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Wyndham Grand, İzmir

Random Biyopsilerin Kolposkopi Uygulamasında Yeri Vardır / Yoktur

Con

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Jinekolojik Onkoloji; Moleküler Tıp; PhD

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KOLPOSKOPİ POZİTİF

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Random biopsy in colposcopy-negative quadrant is not effective in women with positive colposcopy in practice

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- 1997 kadın
- Shanxi Province Cervical Cancer Screening Study I (SPOCCS I)

Efficacy of colposcopic-directed biopsies and random biopsies to detect HGIL+ with correlation to cytology (ThinPrep Pap).

	HSIL+ detected by colposcopic directed biopsy *N* (percent, 95%CI)	HSIL+ detected by random biopsy only *N* (percent, 95%CI)
Cytology = HSIL+ (108)		
Scopy+ (84)	56/84 (66.7, 56.1–76.1)	2/84 (2.4, 0.4–7.6)
1 or 2 quadrants (46)	20/46 (43.5, 30.0–58.0)	2/46 (4.3, 0.7–13.6)
3 or 4 quadrants (38)	36/38 (94.7, 83.7–99.1)	0
Scopy− (24)		6/24 (25, 10.8–44.9)
Cytology = LGIL (91)		
Scopy+ (32)	4/32 (12.5, 4.1–27.5)	1/32 (3.1, 0.2–14.5)
1 or 2 quadrants (26)	2/26 (7.7, 1.3–23.2)	1/26 (3.8, 0.2–17.5)
3 or 4 quadrants (6)	2/6 (33.3, 6.0–73.8)	0
Scopy− (59)		4/59 (6.8, 2.2–15.6)
Cytology = ASCUS (314)[a]		
Scopy+ (81)	3/81 (3.7, 0.95–9.7)	1/81 (1.2, 0.06–5.9)
1 or 2 quadrants (69)	2/69 (2.9, 0.5–9.2)	0
3 or 4 quadrants (12)	1/12 (8.3, 0.4–34.7)	1/12 (8.3, 0.4–34.7)
Scopy− (231)		1/231 (0.4, 0.02–2.1)
Cytology normal (1480)		
Scopy+ (321)	1/321 (0.3, 0.02–1.5)	1/321 (0.3, 0.02–1.5)
1 or 2 quadrants (275)	1/275 (0.4, 0.02–1.8)	0
3 or f 4 quadrants (46)	0	0
Scopy− (1159)		2/1159 (0.2, 0.03–0.6)

[a] 2 scopy unknown.

Results: For women with severe cytological abnormalities (HSIL+) and negative colposcopy, the yield of HSIL+ diagnosed by random biopsy was 25%. On the other hand, the yield of HSIL+ diagnosed by random biopsies in the negative quadrant was no more than 4% when the colposcopy was positive, regardless of the cytological findings. For women with negative HPV, no HSIL+ was found by random biopsy. For women with severe cytological abnormalities (HSIL+) and positive HPV, the yield of HSIL+ diagnosed by random biopsy was 35% when colposcopy was negative. For women with low-grade intraepithelial lesion (LSIL) and positive HPV, the yield of HSIL+ diagnosed by random biopsy was 12.5% when colposcopy was negative.

- ***Random biyopsiler pozitif kolposkopisi olup negatif kadrandan alındığında etkin değil***
  - ***HSIL saptanma oranını arttırmaz***

- ***Kimlere yapılabilir:***
  - **Sitoloji HSIL+ olup negatif kolposkopisi olanlarda**
    - **%25**
  - **Sitoloji LSIL veya HSIL+ ve pozitif HPV olan ancak negatif kolposkopik bulguları olanlarda**
    - **%12.5 / %35**

KOLPOSKOPİ POZİTİF

KOLPOSKOPİK BİYOPSİ SAYISI

Wentzensen et al. 2014
Sonuçlar:

- **Biyopsiler 4'e tamamlanmış..**
- HSIL yakalama duyarlılığı
  - ***1 biyopsi 60.6% (95% CI, 54.8% to 66.6%)***
  - ***2 biyopsi 85.6% (95% CI, 80.3% to 90.2%)***
  - ***3 biyopsi 95.6% (95% CI, 91.3% to 99.2%)***

- Tüm subgruplarda…
- Yakalama oranı ***kolposkopide yüksek gradlı lezyon şüphesi, HSIL sitolojisi ve HPV 16 pozitif*** gruplarda daha yüksek

Yield of HSIL from random biopsies

Directed biopsies	Yield of HSIL based on directed biopsies	Additional yield of consensus random biopsies
None	ND	1/22 (4.5%)
1	11/90 (12.2%)	1/76 (1.3%)
2	33/181 (18.2%)	2/152 (1.3%)
3	66/145 (45.5%)	1/125 (0.8%)

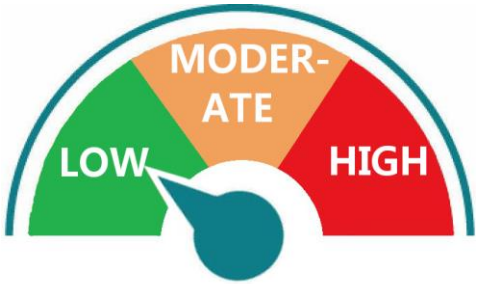
- Few HSIL are detected by random biopsies
- No additional CIN3 are detected by consensus random biopsies

Wentzensen JCO 2014

Redman C, IFCPC2017 Congress, Presidential debate

KOLPOSKOPİ NEGATIF

DÜŞÜK RİSKLİ GRUP



Düşük Riskli Grup

Random Biopsies in Low Risk Women

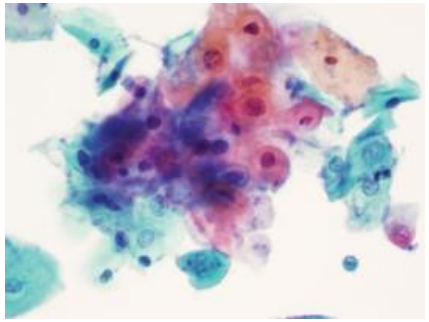
Low-risk group: <HSIL, HPV 16/18-, normal colposcopy						
Study	Manuscript	N	CIN2+	CIN3+	Proportion CIN2+	Proportion CIN3+
ATHENA	Huh 2014	1225	8	2	0.0065	0.0016
ALTS	in preparation	373	4	2	0.0107	0.0054
BD	in preparation	1572	25	11	0.0159	0.0070
Biopsy	in preparation	19	0	0	0.0000	0.0000
Total		3189	37	15	0.0116	0.0047

- Studies have shown that women with a low prior risk and normal colposcopy impression have a very low risk of prevalent precancer
- **But, what about women who are at higher risk?**

Huh, IFCPC2017 Congress, Presidential debate

KOLPOSKOPI NEGATIF

ASCUS GRUBU



European Journal of Obstetrics & Gynecology and Reproductive Biology 207 (2016) 32–36

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Punch biopsy guided by both colposcopy and HR-HPV status is more efficient for identification of immediate high-grade squamous intraepithelial lesion or worse among HPV-infected women with atypical squamous cells of undetermined significance

Z. Ding[a,b], Y. Li[c], A. Chen[b], M. Song[d], Y. Zhang[a,*]

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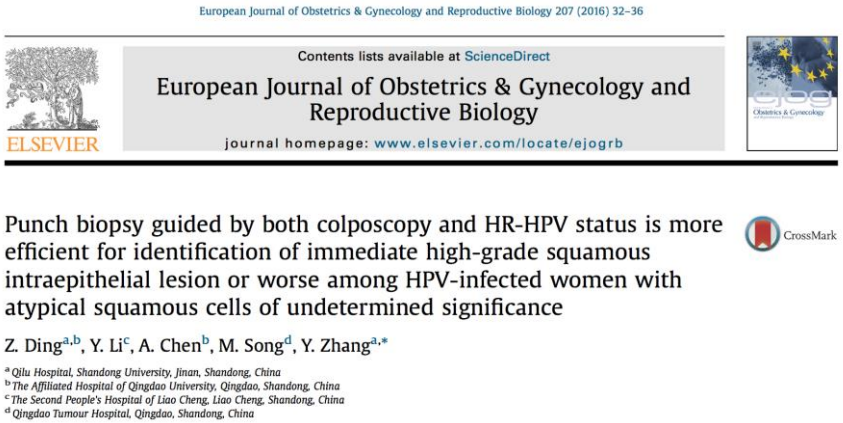
- **620 ASCUS** & **HR-HPV pozitif** kadın
- ***Bulgu varsa kolposkopik biyopsi***
- ***Normal kolposkopik bulgular varsa random bx***
- ***Kolposkopik biyopsi ile servikal patolojilerin uyum oranı %89***



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- ***Kolposkopisi normal*** hasta grubunda, HPV16 pozitifliğini veya virüs yükü yüksekliğini (50 RLU/CO) hesaba katmak HSIL+ saptamadaki duyarlılığı %74.7'den %81.0'e arttırıyor.
- ***Bu grupta random biyopsi düşünülebilir ve HSIL tanısını arttırır***

KOLPOSKOPI NEGATIF

ECC’NIN ROLÜ

Observational Study

Hu et al. Medicine (2017) 96:17

Medicine®

OPEN

Pooled analysis on the necessity of random 4-quadrant cervical biopsies and endocervical curettage in women with positive screening but negative colposcopy

Shang-Ying Hu, MD PhD[a], Wen-Hua Zhang, MD[b,*], Shu-Min Li, MD PhD[b], Nan Li, MD, PhD[b], Man-Ni Huang, MD[b], Qin-Jing Pan, MD[c], Xun Zhang, MD[d], Ying Han, MD[b], Fang-Hui Zhao, MD, PhD[a], Wen Chen, MD, PhD[a], You-Lin Qiao, MD, PhD[a,*]

- **ECC**

- 17 populasyon bazlı tarama çalışması
- 30371 kadın

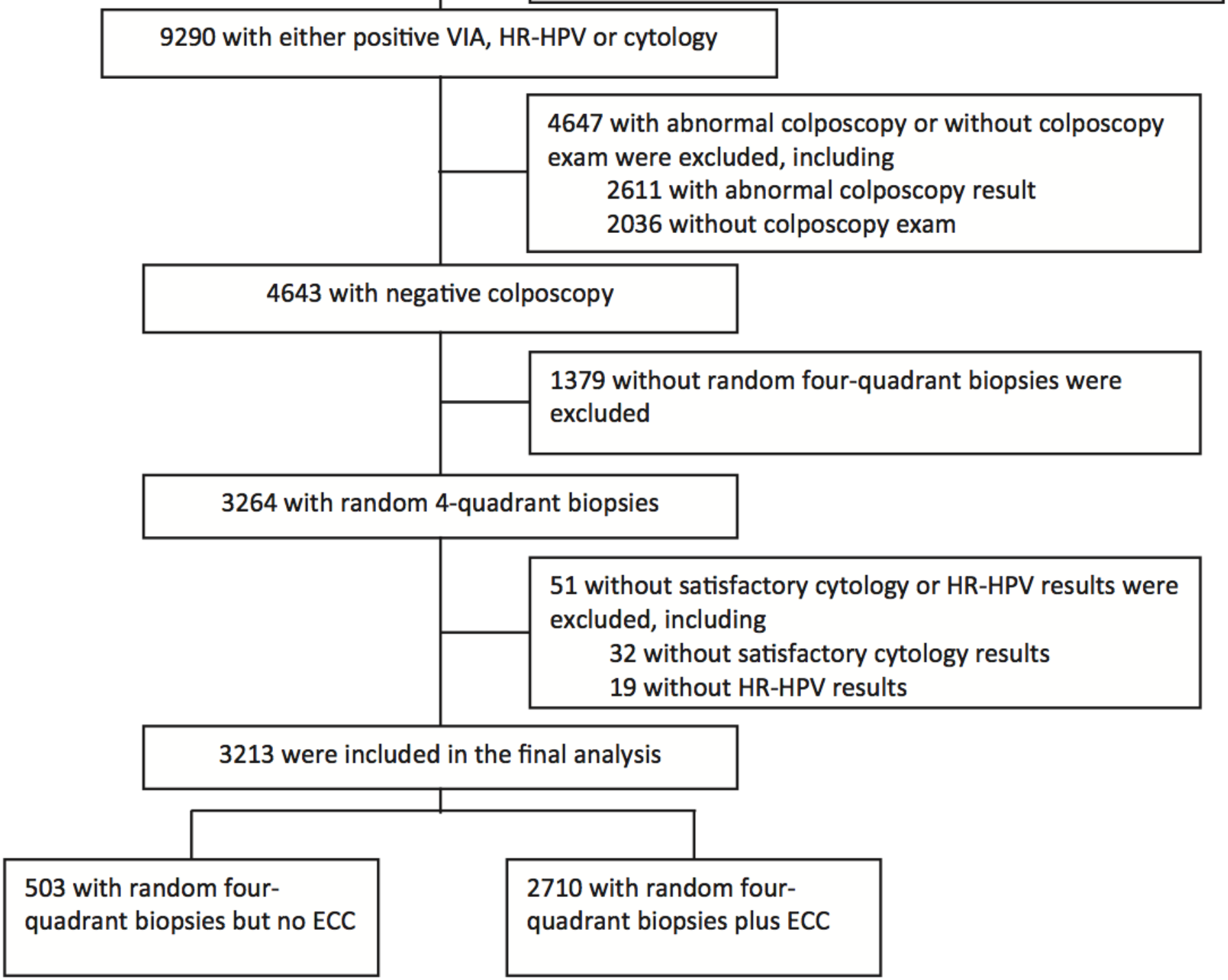
9290 with either positive VIA, HR-HPV or cytology
4647 with abnormal colposcopy or without colposcopy exam were excluded, including
2611 with abnormal colposcopy result
2036 without colposcopy exam
4643 with negative colposcopy
1379 without random four-quadrant biopsies were excluded
3264 with random 4-quadrant biopsies
51 without satisfactory cytology or HR-HPV results were excluded, including
32 without satisfactory cytology results
19 without HR-HPV results
3213 were included in the final analysis
503 with random four-quadrant biopsies but no ECC
2710 with random four-quadrant biopsies plus ECC

Table 5

Proportions of random 4-quadrant biopsies and/or ECC showing CIN2+ and CIN3+.

	CIN2+, n (%)	CIN3+, n (%)
Random 4-quadrant biopsies Yes/ECC Yes*	13 (16.0)	32 (16.5)
Random 4-quadrant biopsies Yes/ECC No	53 (65.4)	144 (74.2)
Random 4-quadrant biopsies No/ECC Yes	15 (18.5)	18 (9.3)
Random 4-quadrant biopsies and/or ECC Yes	81 (100.0)	194 (100.0)

CIN = cervical intraepithelial neoplasia, CIN2+ = cervical intraepithelial neoplasia grade 2 or worse, CIN3+ = cervical intraepithelial neoplasia grade 3 or worse, ECC = endocervical curettage.

* "Yes" means the histological result was CIN2+ or CIN3+, and "No" means less than CIN2 or CIN3, oppositely.

- ***ECC yapılmadan sadece random biyopsi yapılsa CIN2+ lezyonların %18.5'i atlanabilir***

KOLPOSKOPİK BİYOPSİ BAŞARISI

DOI: 10.1111/j.1471-0528.2012.03444.x
www.bjog.org

Systematic review

Accuracy of colposcopy-directed punch biopsies: a systematic review and meta-analysis

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Accepted 3 June 2012. Published Online 13 August 2012.

Selection criteria Articles that compared the colposcopically directed cervical punch biopsy with definitive histology from an excisional cervical biopsy or hysterectomy.

Main results Thirty-two papers comprising 7873 paired punch/definitive histology results were identified. The pooled sensitivity for a punch biopsy defined as test cut-off CIN1+ to diagnose CIN2+ disease was 91.3% (95% CI 85.3–94.9%) and the specificity was 24.6% (95% CI 16.0–35.9%). In most of the studies, the majority of enrolled women had positive punch biopsies. Pooling of the four studies where the excision biopsy was performed immediately after the punch biopsy, and where the rate of positive punch biopsies was considerably lower, yielded a sensitivity of 81.4% and specificity of 63.3%.

Author's conclusion The observed high sensitivity of the punch biopsy derived from all studies is probably the result of verification bias.

The number of punch biopsies

It has been shown that increasing the number of biopsies increases the detection rate of CIN3[55] as does the taking of random biopsies from apparently normal cervical tissue.[56,57] We have demonstrated that the pooled sensitivity for a single punch biopsy is 90%, if one or more punch biopsies are performed this increases to 93%, and if multiple biopsies were always performed then the sensitivity would be in the order of 100% (intergroup heterogeneity $P < 0.001$). This supports Pretorius' findings, who observed that colposcopy-targeted biopsies missed a proportion of high-grade CIN,[57] but that some of the missed disease may be picked up by random biopsies. The TOMBOLA trial identified a false-negative rate associated with punch biopsy but concluded that it did not have an impact on the clinical outcome because missed cases would be picked up at the next round of screening.[58] Missed disease

Colposcopy

When looking at the reason for missed high-grade CIN the question arises as to whether this is a function of colposcopy, either not identifying the abnormality or failing to sample an identified abnormal area. Developments in colposcopy and improvements in the images obtained are associated with improved detection of CIN2+ rates,[59] but apparently normal cervix, even under enhanced imaging, has been shown to contain CIN2+ disease in 25% of cases of women referred to colposcopy with any cytological abnormality or undergoing follow up for a CIN1 or CIN2 lesion.[60] Therefore this implies that it is colposcopy rather than the punch biopsy itself that is the limiting factor for detecting CIN2+ because a targeted biopsy cannot be used to detect disease that is not visible.

Sorun…

Need for adjunctive technologies

Redman C, IFCPC2017 Congress, Presidential debate

- ***Kolposkopi pozitif olgularda random biyopsinin ek yararı görünmemekte***

- ***Kolposkopi + grupta biyopsi sayısının arttırılması faydalı***

- ***Düşük riskli gruplarda random biyopsinin ek yararı yok***

- ***Kolposkopi negatif vakalarda random biopsilerin yeri olabilir***
  - ***HPV 16 + ve ASCUS grubu öne çıkıyor***
  - ***Mutlaka ECC eklenmeli***

- ***Teşekkürler…***