomografi üreteral tutulmayı göstermesi bakımından değerli)

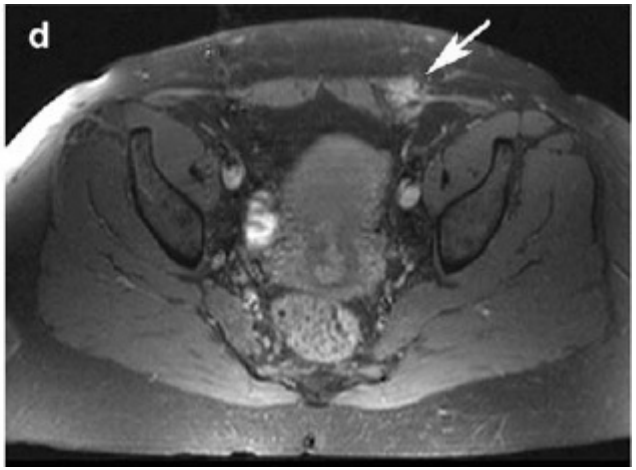
Eur Radiol (2010) 20: 1267–1276
DOI 10.1007/s00330-009-1658-1

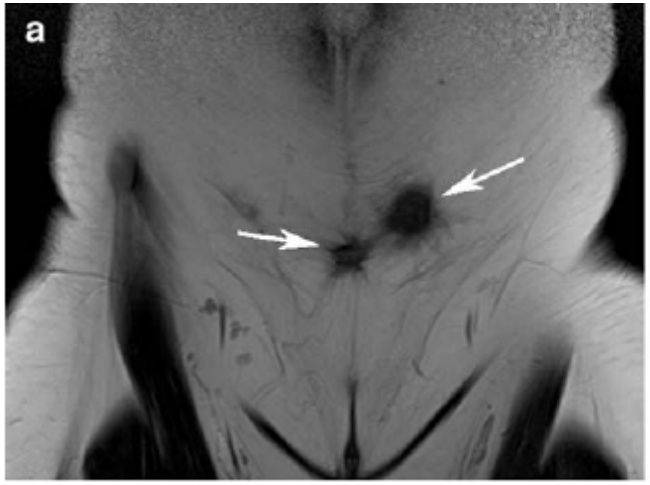
UROGENITAL

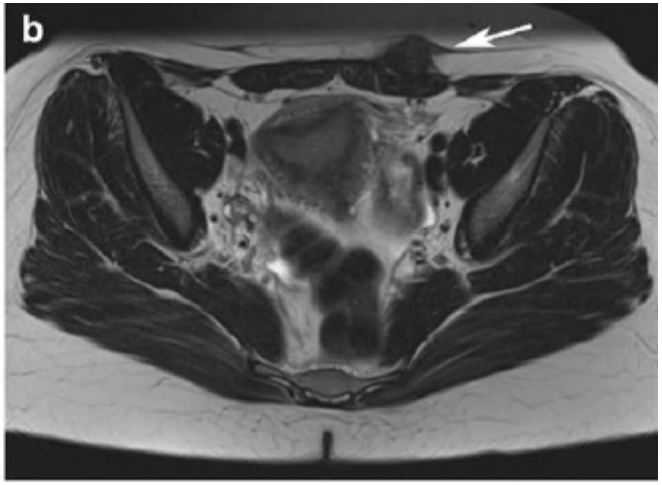
Milou P. H. Busard
Velja Mijatovic
Cees van Kuijk
Peter G. A. Hompes
Jan Hein T. M. van Waesberghe

Appearance of abdominal wall endometriosis on MR imaging









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doi:10.1093/humrep/deq141

human reproduction OPINION Gynaecology

Non-invasive diagnosis of endometriosis: the goal or own goal?

Edgardo Somigliana[1,2], Paolo Vercellini[1,2,3], Paola Vigano'[2,*], Laura Benaglia[1,3], Pier Giorgio Crosignani[4], and Luigi Fedele[1,3]

Screening rules: does endometriosis fit the model?

Table I Main desirable characteristics of a screening test and degree of satisfaction for endometriosis.

Items	Explanation	Degree of satisfaction
1. Health relevance	Is the condition an important health problem (significant risk of mortality or morbidity)?	+ +
2. Acceptability of the disease	Is the disease acceptable in the population?	−
3. Natural course	Does the condition have a recognizable latent or early symptomatic phase? Is the natural history of the condition well-understood?	−
4. Acceptability of the test	Is the test (and its consequences in terms of further diagnostic testing and subsequent treatment) acceptable to the population?	+
5. Effectiveness of treatment	Is early treatment of the condition effective? Does diagnosis of the disease before symptoms occur results in better outcome than waiting for symptoms?	+
6. Consensus	Does a consensus exist regarding proper management of abnormal test results?	− −
7. Complication balance	Is the risk of complication from the test and subsequent evaluation and treatment lower than the risk of morbidity and mortality from the disease?	+
8. Cost-benefits balance	Are the costs of testing and treating asymptomatic disease acceptable? Do the objectives of the program justify the costs?	+/−

Adapted from Peters *et al.* (1996) and Massad (2008).
A five-points scale was used to evaluate the degree of satisfaction. It is as follows: not at all (− −), mainly unsatisfied (−), unclear (+/−), partly satisfied (+) and satisfied to a large extent (+ +).
Judgement was independently done by all the authors and a consensus was reached by discussion if controversies emerged.

Endometrial Biyopsi;
Sinir liflerinin gösterilmesi

- Endometrial örneklemdeki fonksiyonel tabakada , endometriozisi bulunan hastalarda, olmayanlara göre artmış sinir lifi (primer olarak myelinize olmamış duyusal C lifleri ve Aδ) gösterilmiştir.

- Protein gene product 9.5 (PGP 9.5), vasoaktif intestinal peptid (VIP) ve substance P için boyama pozitif ancak nörofilament için negatif saptanmıştır.
    - Al-Jefout… M Diagnosis of endometriosis by detection of nerve fibres in an endometrial biopsy: a double blind study. Hum Reprod. 2009;24:3019–3024.
    - Bokor A… Density of small diameter sensory nerve fibres in endometrium: a semi-invasive diagnostic test for minimal to mild endometriosis. Hum Reprod. 2009;24:3025–3032.

Human Reproduction Vol.21, No.3 pp. 782–787, 2006
Advance Access publication October 27, 2005.
doi:10.1093/humrep/de

High density of small nerve fibres in the functional layer of the endometrium in women with endometriosis

N.Tokushige[1,3], R.Markham[1], P.Russell[2] and I.S.Fraser[1]

Table I. Small unmyelinated nerve fibre density in the functional layer of endometrium (per mm^2, mean±SD) in women with and without endometriosis

	n	Mean±SD	Range
Hysterectomy specimens: endometriosis			
Menstrual	1	7	7
Proliferative	2	6	5–6
Secretory	7	15±5	9–23
Total	10	11±5	
Hysterectomy specimens: no endometriosis			
Menstrual	5	0	0
Proliferative	16	0	0
Secretory	14	0	0
Total	35	0	
Curettage specimens: endometriosis			
Menstrual	3	7±1	6–8
Proliferative	9	5±1	3–6
Secretory	13	13±6	7–30
Total	25	10±7	
Curettage specimens: no endometriosis			
Menstrual	7	0	0
Proliferative	20	0	0
Secretory	20	0	0
Total	47	0	0

Nerve fibres were stained with PGP9.5.
$P<0.001$ for endometriosis versus no endometriosis.

Human Reproduction, Vol.24, No.12 pp. 3025–3032, 2009
Advanced Access publication on August 18, 2009 doi:10.1093/humrep/dep283

human reproduction ORIGINAL ARTICLE *Gynaecology*

Density of small diameter sensory nerve fibres in endometrium: a semi-invasive diagnostic test for minimal to mild endometriosis

A. Bokor[1], C.M. Kyama[1], L. Vercruysse[1], A. Fassbender[1], O. Gevaert[2], A. Vodolazkaia[1], B. De Moor[2], V. Fülöp[3], and T. D'Hooghe[1,4,5]

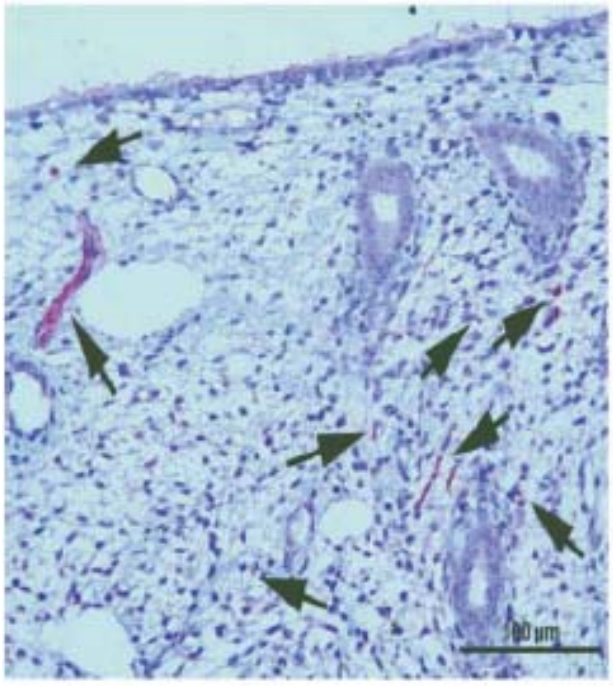
	Endometriosis (n = 20)	Controls (n = 20)
Age (years, mean ± SD)	33 ± 10	32 ± 5
Gravidity/parity (mean ± SD)	0.1 ± 0.3/0.05 ± 0.22	0.35 ± 0.87/0.15 ± 0.7
Primary/secondary infertility [n (%)]	18 (90)/2 (10)	17 (85)/3 (15)
Chronic pelvic pain [n (%)]	0 (0)	0 (0)
Dysmenorrhoea [n (%)]	3 (15)	2 (10)
Dyspareunia [n (%)]	0 (0)	1 (5)
Concurrent hormonal medication [n (%)]	0 (0)	0 (0)
Previous treatment for infertility [n (%)]	3 (15)	4 (20)
Ovulation induction	1 (5)	0 (0)
Laparoscopic surgery	2 (10)	4 (20)
Indication for surgery [n (%)]		
Infertility	2 (10)	4 (20)
Pelvic pain	0 (0)	0 (0)
Ethnicity [n (%)]		
Caucasian	20 (100)	19 (95)
Asian	0 (0)	1 (5)

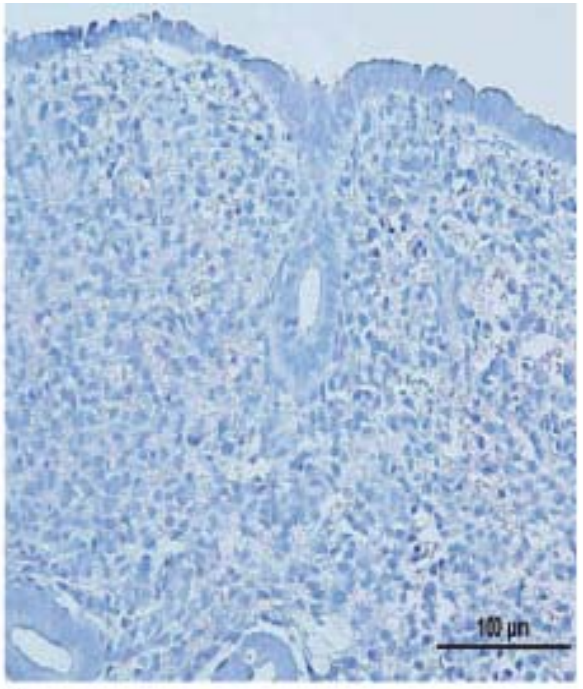
Table II Quantitative assessment of the endometrial nerve fibre density stained against different neural markers in patients with and without endometriosis

Marker	EM nerve fibre density: total number of nerve fibres/mm^2 EM surface area screened [median (range), mean ± SD]		Total number of nerve fibres present in total EM surface area screened/patient [median (range), mean ± SD]		Total EM surface area screened (mm^2)/patient [median (range), mean ± SD]
	Endo (n = 20)	Control (n = 20)	Endo (n = 20)	Control (n = 20)	
PGP9.5	2.30 (0–9.23), 2.62 ± 2.19‡	0.0 (0–0.79), 0.21 ± 0.28‡	9 (0–32), 11.10 ± 7.92‡	0 (0–5), 1.20 ± 1.73‡	5.74 (2.13–10.55), 5.65 ± 2.02
NPY	1.73 (0–18.05), 2.52 ± 3.91‡	0.0 (0–0.62), 0.15 ± 0.23‡	5 (0–31), 7.7 ± 7.76‡	0 (0–5), 1.05 ± 1.70‡	5. 84 (1.57–9.82), 5.68 ± 2.44
CGRP	1.58 (0–4.9), 1.94 ± 1.58‡	0.0 (0–0.68), 0.08 ± 0.19‡	5 (0–31), 6.85 ± 7.2‡	0 (0–3), 0.45 ± 0.99‡	5.54 (1.89–10.05), 5.53 ± 2.70
SP	1.50 (0–8.45), 2.29 ± 2.2‡	0.0 (0–0.56), 0.1 ± 0.2‡	6 (0–27), 7.95 ± 7.04‡	0 (0–3), 0.55 ± 1.05‡	5. 92 (1.43–10.07), 5.54 ± 2.5
VIP	0.71 (0–16.79), 2.37 ± 3.77‡	0.0 (0–0.43), 0.06 ± 0.15‡	4.5 (0–22), 7.75 ± 6.9‡	0 (0–3), 0.85 ± 1.95‡	5.84 (1.01–9.81), 5.63 ± 2.12
NF	0.0 (0–0.45), 0.02 ± 0.10¶	0.0 (0–4.68), 0.25 ± 1.04¶	0 (0–1), 0.05 ± 0.22¶	0 (0–30), 1.60 ± 6.70¶	6.19 (1.73–9.99), 5.92 ± 2.32

EM, endometrium; Endo, patients with endometriosis; Control, women with a normal pelvis.
‡$P < 0.0001$.
¶NS.

least-squares support vector machines (LS-SVM) modelling
Leave-one-out cross-validation (LOO-CV) analysis.





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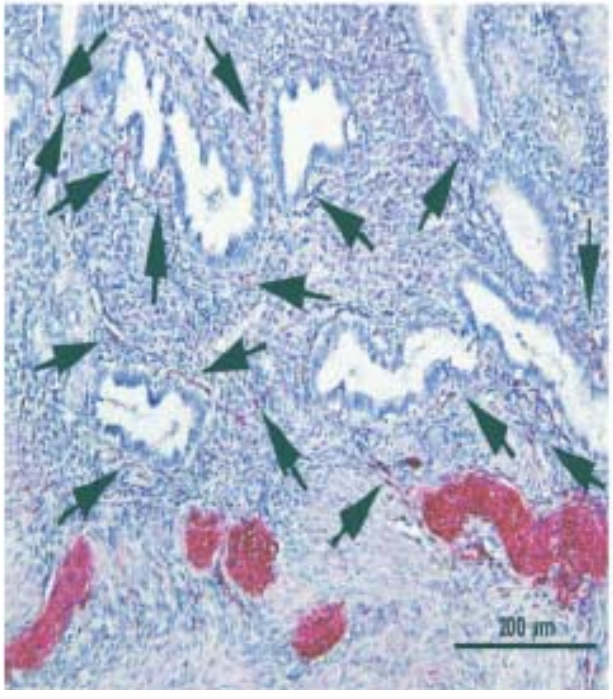

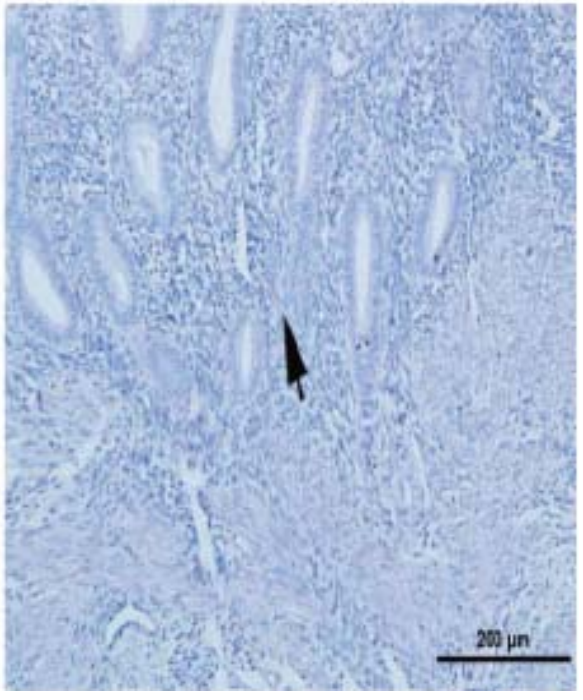

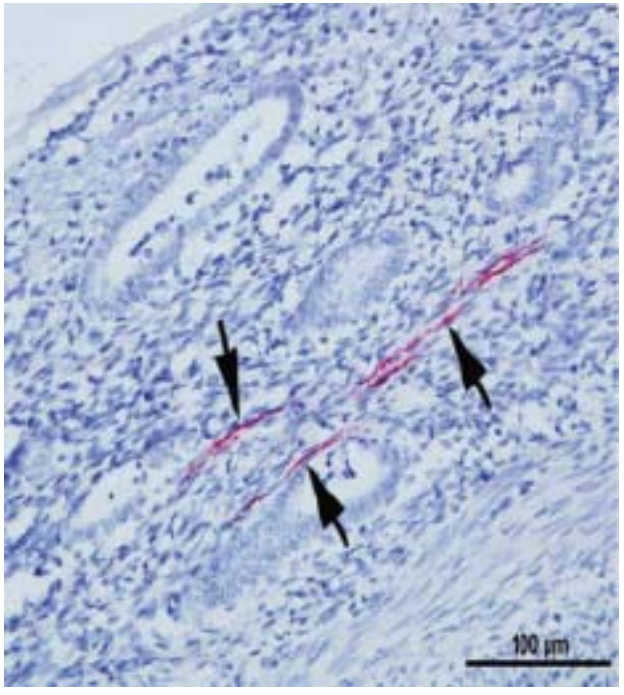

Pelvik ağrı semptomu bulunan kadınlarda endometriumun fonksiyonel tabakasında PGP9.5- pozitif sinir lifi dansite ve yüzdesi (sayı/mm2).

Endometriozisle birlikte adenomyozis			
Proliferatif	22	0.7 (0_2.8)	59.1% (13/22)
Sekretuvar	11	0.5 (0_1.9)	63.6% (7/11)
Toplam	33	0.6 (0_2.8)	60.6% (20/33)
Tek başına endometriozis			
Proliferatif	8	1.3 (0_2.4)	66.7% (6/8)
Sekretuvar	10	1.9 (0_3.0)	90.0% (9/10)
Toplam	18	1.5 (0_3.0)	83.3% (15/18)
Tek başına adenomyozis			
Proliferative	15	0.6 (0_7.0)	53.3%(8/15)
Sekretuvar	11	0.3 (0_2.4)	54.5%(6/11)
Toplam	26	0.5 (0_7.0)	53.9% (14/26)
Myom			
Proliferatif	8	0.8 (0_5.8)	75.0% (6/8)
Sekretuvar	5	0.7 (0_2.5)	60.0% (3/5)
Toplam	13	0.6 (0_5.8)	69.2% (9/13)

Zhang. Endometrial innervation and pain in women. Fertil Steril 2009.

- Fonksiyonel endometrial tabakada PGP9.5-immunoreaktif küçük sinir lifi, tanısı ne olursa olsun sadece ağrı bulunan olgularda.
- Birim alanda bulunan sinir sayısı, ağrı bulunan olgularda, tanıya göre farklılık göstermiyor.
    - Zhang. Endometrial innervation and pain in women. Fertil Steril 2009

- Adenomyozis veya myomu bulunan olgularda PGP9.5-immunoreaktif küçük sinir lifi sayısı ağrı olsun veya olmasın farklılık göstermiyor
    - Zhang X Innervation of endometrium and myometrium in women with painful adenomyosis and uterine fibroids Fertility and Sterility 2010, Vol. 94, 730-737

Semi- invaziv diğer işlemler

- Sistoskopi (Mesane endometriozisi)
- Sigmoidoskopi veya kolonoskopi (transmural barsak lezyonları)
- Ultrasound-guided fine needle aspiration (rektosigmoid, rektovaginal septum, veya abdominal skarlarda).

Laparoskopi

- Endometriozis düşünülen patolojilerin sadece %54 to % 67 ‘si histolojik olarak konfirme edilebilmektedir.
- Klinik olarak endometriozis şüphelenilen olguların %18 ‘inde patolojide endometriozisi düşündüren bulguya rastlanmamaktadır.
    - Walter AJ. Endometriosis: correlation between histologic and visual findings at laparoscopy. Am J Obstet Gynecol. 2001;184: 1407–1411.

- %20 endometriozis prevalansını öngören bir meta analizde laparoskopideki pozitif bulguların yaklaşık yarısının histolojik tanı ile uyumsuz olduğu bildirilmiştir.
    - Wykes CB Accuracy of laparoscopy in the diagnosis of endometriosis: a systematic quantitative review. BJOG. 2004;111:1204–1212.

- Bu durumu oluşturabilecek diğer lezyonlar; peritoneal lezyonlar, inflamatuvar değişiklikler, hemangiom, yabancı cisim reaksiyonu, mezotelial hiperplazi ve hemosiderin depozitleri olabilir.

Detection of peritoneal endometriotic lesions by autofluorescence laparoscopy

Olaf Buchweitz, MD,[a] Annette Staebler, MD,[b] Joke Tio, MD,[a] Ludwig Kiesel, MD[a]

Departments of Obstetrics and Gynaecology[a] and Pathology,[b] University of Münster, Münster, Germany

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- Floresan yöntemiyle laparoskopi son yıllarda uygulanmaya başlayan yeni bir yöntem olarak karşımıza çıkmaktadır.
- Özellikle gözle görülmesi zor veya olanaksız lezyonların tanınmasında kullanılma amaçlıdır.

- Otofloresan laparoskopinin etkinliğini artırmak için alternatif yöntem olarak eksojen duyarlaştırıcılar verilebilir.
- Endojen floroforlar arasında; triptofan ve kollajen bulunmaktadır
- Mavi ışığın, özellikle sistemik 5-aminolevulinik asid (5-ALA) uygulamasından sonra kullanımı, non-pigmente ve occult lezyonların tanısını anlamlı olarak artırmaktadır.
- Nonpigmente endometriotik lezyonların görülme olasılığını ışığı duyarlaştırıcı protoporfirin IX (PP IX) güçlendirmektedir.

Table IV Relative gain in sensitivity as a result of fluorescence diagnosis induced by 5-ALA and autofluorescence in the diagnosis of nonpigmented endometriotic lesions compared with white light diagnosis

Author	Patients	Method	Sensitivity WL/FD	Relative gain in sensitivity
Malik et al[1]	31	PDD	69/100%	1.45
Hillemanns et al[3]	15	PDD	ni	ni
Malik et al[9]	51	PDD	48/94%	1.95
Buchweitz et al[4]	24	PDD	58/92%	1.59
Demco[7]	25	AF	ni	ni
Buchweitz	83	AF	65/92%	1.41

FD, Fluorescence diagnosis with or without exogenous photosensitizers; *PDD*, fluorescence diagnosis after exogenous administration of 5-ALA; *WL*, white light diagnosis; *AF*, autofluorescence; *ni*, no information.

Diagnosis method	Endometriosis
White light	
Sensitivity	32/49 (65%)
Specificity	45/66 (68%)
White light + autofluorescence	
Sensitivity	45/49 (92%)
Specificity	56/66 (84%)

In 83 patients under clinical suspicion of endometriosis, the site was assessed in both white light mode and then in autofluorescence mode. It was possible to identify 77 lesions that corresponded visually to nonpigmented peritoneal lesions in white light mode and/or had circumscribed reduced autofluorescence in autofluorescence mode. In addition, we obtained 38 control biopsy specimens without conspicuous features in white light and autofluorescence mode. It was possible to detect endometriosis histologically in 49 lesions. Sixty-six lesions had no endometrioid glands or stroma.

	Normal autofluorescence		Reduced autofluorescence	
Morphology	n	Hist pos	n	Hist pos
Red	1	0 (0%)	22	20 (90.9%)
Adhesion-like	5	1 (20%)	4	3 (75%)
Vesicular	6	0 (0%)	6	6 (100%)
White	10	2 (20%)	9	7 (77.8%)
Black	0		30	25 (83.3%)
Inconspicuous	38	1 (2.6%)	14	9 (64.2%)
Endometrioma	21	16 (76.2%)	0	
Deep infiltrating	32	30 (93.7%)	0	

Thirty-eight control biopsy specimens were taken from normal-looking peritoneum with normal autofluorescence. In 14 cases normal-looking peritoneum revealed reduced autofluorescence. *Hist pos*, Histologically positive.

Normal görünen ve lezyon bulunmayan laparoskopilerdeki periton biyopsilerinde histolojik %6 oranında endometriozis tanısı konulmuş, eğer hasta infertil asemptomatikse bu oran %25 olarak bildirilmiştir.

- Balasch J, Creus M, Fabregues F. Visible and non-visible endometriosis at laparoscopy in fertile and infertile women and in patients with chronic pelvic pain: a prospective study. Hum Reprod. 1997; 12:1794–1799.

•Histolojik olarak endometriozis tanısı konulamayan olgularda patolojik tanı; fibrozis (Gian 2005)

•Evre ilerledikçe histolojik tanı doğrulama olasılığı daha fazla (%82.1), Spesmen büyük oldukça tanı konulma şansı daha da artmakta.

•Bishry GE. Correlation between laparoscopic and histological diagnosis in patients with endometriosis Journal of Obstetrics and Gynaecology, July 2008; 28(5): 511–515

- Zamanla histolojik tanı olasılığı artmakta, nedeninin patologlara bu tür materyallerin daha önceden gönderilmemiş olması ve negatif sonuçlar daha çok çalışma başlangıcında alınmış.

- Daha sonra patoloğa giden formlar incelendiğinde etiketlemenin peritoneal lezyon olarak yapıldığı ve bunlarda daha çok non spesifik fibrozis lehine sonuç verildiği bildirilmekte

- Daha sonra fark edilip endometriotik lezyon olduğu lokalizasyonu ve evresinin belirtilmiş; tanı oranının anlamlı olarak yükseldiği bildirilmektedirler
    - Bishry GE. Correlation between laparoscopic and histological diagnosis in patients with endometriosis Journal of Obstetrics and Gynaecology, July 2008; 28(5): 511–515

Lezyon tipine göre değerlendirmede

- Kırmızı lezyonlarda %100,
- Siyah lezyonlarda %92,
- Beyaz lezyonlarda %31 oranında endometriozis tanısı bildirilmiş.
    - » Moen and Halvorsen (1992), Mettler et al. (2003)

A logistic model for the prediction of endometriosis

Barbara J. Stegmann, M.D., M.P.H.,[a] Michele Jonsson Funk, Ph.D.,[b] Ninet Sinaii, Ph.D., M.P.H.,[c] Katherine E. Hartmann, M.D., Ph.D.,[d] James Segars, M.D.,[a] Lynnette K. Nieman, M.D.,[a] and Pamela Stratton, M.D.[a]

Fertility and Sterility® Vol. 91, No. 1, January 2009

•Ovarian fossa, kolon veya appendiksteki endometriozis düşünülen lezyonların histolojik olarak tanı alma olasılığı, uterus, over, tuba, cul-de-sac, veya uterosakral ligamenttekilere göre %25 oranında daha fazla

•Endometriotik odaktaki lezyon çapı her mm artış için %5 artan oranda histoloji ile doğrulanmaktadır.

TABLE 1

Distribution of lesion characteristics, odds ratios for association of lesion characteristics with histologically confirmed endometriosis, and calculated probability of histologically confirmed endometriosis of each characteristic (derived from the model after adjustment of all other variables).

Lesion characteristics	n (%)	Odds ratio (95% confidence interval)	Adjusted probability % of endo+ (95% confidence interval)	% Change from referent
Location[a]				
Bladder peritoneum, round or broad ligament, sidewall	129 (26.5)	0.42 (0.25, 0.71)	0.44 (0.15, 0.78)	−22
Uterus, ovary, fallopian tube	106 (21.8)	0.50 (0.26, 0.97)	0.49 (0.18, 0.81)	−17
Cul-de-sac, uterosacral ligaments (referent)	196 (40.3)	—	0.66 (0.30, 0.89)	—
Ovarian fossa, colon, appendix	56 (11.5)	1.18 (0.70, 1.98)	0.69 (0.34, 0.91)	3
Color groups[b]				
Red or white	251 (51.6)	—	0.66 (0.30, 0.89)	—
Blue, black, brown, endometrioma	136 (27.9)	1.21 (0.76, 1.93)	0.69 (0.33, 0.91)	3
Mixed colors	100 (20.5)	1.87 (1.05, 3.34)	0.78 (0.44, 0.94)	12
Race[c]				
Nonwhite	82 (16.8)	0.67 (0.40, 1.12)	0.56 (0.22, 0.85)	10
White (referent)	405 (83.2)	—	0.66 (0.30, 0.89)	—
Stage[d]				
I	99 (20.3)	0.49 (0.31, 0.79)	0.48 (0.17, 0.81)	−18
II, III, IV	388 (79.7)	—	0.66 (0.30, 0.89)	—

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	Median (range)	Odds ratio per unit increase (95% confidence interval)		
Width of lesion (mm)[d]	5 (1–90)	1.05 (1.02, 1.09)		
2.7			0.59 (0.25, 0.87)	−7
7.7 (mean, referent)			0.66 (0.30, 0.89)	—
12.7			0.71 (0.35, 0.92)	4
17.7			0.76 (0.40, 0.94)	8
22.7			0.80 (0.45, 0.95)	10
BMI (kg/m^2)[e]	24.3 (17.2–4.5)	0.97 (0.93, 1.01)		
35			0.59 (0.19, 0.90)	−4
30			0.62 (0.24, 0.90)	−2
25 (mean, referent)			0.66 (0.30, 0.89)	—
20			0.68 (0.36, 0.89)	2
15			0.71 (0.43, 0.89)	4
Age (y)[f]	31 (17–46)	1.01 (0.98, 1.04)		
21.4			0.63 (0.32, 0.87)	−2
26.4			0.64 (0.31, 0.88)	0
31.4 (mean, referent)			0.66 (0.30, 0.89)	—
36.4			0.66 (0.29, 0.91)	1
41.4			0.67 (0.28, 0.92)	2

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- Multivaryan lojistik regresyon, “artificial neural networks” ve “least-squares support vector machines” (LS-SVM), tanı testlerinin prediktif performansının arttırılmasında kullanılmakta (Van Holsbeke et al., 2009)
- Klinik araştırmalarda, küçük data gruplarının belirlenmesinde “Leave-one-out cross-validation” (LOO-CV) tercih edilmekte (Hedenfalk., 2001; Hoshida, 2008).

Genetik çalışmalar (polimorfizm, lokus belirleme)

- Semptom varlığı ve infertilite bulunan endometriozisli olgularda p53 codon 72 gen polimorfizminin tanının desteklenmesinde moleküler marker olarak kullanılabileceği ileri sürülmüştür.
    - Ribeiro Júnior CL, Arruda JT, Silva CT, Moura KK. Analysis of p53 codon 72 gene polymorphism in Brazilian patients with endometriosis. Genet Mol Res 2009;8:494-9

- Kromozom 7p13–15 endometriozis ilişkisi?
    - Zondervan K.Human Reproduction Vol.22, No.3 pp. 717–728, 2007

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A Functional Promoter Polymorphism in *NFKB1* Increases Susceptibility to Endometriosis

Bin Zhou,[1,*] Li Rao,[2,*] Ying Peng,[2] Yanyun Wang,[3] Mingrong Qie,[4] Zhu Zhang,[4] Yaping Song,[1] and Lin Zhang[1]

TABLE 1. DISTRIBUTION OF THE −94 INSERTION/DELETION ATTG POLYMORPHISM IN THE *NFKB1* GENE IN ENDOMETRIOSIS PATIENTS AND CONTROL SUBJECTS

	Patients, n = 206	*Hospital control subjects*			*Community control*			*All control subjects*		
		n = 173	*OR*	p-*Value*	n = 192	*OR*	p-*Value*	n = 365	*OR*	p-*Value*
NFKB1 −94 genotype (%)										
$ATTG_1/ATTG_1$	19 (9.2)	29 (16.8)			35 (18.2)			64 (17.5)		
$ATTG_1/ATTG_2$	64 (31.1)	78 (45.1)	1.252 (0.643–2.438)	NS	88 (45.8)	1.340 (0.703–2.553)	NS	166 (45.5)	1.299 (0.722–2.337)	NS
$ATTG_2/ATTG_2$	123 (59.7)	66 (38.2)	2.844 (1.483–5.455)	**0.001**	69 (35.9)	3.284 (1.746–6.175)	**8.92E-007**	135 (37.0)	3.069 (1.740–5.412)	**7.93E-007**
NFKB1 −94 allele (%)										
$ATTG_1$	102 (24.8)	136 (39.3)	1.968 (1.442–2.686)	**1.74E-005**	158 (41.1)	2.125 (1.571–2.875)	**8.52E-007**	294 (40.3)	2.049 (1.567–2.680)	**1.24E-007**
$ATTG_2$	310 (75.2)	210 (60.7)			226 (58.9)			436 (59.7)		

Boldfaced values indicate a significant difference at the 5% level.
NS, not significant; OR, odds ratio.

Moleküler araştırmalar

- HOXA-10 fazla ekspresyonu, desidualize hücrelerde, IGFBP1 mRNA azalması ile kendini göstermekte, tam tersi durumda, IGFBP1 mRNA H1db cAMP varlığına rağmen artmaktadır.
- HOXA10 seviyesindeki azalma endometriozisteki uterin çevrenin değişmesiyle görülebilir

- Kim JJ, Taylor HS, Lu Z, Ladhani O, Hastings JM, Jackson KS, *et al. Altered* expression of HOXA10 in endometriosis: potential role in decidualization. Mol Hum Reprod 2007;13:323-32.

Teşekkürler