Rutin Pratiği Değiştirecek Literatür Güncellemesi "Cerrahi"

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Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23–01): a phase 3 randomised controlled trial

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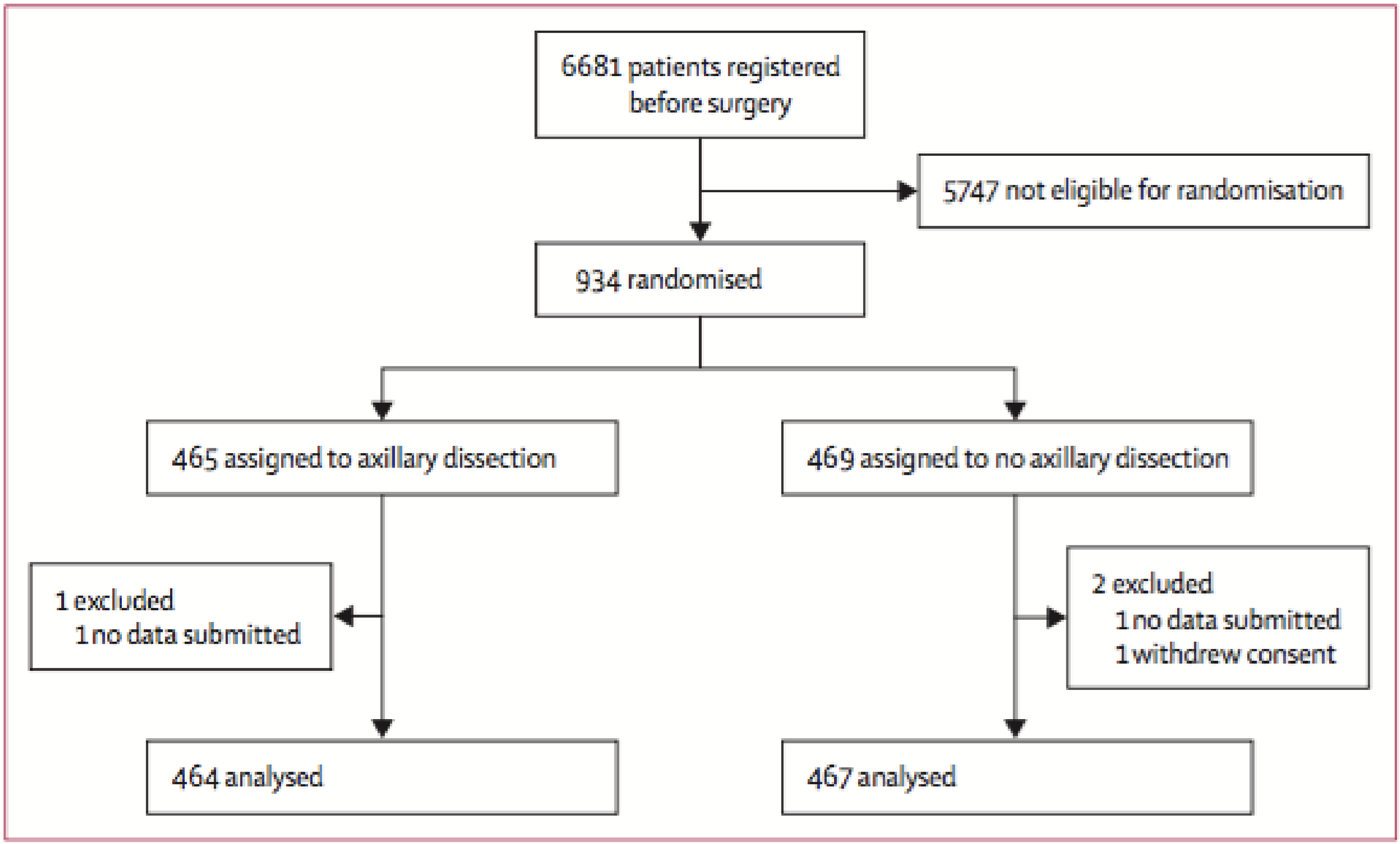
Amaç

- (T1-2) SLNB'de bir veya daha fazla mikrometastatik lenf nodu varlığında ALND ???

Metod

- 27 merkez
- 2001-2010
- Tümör çapı en fazla 5 cm
- cN0 hastalar
- Meme cerrahisi mastektomi veya MKC
- Mikrometastaz ≤ 2mm veya izole tm hüc


6681 patients registered before surgery
5747 not eligible for randomisation
934 randomised
465 assigned to axillary dissection
469 assigned to no axillary dissection
1 excluded
1 no data submitted
2 excluded
1 no data submitted
1 withdrew consent
464 analysed
467 analysed

SLNB

- Tüm SLN'ları 50-200 µm'lik kesitler
- HE ile değerlendirme
- Mikrometastaz şüphesi varsa sitokeratin immün boyama

Hasta Özellikleri

	Axillary dissection (n=464)	No axillary dissection (n=467)
Age (years)		
Median (range)	53 (28–81)	54 (26–81)
Preoperative sentinel-node biopsy		
No	287 (62%)	286 (61%)
Yes	177 (38%)	181 (39%)
Menopausal status		
Pre	204 (44%)	207 (44%)
Post	260 (56%)	260 (56%)

Hasta Özellikleri

	Axillary dissection (n=464)	No axillary dissection (n=467)
Pathological tumour size		
<2 cm	316 (68%)	322 (69%)
2–2·9 cm	106 (23%)	112 (24%)
≥3 cm	35 (8%)	28 (6%)
Unknown	7 (2%)	5 (1%)
Oestrogen receptor status		
Negative	51 (11%)	40 (9%)
Positive	409 (88%)	425 (91%)
Unknown	4 (<1%)	2 (<1%)

Hasta Özellikleri

	Axillary dissection (n=464)	No axillary dissection (n=467)
Progesterone receptor status		
Negative	108 (23%)	115 (25%)
Positive	352 (76%)	350 (75%)
Unknown	4 (<1%)	2 (<1%)
Sentinel-node tumour size		
≤1 mm	323 (70%)	320 (69%)
1·1–2 mm	131 (28%)	135 (29%)
>2 mm	10 (2%)	11 (2%)
Unknown	0	1 (<1%)

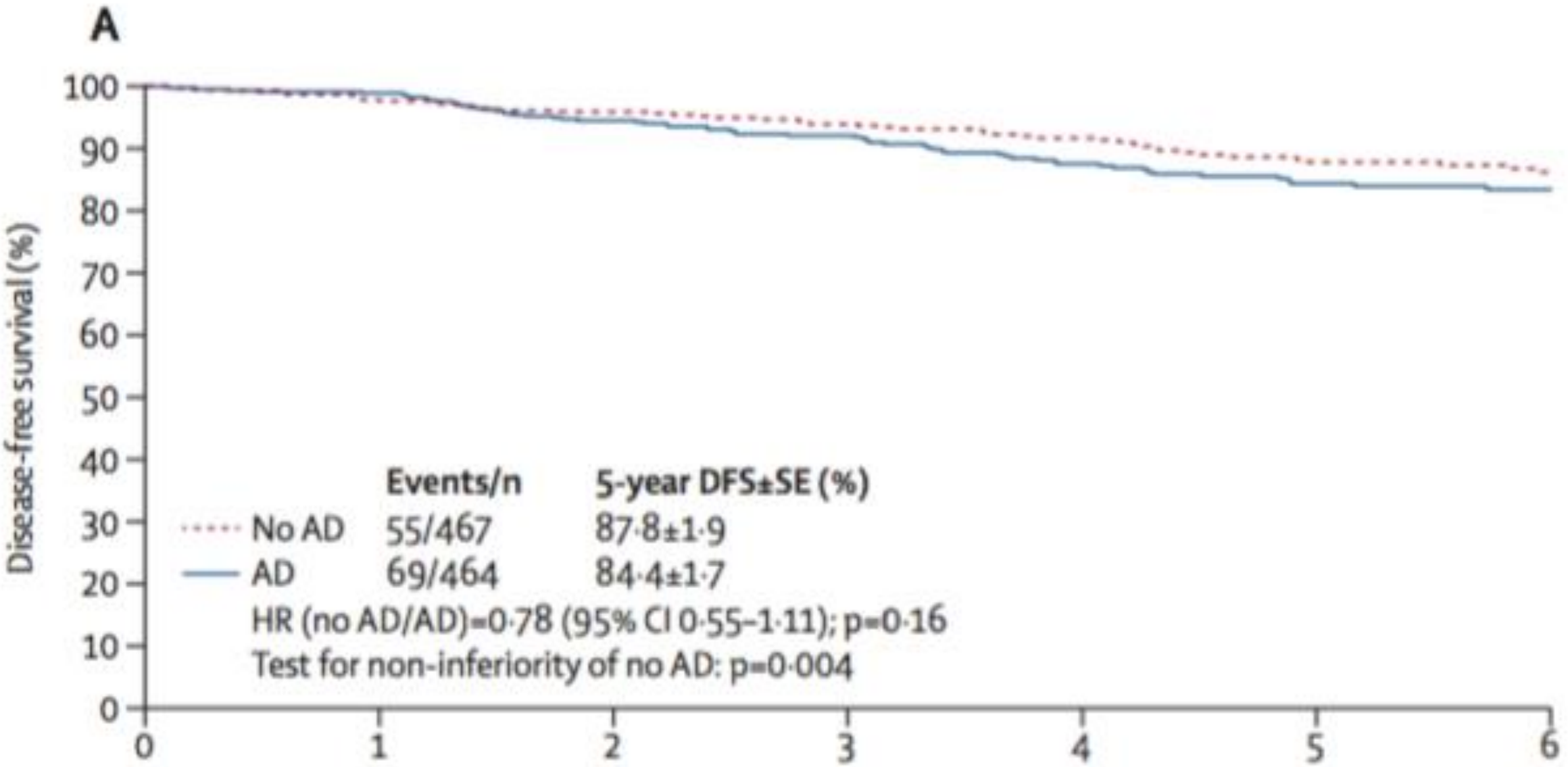
Hasta Özellikleri

	Axillary dissection (n=464)	No axillary dissection (n=467)
Number of sentinel-nodes removed		
1	226 (49%)	254 (54%)
2	153 (33%)	134 (29%)
3	52 (11%)	50 (11%)
4	15 (3%)	21 (4%)
5	11 (2%)	5 (1%)
≥6	7 (2%)	3 (<1%)
Median (range)	2 (1–9)	1 (1–8)

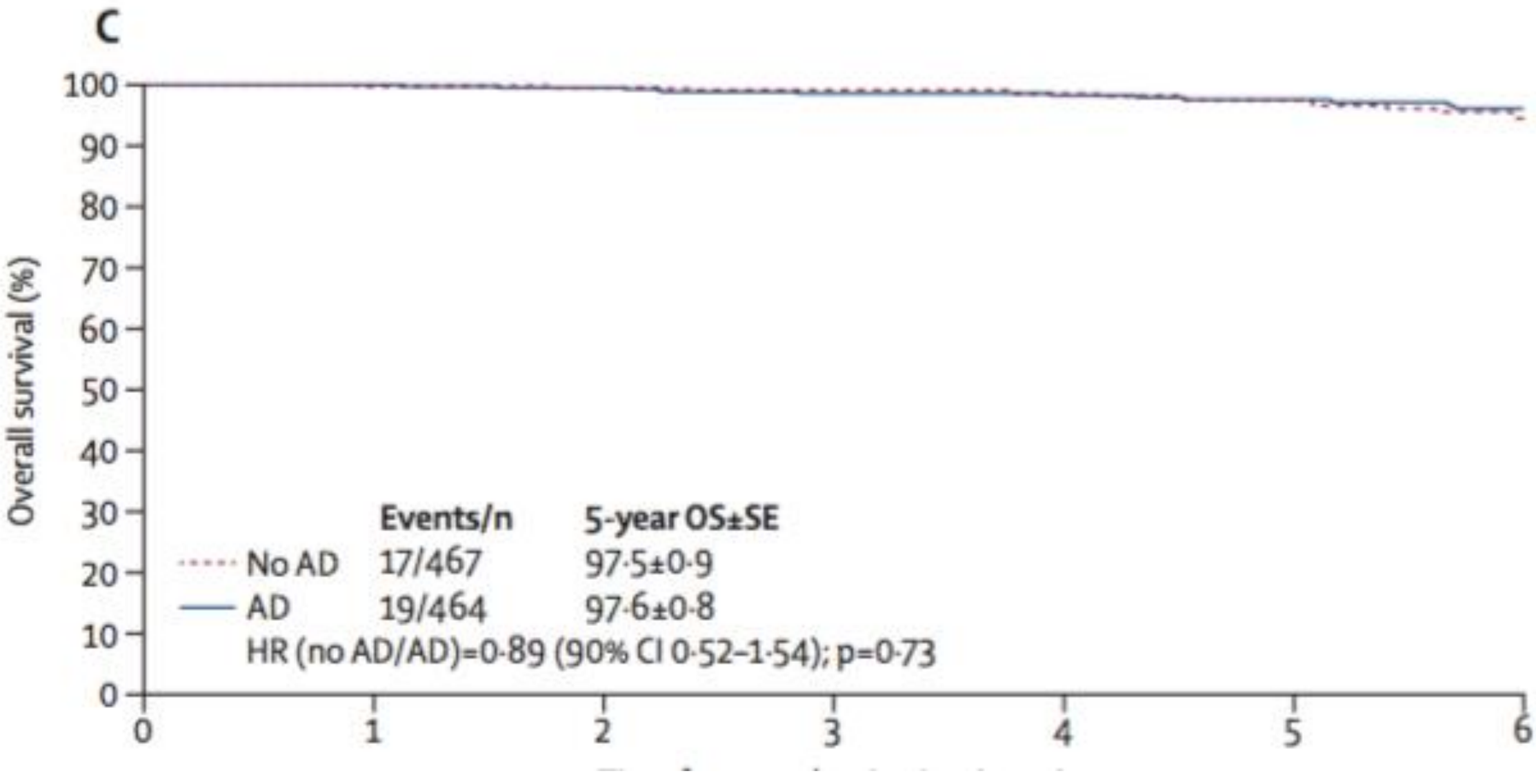
Hasta Özellikleri

	Axillary dissection (n=464)	No axillary dissection (n=467)
Number of metastatic sentinel-nodes		
1	440 (95%)	450 (96%)
2	23 (5%)	17 (4%)
3	1 (<1%)	0
Number of axillary nodes removed		
Median (range)	21 (1–44)	2 (1–29)
Additional involved nodes		
No	405 (87%)	455 (97%)
Yes	59 (13%)	12 (3%)
Internal mammary nodes removed		

Hastalıksız Sağ Kalım



Sağ Kalım


C
Overall survival (%)
100
90
80
70
60
50
40
30
20
10
0
0
1
2
3
4
5
6
Events/n
5-year OS±SE
No AD 17/467 97·5±0·9
AD 19/464 97·6±0·8
HR (no AD/AD)=0·89 (90% CI 0·52–1·54); p=0·73

Cerrahi komplikasyonlar

	Axillary dissection (n=447)	No axillary dissection (n=453)	p value†
Sensory neuropathy	82 (18%)	55 (12%)	0·012
Grade 1	60 (13%)	40 (9%)	
Grade 2	15 (3%)	6 (1%)	
Grade 3	1 (<1%)	0	
Grade 4	0	0	
Unknown grade	6 (1%)	9 (2%)	
Lymphoedema	59 (13%)	15 (3%)	<0·0001
Grade 1	33 (7%)	10 (2%)	
Grade 2	20 (4%)	3 (<1%)	
Grade 3	2 (<1%)	0	
Grade 4	1 (<1%)	0	
Unknown grade	3 (<1%)	2 (<1%)	
Motor neuropathy	37 (8%)	13 (3%)	0·0004
Grade 1	25 (6%)	11 (2%)	
Grade 2	9 (2%)	1 (<1%)	
Grade 3	3 (<1%)	1 (<1%)	
Grade 4	0	0	
Unknown grade	0	0	

Aksiller Nüks

- AD uygulanan - %0.2
- AD uygulanmayan- %0.86

Tartışma

- %92 hasta 3 cm'den küçük tümör
- %91'ine MKC
- %96'sına adjuvan sistemik tedavi
- Benzer hasta özellikleri varlığında ALND uygulanmayabilir

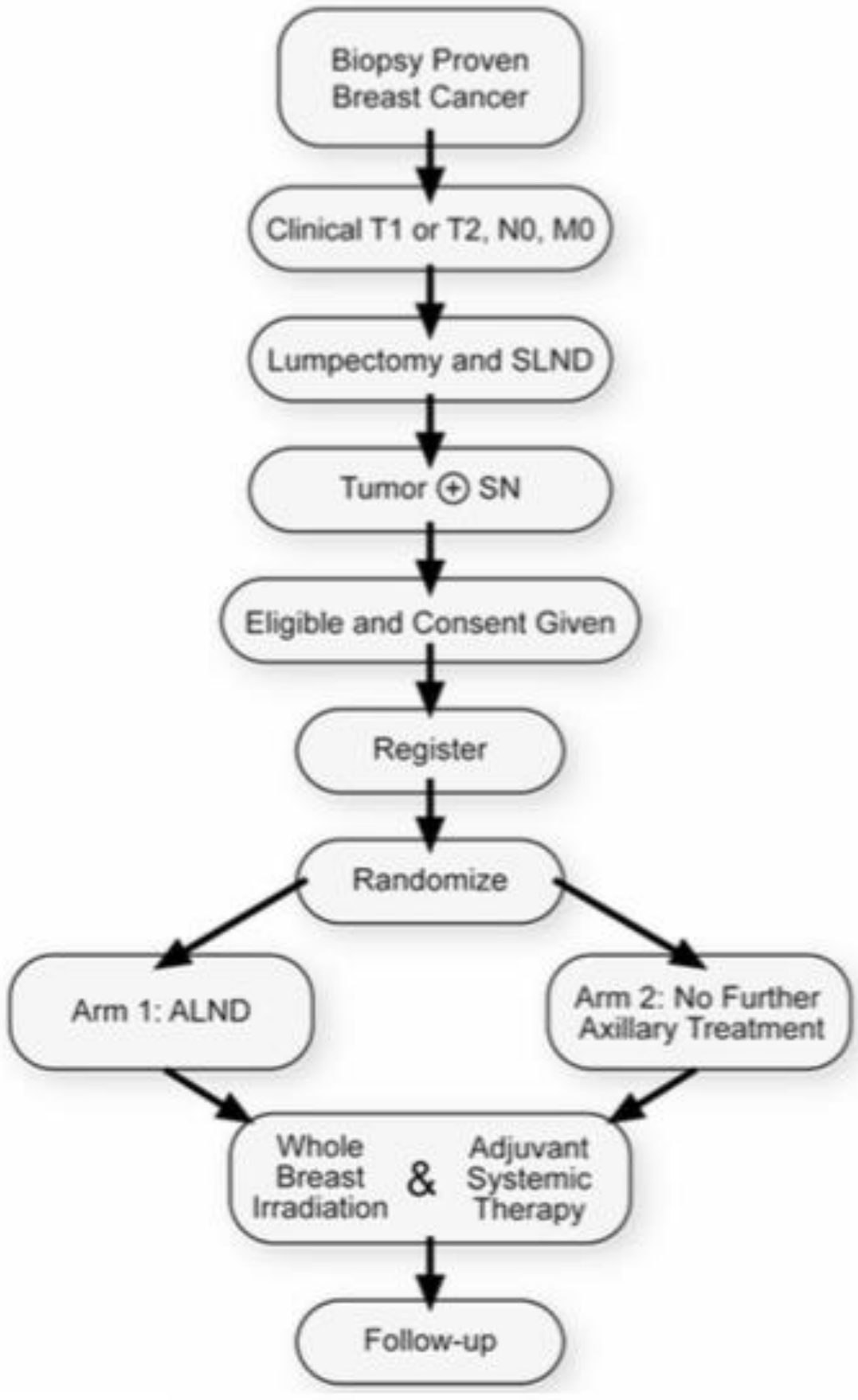
Tartışma

- AD uygulanan grupta non-SLN metastaz oranı %13
- AD uygulanmayan grupta aksiller nüks oranı %1’den az
- 927 hastaya (>%99) RT veya KT veya her ikisi

Tartışma

- ACOSOG Z0011
  - T1-2, cN0,M0 iki gruba randomize edilmiş
    - SLNB sonrası 3’den az makrometastazı olan 856 hasta
      - Tamamlayıcı AD
      - Sadece SLNB (aksillaya ek RT yok)

Z0011 Study Design Schema



Tartışma

- ACOSOG Z0011
  - Ortalama takip 6.3 yıl
  - Sağ kalım farkı yok
  - Adjuvan tedavi ve RT uygulanacak sınırlı aksiller hastalığı olan hastalarda ek cerrahi uygulanmayabilir

Original Investigation

Sentinel Lymph Node Surgery After Neoadjuvant Chemotherapy in Patients With Node-Positive Breast Cancer
The ACOSOG Z1071 (Alliance) Clinical Trial

Judy C. Boughey, MD; Vera J. Suman, PhD; Elizabeth A. Mittendorf, MD, PhD; Gretchen M. Ahrendt, MD; Lee G. Wilke, MD; Bret Taback, MD; A. Marilyn Leitch, MD; Henry M. Kuerer, MD, PhD; Monet Bowling, MD; Teresa S. Flippo-Morton, MD; David R. Byrd, MD; David W. Ollila, MD; Thomas B. Julian, MD; Sarah A. McLaughlin, MD; Linda McCall, MS; W. Fraser Symmans, MD; Huong T. Le-Petross, MD; Bruce G. Haffty, MD; Thomas A. Buchholz, MD; Heidi Nelson, MD; Kelly K. Hunt, MD; for the Alliance for Clinical Trials in Oncology

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Published online October 7, 2013.

Amaç

- Antrasiklin ve taksan
  - Nodal hastalıkta eradikasyon %30-40
  - ALND faydası ?
    - ALND uygulamamak için yanlış negatiflik oranı düşük olmalı
- Biyopsi ile kanıtlanmış cN1 olgularda kemoterapiyi takiben SLNB'de yanlış negatiflik oranını (FNR) belirlemek

Metod

- 136 merkez
- 2009-2011
- T0-4, N1-2, M0 ve neoadjuvan KT
- KT öncesi aksiller İİAB veya kalın İB ile kanıtlanmış hastalar

Metod

- AJCC evreleme- cN1 ve cN2 hastalar
- KT’den sonra SLNB ve ALND
- Mavi boya, radyokolloid veya her ikisi
- Aynı zamanda cerrahi sırasında şüpheli lenf nodları eksize edilmiş
- HE ile değerlendirme

Characteristics	No. (%)	
	cN1 Cohort (n = 663)	cN2 Cohort (n = 38)
Age, y		
18-39	120 (18.1)	4 (10.5)
40-49	213 (32.1)	15 (39.5)
50-59	197 (29.7)	10 (26.3)
60-69	112 (16.9)	5 (13.2)
≥70	21 (3.2)	4 (10.5)
Clinical T category at diagnosis[b]		
T0/Tis	5 (0.8)	2 (5.3)
T1	86 (13.0)	5 (13.2)
T2	372 (56.1)[c]	13 (34.2)
T3	175 (26.4)	10 (26.3)
T4	25 (3.8)	8 (21.1)

Characteristics	No. (%)	
	cN1 Cohort (n = 663)	cN2 Cohort (n = 38)
Approximated subtype		
ERBB2-positive (formerly *HER2*)	197 (29.7)	12 (31.6)
Hormone receptor–positive/ *ERBB2*-negative	301 (45.4)	14 (36.8)
Triple receptor–negative	156 (23.5)	10 (26.3)
Insufficient information to classify/ no invasive breast tumor/ prior breast surgery	9 (1.4)	2 (5.3)
Tumor histology		
IDC	590 (89.0)	30 (79.0)
ILC	37 (5.6)	1 (2.6)
Mix of IDC and ILC	11 (1.7)	0
Invasive carcinoma, other	20 (3.0)	5 (13.2)
DCIS	2 (0.3)	0
No breast disease, stage T0	3 (0.5)	2 (5.3)

Characteristics	No. (%)	
	cN1 Cohort (n = 663)	cN2 Cohort (n = 38)
Type of axillary lymph node biopsy		
Fine-needle aspiration	259 (39.1)	13 (34.2)
Core-needle biopsy	404 (60.9)	25 (65.8)
Clip placed in axilla		
Yes	214 (32.3)	16 (42.1)
No	448 (67.6)	22 (57.9)
Not stated	1 (0.2)	0

Characteristics	No. (%)	
	cN1 Cohort (n = 663)	cN2 Cohort (n = 38)
Neoadjuvant chemotherapy regimen		
Anthracycline and a taxane	499 (75.3)	24 (63.2)
Anthracycline	41 (6.2)	3 (7.9)
Taxane	112 (16.9)	10 (26.3)
No anthracycline and no taxane	11 (1.7)	1 (2.6)
Chemotherapy completed	609 (91.9)	33 (86.8)
Reason chemotherapy discontinued		
Disease progression	6 (0.9)	1 (2.6)
Intolerable adverse effects	38 (5.7)	4 (10.5)
Refusal	5 (0.7)	0
Lack of tumor response	3 (0.4)	0
Physician discretion	1 (0.2)	0
Desire for alternative therapy	1 (0.2)	0

Characteristics	No. (%)	
	cN1 Cohort (n = 663)	cN2 Cohort (n = 38)
Findings on axilla after chemotherapy		
No palpable adenopathy	556 (83.9)	26 (68.4)
Palpable lymph nodes	76 (11.5)	8 (21.1)
Fixed or matted lymph nodes	2 (0.3)	2 (5.3)
Not reported	29 (4.4)	2 (5.3)
Type of breast surgery after chemotherapy		
Partial mastectomy	266 (40.1)	11 (28.9)
Total mastectomy	395 (59.6)	25 (65.8)
None	2 (0.3)	2 (5.3)
Type of axillary surgery		
SLN	2 (0.3)	0
SLN with no SLN identified and ALND	46 (6.9)	4 (10.5)
SLN with SLN identified and ALND	603 (91.0)	34 (89.5)
ALND	12 (1.8)	0

Variable	No. (%)	
	cN1 (n = 651)	cN2 (n = 38)
Mapping agent used		
Blue dye	25 (3.8)	3 (7.9)
Radiolabeled colloid	109 (16.7)	7 (18.4)
Both	517 (79.4)	28 (73.7)
Timing of radiolabeled colloid injection		
Day before surgery	160 (24.6)	5 (13.2)
Morning of surgery	466 (71.6)	30 (78.9)
Not used	25 (3.8)	3 (7.9)

Variable	No. (%)	
	cN1 (n = 651)	cN2 (n = 38)
Injection sites		
Subareolar/periareolar	404 (62.1)	31 (81.6)
Peritumoral	56 (8.6)	1 (2.6)
Intradermal	17 (2.6)	2 (5.3)
Multiple sites	147 (22.6)	2 (5.3)
Not specified	27 (4.1)	2 (5.3)
No. of SLNs examined		
0	46 (7.1)	4 (10.5)
1	78 (12.0)	8 (21.1)
2	155 (23.8)	10 (26.3)
3	148 (22.7)	6 (15.8)
4	90 (13.8)	5 (13.2)
≥5	134 (20.6)	5 (13.2)

cN1 Hastalarda FNR

- En az 2 SLN eksize edilen hasta sayısı 525

- 215 (%41)hastada patolojik tam yanıt

- 310 hastada rezidüel nodal hastalık

  - 108 SLN ile

  - 163 ALND ve SLN ile

  - **39 Sadece ALND da (%12.6) yanlış negatiflik**

Table 3. Factors Affecting the Likelihood of a False-Negative Sentinel Lymph Node Finding in the 310 Women With cN1 Disease at Presentation, 2 or More SLNs Examined, and Residual Nodal Disease After Neoadjuvant Chemotherapy

	False-Negative SLN Findings, No. (Total)	FNR (95% CI), %	Fisher Exact Test, *P* Value
Age, y			
18.0-49.9	20 (150)	13.3 (8.3-19.8)	.73
≥50.0	19 (160)	11.9 (7.3-17.9)	
BMI			
≥25.0	25 (227)	11.0 (7.3-15.8)	.18
<25.0	14 (83)	16.9 (9.5-26.7)	
Clinical T category prior to chemotherapy			
Tis, T0, T1, or T2	32 (225)	14.2 (9.9-19.5)	.18
T3 or T4	7 (85)	8.2 (3.4-16.2)	
Chemotherapy duration, mo			
≤4.0	20 (201)	10.0 (6.2-15.0)	.07
≥4.1	19 (109)	17.4 (10.8-25.9)	
Palpable, fixed, or matted nodes after chemotherapy[a]			
Yes	10 (52)	19.2 (9.6-32.5)	.17
No	28 (247)	11.3 (7.7-16.0)	
Mapping agents used			
Single	12 (59)	20.3 (11.0-32.8)	.05
Dual	27 (251)	10.8 (7.2-15.3)	
Multiple injection sites[b]			
Yes	5 (70)	7.1 (2.4-15.9)	.21
No	30 (225)	13.3 (9.2-18.5)	
No. of SLNs examined			
2	19 (90)	21.1 (13.2-31.0)	.007
≥3	20 (220)	9.1 (5.6-13.7)	

Tartışma

- cN1 tümörlerde kemoterapi sonrası yanlış pozitiflik oranı(%12.6), cN0 tümörlerde beklenenden (%10) daha yüksek
- Kombine yöntemde oran %10.8
- NSABP B-27 çalışmasında cN0 hastalarda %9.3

Tartışma

- 3 ve daha fazla SLN varlığında yanlış pozitiflik oranı %9.1
- NSABP B-32 (kemoterapi öncesi)
  - 1 SLN %18
  - 2 SLN %10
  - 3 SLN %7

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ORIGINAL ARTICLE – GUIDELINE AND META-ANALYSIS

Society of Surgical Oncology–American Society for Radiation Oncology Consensus Guideline on Margins for Breast-Conserving Surgery With Whole-Breast Irradiation in Stages I and II Invasive Breast Cancer

Meena S. Moran, MD[1], Stuart J. Schnitt, MD[2], Armando E. Giuliano, MD[3], Jay R. Harris, MD[4], Seema A. Khan, MD[5], Janet Horton, MD[6], Suzanne Klimberg, MD[7], Mariana Chavez-MacGregor, MD[8], Gary Freedman, MD[9], Nehmat Houssami, MD, PhD[10], Peggy L. Johnson[11], and Monica Morrow, MD[12]

Amaç

- MKC oldukça sık uygulanmasına rağmen optimal cerrahi sınır ile ilgili fikir birliği yok
- Genişletici cerrahi rezeksiyon sık (%25)
- Görüntüleme, sistemik tedavide gelişmeler
- **Optimal cerrahi sınır ??**

Metod

- 1965-2013 yılları arasında cerrahi sınır ile ilgili makaleler
  - Evre 1-2 meme kanseri
  - Neoadjuvan KT ø
  - DCİS ø
  - MKC ve WBRT
  - Mikroskopik cerrahi sınır kantitatif olarak bildiren
  - Ortanca/ortalama takip süresi 4 yıl
  - Yaş bilgisi olan

Metod

- Toplam 33 çalışma
- 28162 hasta
- 1506’sında IBTR (median prevelans %5.3)
- Median takip 79.2 ay

Pozitif Cerrahi Sınır

Relationship between IBTR and margin status

	No. of studies	No. of participants	Adjusted OR of IBTR[a]	95% CI	*P* (association)
Margin category (model one)		28,162			<0.001
Close/positive	33	6,178	1.96	1.72–2.24	
Negative	33	21,984	1.0	—	
Margin category (model two)		13,081			<0.001
Positive	19	1,641	2.44	1.97–3.03	
Close	19	2,407	1.74	1.42–2.15	
Negative	19	9,033	1.0	—	—
Threshold distance (model two)[b]					0.90
1 mm	6	2,376	1.0	—	—
2 mm	10	8,350	0.91	0.46–1.80	—
5 mm	3	2,355	0.77	0.32–1.87	—

Pozitif Cerrahi Sınır

Impact of margin width on IBTR adjusted for individual covariates and follow-up

Covariate	No. of studies	Threshold distance negative margin: adjusted OR (mm)			*P* (association)
		1	2	5	
Age	18	1.0	0.53	0.77	0.53
Endocrine therapy	16	1.0	0.95	0.90	0.95
Radiation boost	18	1.0	0.86	0.92	0.86

OR odds ratio. *IBTR* ipsilateral breast tumor recurrence. *CI* confidence interval

Teşekkürler