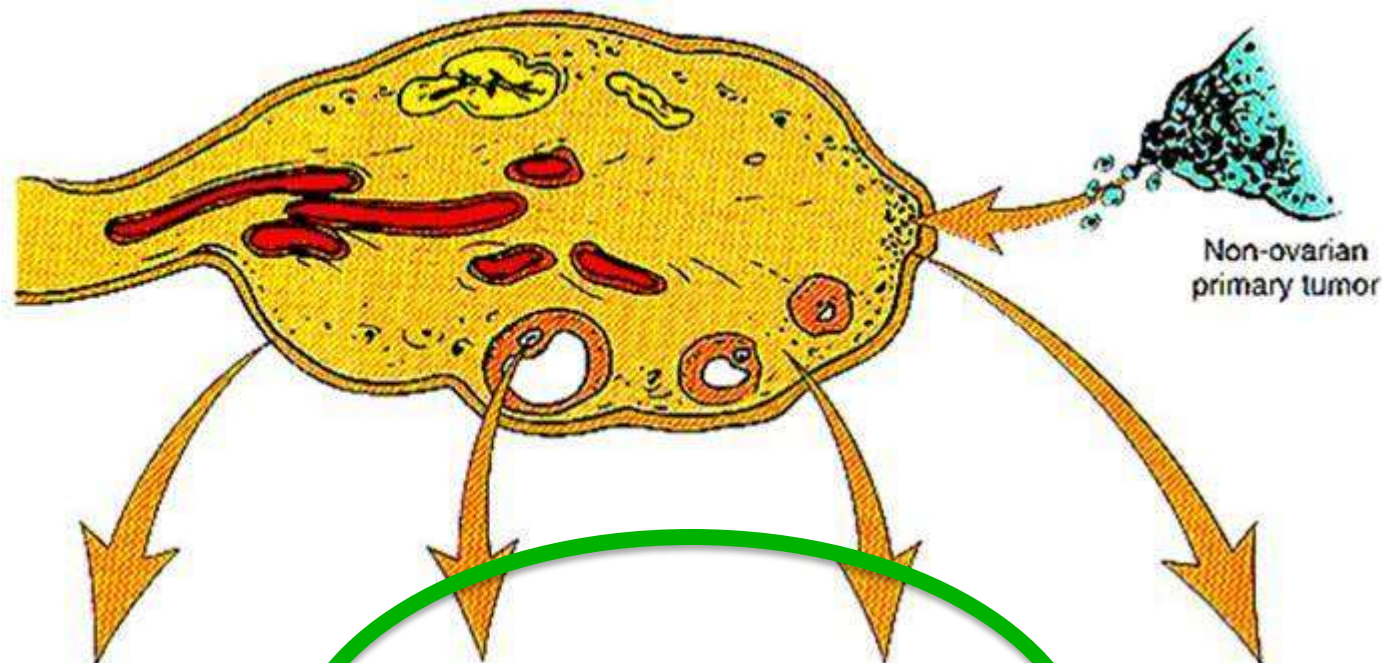




Türk Jinekoloji ve
Obstetrik Derneği
İZMİR ŞUBESİ

İntraoperatif Saptanan Epitelyal Olmayan Over Tümörlerinde Yönetim

Prof. Dr. Tefvik GÜVENAL
Celal Bayar Üniversitesi
Manisa



ORIGIN	SURFACE EPITHELIAL CELLS (Surface epithelial-stromal cell tumors)	GERM CELL	SEX CORD-STROMA	METASTASIS TO OVARIES
Overall frequency	65%-70%	15%-20%	5%-10%	5%
Proportion of malignant ovarian tumors	90%	%5	%3-5	5%
Age group affected	20+ years	0-25+ years	All ages	Variable
Types	<ul style="list-style-type: none"> • Serous tumor • Mucinous tumor • Endometrioid tumor • Clear cell tumor • Brenner tumor • Cystadenofibroma 	<ul style="list-style-type: none"> • Teratoma • Dysgerminoma • Endodermal sinus tumor • Choriocarcinoma 	<ul style="list-style-type: none"> • Fibroma • Granulosa-theca cell tumor • Sertoli-Leydig cell tumor 	

Table 1. Classification of germ cell tumor (GCTs)

Primitive GCTs

Dysgerminoma

Yolk sac tumor

Embryonal carcinoma

Others

Mixed GCTs (specify components)

Biphasic or triphasic teratoma

Immature teratoma

Mature teratoma

Monodermal teratoma and somatic-type tumors associated with teratoma

Table 3. Classification of sex cord-stromal tumors (SCSTs) and steroid cell tumors

Ovarian stromal tumors with sex cord elements

Adult granulosa cell tumor

Juvenile granulosa cell tumor

Sertoli-Leydig cell tumors

Gynandroblastoma

Sex cord tumor with annular tubules

Others

Pure stromal tumors

Fibroma and thecoma, typical, cellular and mitotically active

Malignant tumors (fibrosarcoma)

Other ovarian stromal tumors

Ovarian stromal tumor with minor sex cord elements

Sclerosing stromal tumor

Signet-ring stromal tumor

Microcystic stromal tumor

Ovarian myxoma

Stromal-Leydig cell tumor

Steroid cell tumors

Stromal luteoma, Leydig cell tumor

Steroid cell tumor, not otherwise specified

İnsidans

- Germ hücreli tümörler 3.7/100.000
 - Çoğunlukla gençlerde
 - Adölesan öncesi malign over tm. %80'i
- Sex Cord Stromal tümörler 2.1/100.000
 - Çoğunlukla yetişkinlerde

Non-epitelyal tümörler

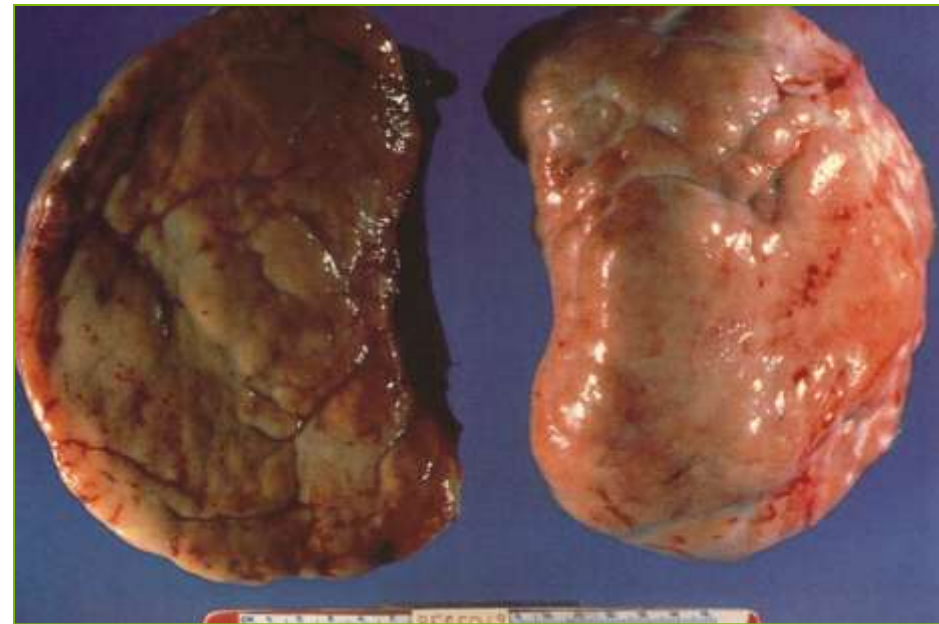
- Daha genç kadınlarda görülür
- Daha erken evrededir
 - %60-70 stage I
- Genellikle bir overe sınırlıdır
- Kemoterapiye daha duyarlıdır
- Kür oranları yüksektir
- Doğal seyri, prezentasyonu ve yönetimi epitelyal over tümörlerinden farklılık gösterir

Önemli noktalar***

- Bu tümörler hızlı büyüyen tümörlerdir ve hızla büyük boyutlara ulaşabilirler
- İlk operasyon bazen acil durumlarda (torsiyon ya da rüptür) yapılabilir ve cerrah her zaman onkoloji konusunda deneyimli değildir
- Bu hastaların çoğu gençtir ve fertilitatesini korumaya çalışmak önemlidir

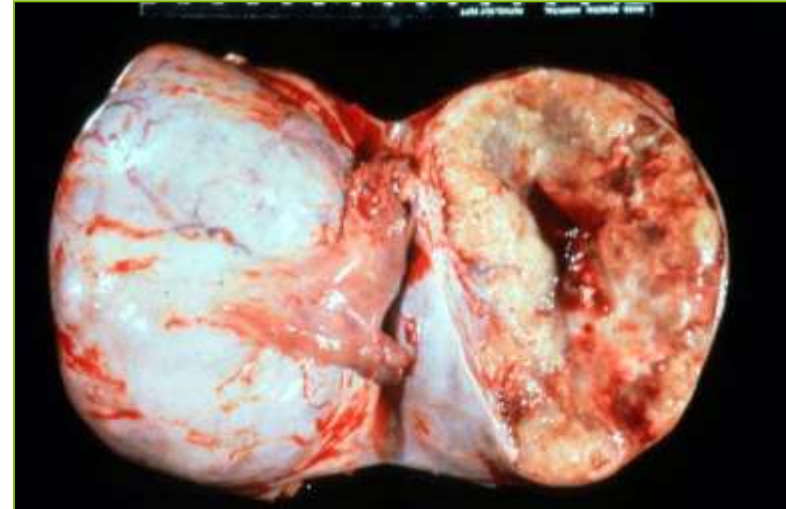
Disgerminomlar

- Pür ya da mikst halde
- Bilateralite oranı %10-20
- Stage Ia %65-75
- Stage Ib %10-15
- Stage II ve III %15
- Stage IV %4



Endodermal Sinüs (Yolk Sak) Tm

- Çok hızlı büyür, agresif bir tümördür
- Ort.yaş 19
- Çoğunlukla unilateral
- Boyutları büyüktür (10-30 cm)
- Serum AFP düzeyleri artar



Matür Kistik Teratom (Dermoid)

- Sık görülür
- Genç yaşlarda sık
- Rüptür, torsiyon ve malign dejenerasyon olabilir
- Torsiyon daha büyük tümörlerde oluşmaktadır (ortalama 11 cm vs 6 cm)
- Malign transformasyon riski, %1-2 ve 40 yaş üstünde artmaktadır (SCC daha sık)

İmmatür teratom

- Tüm over teratomlarının %3
- Çoğu unilateral ve solid
- Tümör grade prognostik (grade 1, 2, ve 3)

Table 12–7. IMMATURE (MALIGNANT) TERATOMAS

GRADE	NO.	TUMOR DEATHS (%)
1	22	4 (18)
2	24	9 (37)
3	10	7 (70)

TABLE 2**Types of malignant tumor associated with ovarian teratoma**

Types of malignant tumor	No. of patients (%)
Immature ovarian teratoma	24 (68.6)
Mucinous adenocarcinoma combined with ipsilateral mature teratoma	1 (2.8)
Mucinous borderline tumor combined with ipsilateral mature teratoma	3 (8.6)
Mucinous borderline tumor with contralateral mature teratoma	2 (5.8)
Serous borderline tumor combined with ipsilateral mature teratoma	1 (2.8)
Granulosa cell tumor arising in teratoma	2 (5.8)
Squamous cell carcinoma arising in teratoma	1 (2.8)
Thyroid papillary cancer arising in teratoma	1 (2.8)
Total	35

Kim. Clinical characteristics of ovarian teratoma. Am J Obstet Gynecol 2011.

580 olgunun 35'inde malignite (%6.1)

**Table 1**

Patient's age and characteristics of OT cases studied

Characteristic	Group 1 (MCT; n = 922)	Group 2 (malignant/ potentially malignant; n = 26)	Group 3 (IT; n = 8)
Age (y), mean \pm SD	38.8 \pm 14.3	48.7 \pm 18.1	23 \pm 8.1
Tumor site, n (%)	956 olgu		
Left	410 (44.5)	12 (46.2)	4 (50)
Right	417 (45.2)	11 (42.3)	2 (25)
Bilateral	62 (6.7)	0	1 (12.5)
Other	0	1 (3.8)	1 (12.5)
Unknown	33 (3.6)	2 (7.7)	0
Tumor size (cm), mean \pm SD	Frozen Section oranı %33.2		
	6.2 \pm 4.1	11.9 \pm 5.5	7.0 \pm 3.5
Tumor size (cm), range	Malignite oranı %2.7		
	0.3-45	1.1-26	4-15

Abbreviation: IT, immature teratoma.

Granüloza hücreli tümör

- Granüloza hücreli tmler yak.%70' ini oluşturur
- **Adult** (%95) (ort.yaş 52)
- **Juvenil** tip (<10 yaş %44)
- Histopatolojik malign tümörlerdir
- Seyri yavaş, prognozları iyidir
- İnhibin spesifik bir markırdır
 - İnhibin B tercih edilmelidir (A' ya göre sen/spe yük)



Granüloza hücreli tm

**Table 12–9. GRANULOSA CELL TUMOR
(76 PATIENTS)**

ENDOMETRIAL HISTOLOGY	NO.	%
Proliferative endometrium	19	25
Atrophic endometrium	5	7
Hyperplastic endometrium	42	55
Adenocarcinoma	10	13

Granüloza hücreli tümörlerde endometrial örnekleme yapılmalıdır

Sertoli Leydig hücreli tm

- Çoğunlukla düşük grade' li tümörlerdir,
- Androjen salgılar (virilizasyon %70-85)
- Prognostik faktörler grade ve stage
 - Grade 1, klinik olarak benign
 - Grade 2, klinik %11 malign
 - Grade 3i klinik %59 malign
- Overall 5 y sağkalım %70' dir
- İleri evrede prognoz kötüdür



Tümör markırları

Histology	AFP	hCG	LDH	CA-125	İnhibin
Dysgerminoma	-	+	+	+	-
Endodermal sinus tumor	+	-	+	+	-
Immature teratoma	+	-	-	+	-
Embryonal CA	+	+	-	-	-
ChorioCA	-	+	-	-	-
Granulosa Cell Tm	-	-	-	+	+

İntraoperatif Tanı

- Şüpheli kitle
 - Frozen Section
- Rastlantısal
 - Sezaryen
 - %30-55 Matür kistik teratom
 - Abdominal ve pelvik operasyonlar



Cochrane
Library

Cochrane Database of Systematic Reviews

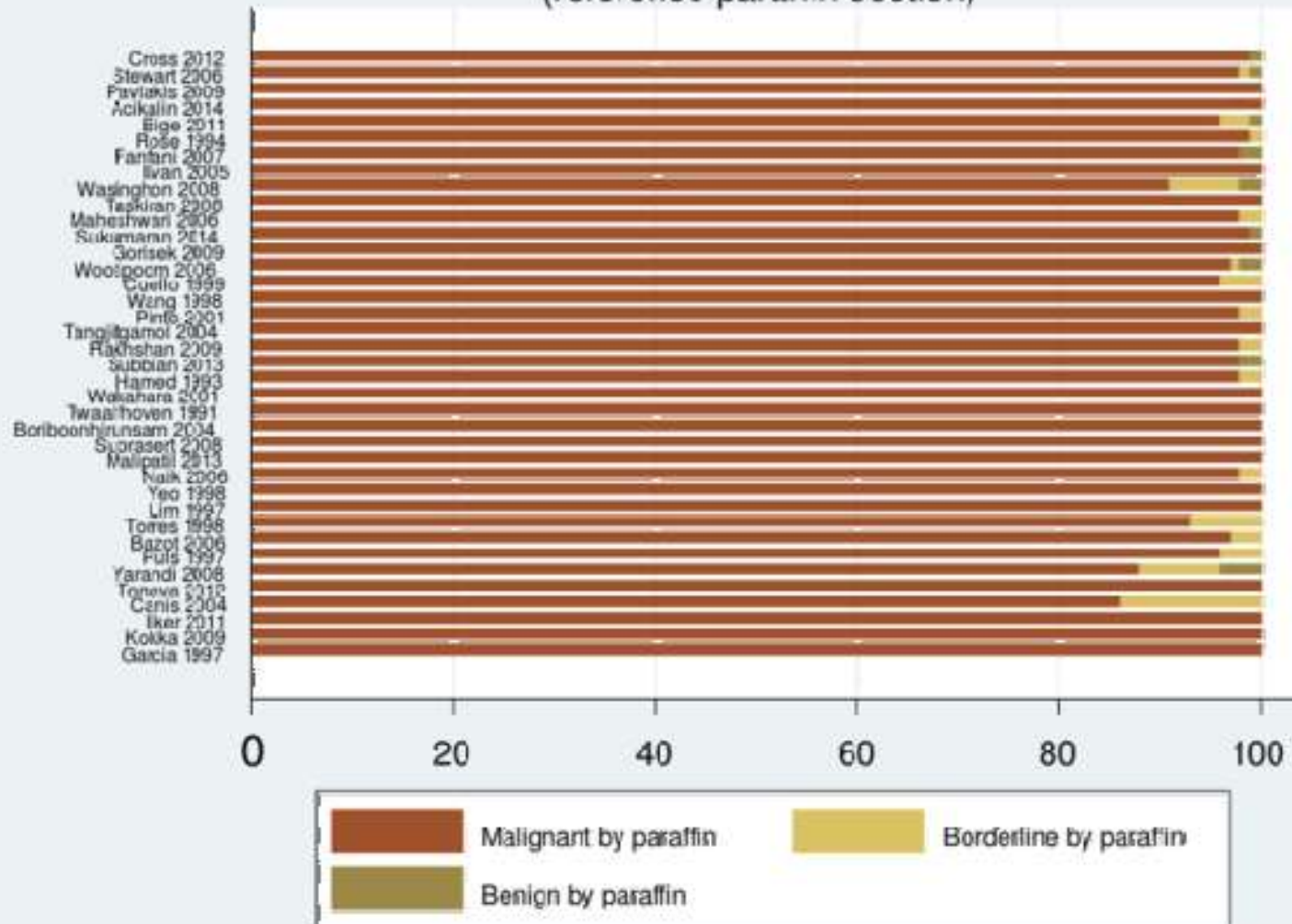
Intraoperative frozen section analysis for the diagnosis of early stage ovarian cancer in suspicious pelvic masses (Review)

Ratnavelu NDG, Brown AP, Mallett S, Scholten RJPM, Patel A, Founta C, Galaal K, Cross P, Naik R

2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Figure 15. Frozen section result malignant: final diagnosis by reference standard

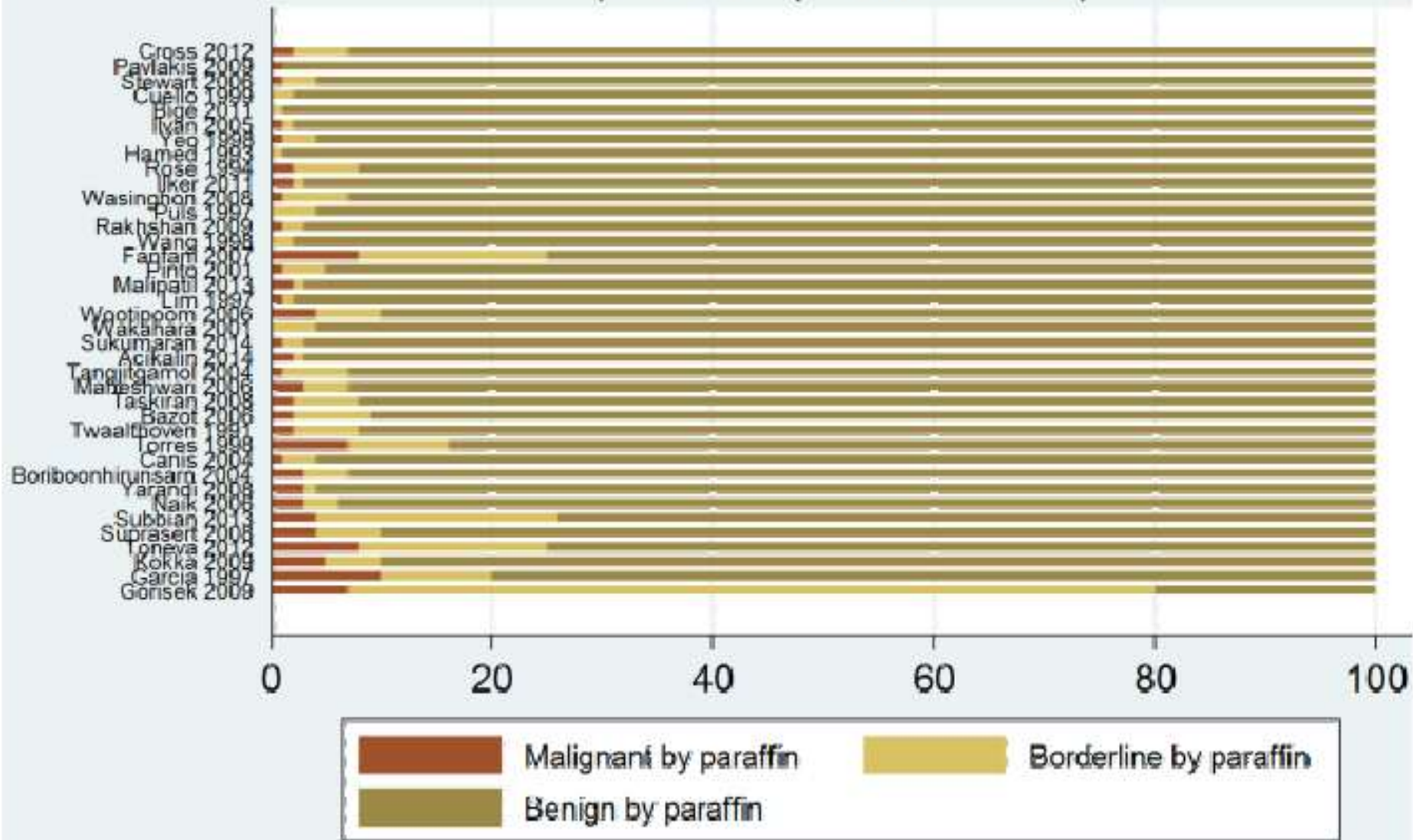
Frozen section malignant: % final diagnosis
(reference paraffin section)



Ordered by number of malignant, with largest at top

Figure 14. Frozen section result benign: final diagnosis by reference standard

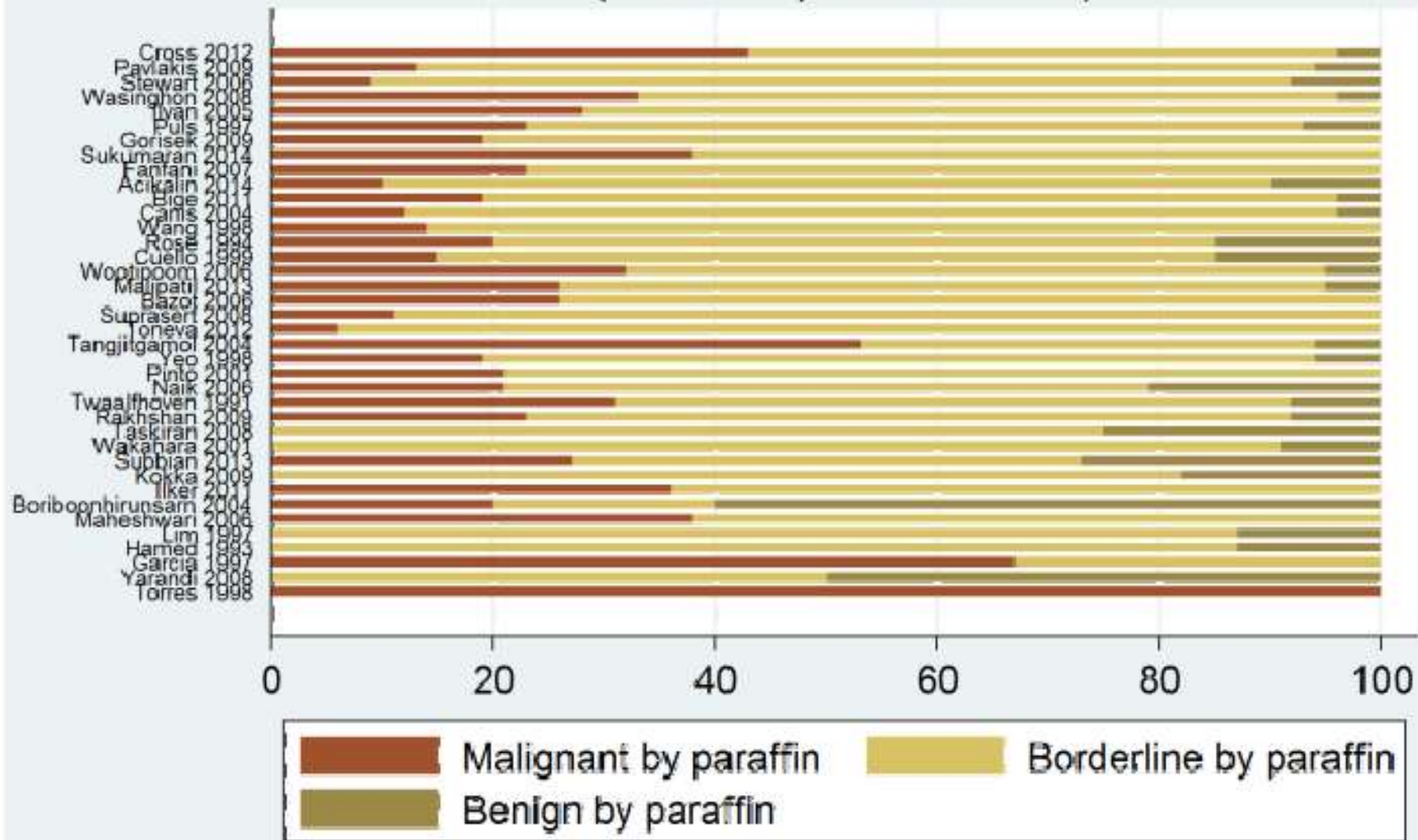
Frozen section benign: % final diagnosis (reference paraffin section)



Ordered by number of benign, with largest at top

Figure 16. Frozen section result borderline: final diagnosis by reference standard

Frozen section borderline: % final diagnosis (reference paraffin section)



Ordered by number of borderline, with largest at top

Table 1 Distribution of ovarian lesions evaluated by frozen section

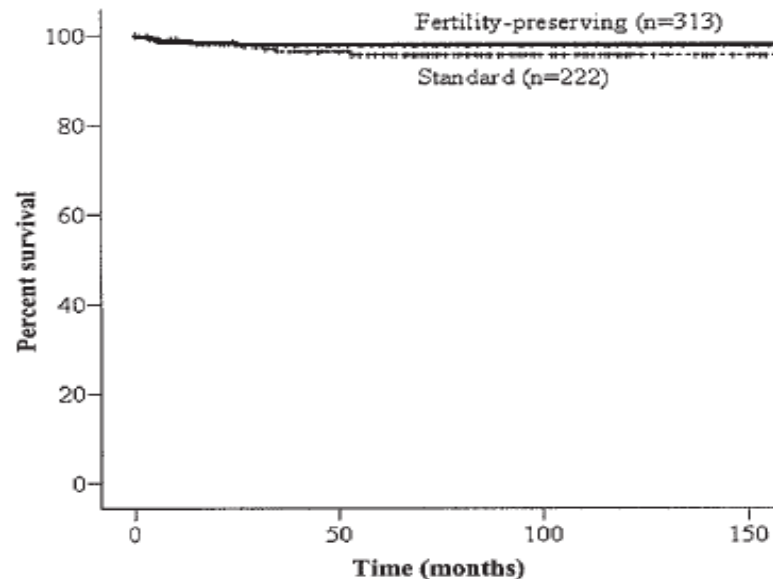
		Benign frequency	Borderline frequency	Malignant frequency
Benign non-neoplastic cysts	Endometriotic cyst	21	0	0
	Paratubal cyst	4	0	0
	Abscess	5	0	0
	Follicular cyst	3	0	0
	Corpus luteal cyst	8	0	0
	Chronic granulomatous inflammation	4	0	0
Surface epithelial tumors	Serous tumors	14	4	11
	Mucinous tumors	19	2	6
	Endometrioid carcinoma	0	0	3
	Clear cell carcinoma	0	0	1
	Brenner tumor	1	0	0
	Transitional cell carcinoma	0	0	1
	Adenocarcinoma, NOS	0	0	3
	Malignant mixed mullerian tumor	0	0	1
Germ cell tumors	Dysgerminoma	0	0	1
	Teratoma	20	0	1
Sex cord stromal tumors	Adult granulosa cell tumor	4	0	0
	Fibroma thecoma	4	0	0

Tedavi

- Cerrahi \pm Adjuvan Kemoterapi
- Cerrahi (ilk tedavi)
 - Tanı ve evreleme
 - Tümörün tam olarak alınması
- **Fertility koruyucu cerrahi (USO, Kistektomi)**
 - Genç kadınlarda
 - İleri evrelerde de düşünülmelidir
- Debulking cerrahi
 - Mümkün olduğunca tümörü çıkartmak
 - Major cerrahi işlemler (Kemoterapide gecikmeye neden)

The Influence of Conservative Surgical Practices for Malignant Ovarian Germ Cell Tumors

JOHN K. CHAN, MD,^{1*} KRISHNANSU S. TEWARI, MD,² SARAH WALLER, MD,³ MICHAEL K. CHEUNG, BA,¹
JACOB Y. SHIN, BA,¹ KATHRYN OSANN, PhD,⁴ AND DANIEL S. KAPP, MD, PhD⁵



Numbers at risk				
FPS ^a	313	181	81	14
Standard ^b	222	133	51	12

^a fertility-preserving surgery
^b hysterectomy and debulking

Fig. 4. Kaplan-Meier disease-specific survival by surgical treatment ($P = 0.26$).

Ooferektomi vs. Kistektomi

- Genellikle konservatif cerrahi USO'dur
- Kistektomi uygun olabilir, ancak standart yaklaşım henüz değildir.
- Kistektomi sonrası
 - Yakın gözlem
 - Tekrar cerrahi (Ooferektomi ile cerrahi evreleme)
 - Kemoterapi



Cerrahi Evreleme

- Vertikal midline insizyon
- Batın sitolojisi
- Abdomen ve pelvik kavitenin dikkatli explorasyonu
- Karşı overin değerlendirilmesi
- Random biyopsiler
 - Omentum, parakolik, pelvik yan duvar, cul-de-sac, vezikouterin periton ve diyafram
- Pelvik ve para-aortik lenf nodu sampling/diseksiyon ?

The prevalence and prognostic impact of lymph node metastasis in malignant germ cell tumors of the ovary

Sanjeev Kumar^{a,d,*}, Jay P. Shah^{a,d}, Christopher S. Bryant^{a,d}, Anthony N. Imudia^{a,d},
Michele L. Cote^{a,c,d}, Rouba Ali-fehmi^{b,d}, John M. Malone Jr.^{a,d}, Robert T. Morris^{a,d}

SEER data, 1988-2004; 1296 olgu
613 LND +
683 LND -

Tip	LN +
Disgerminoma (n=147)	%28
Malign teratoma (n=356)	%6
Mikst GH ve non-disgerminoma (n=180)	%16

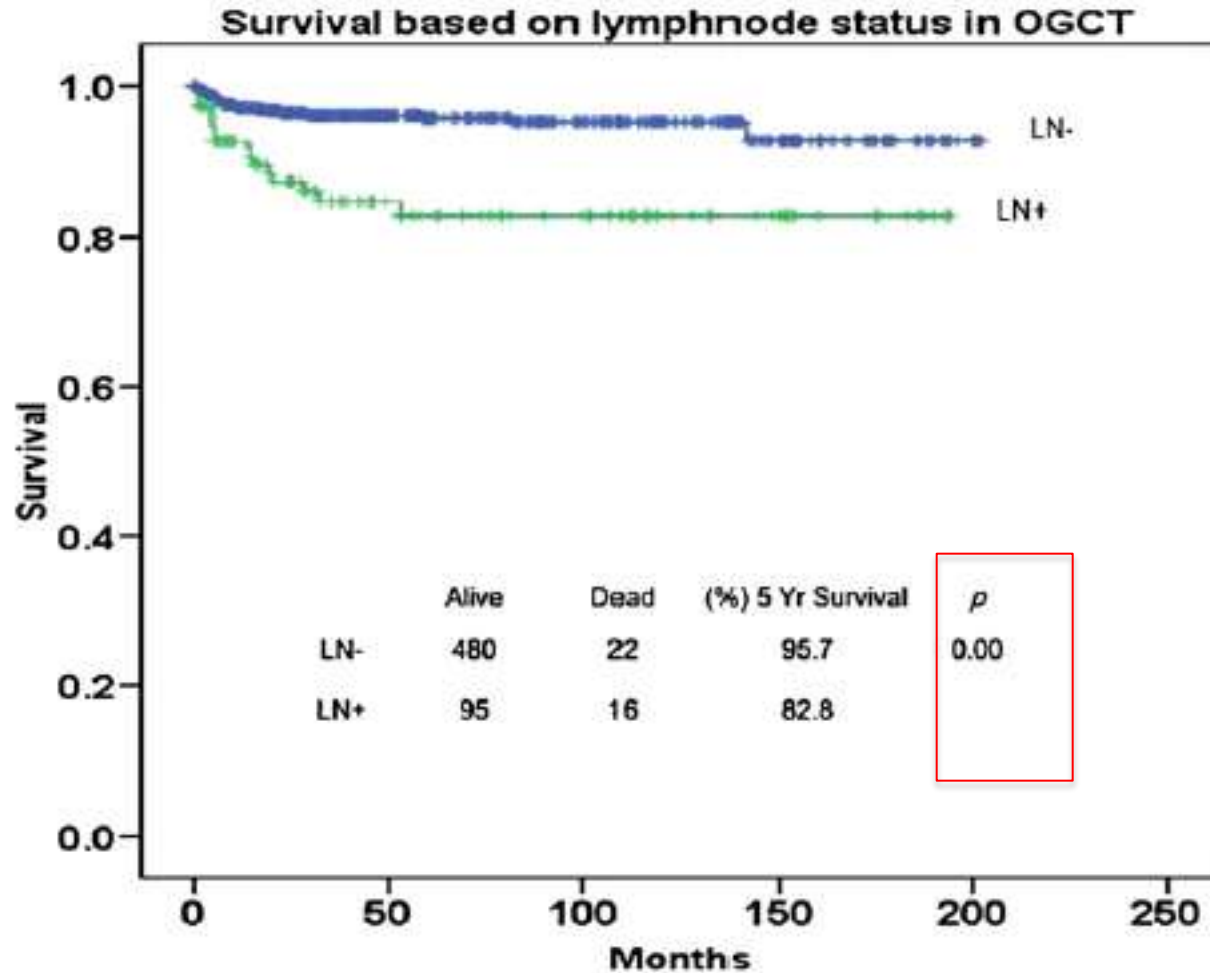


Fig. 1. Survival difference between patients with (LN+) and without (LN-) Lymph node involvement in germ cell tumors of the ovary (OGCT). *p*-represents log rank analysis. *X*-axis time in months, *Y*-axis (%) survival.

Germ hücreli tm LN metastazi

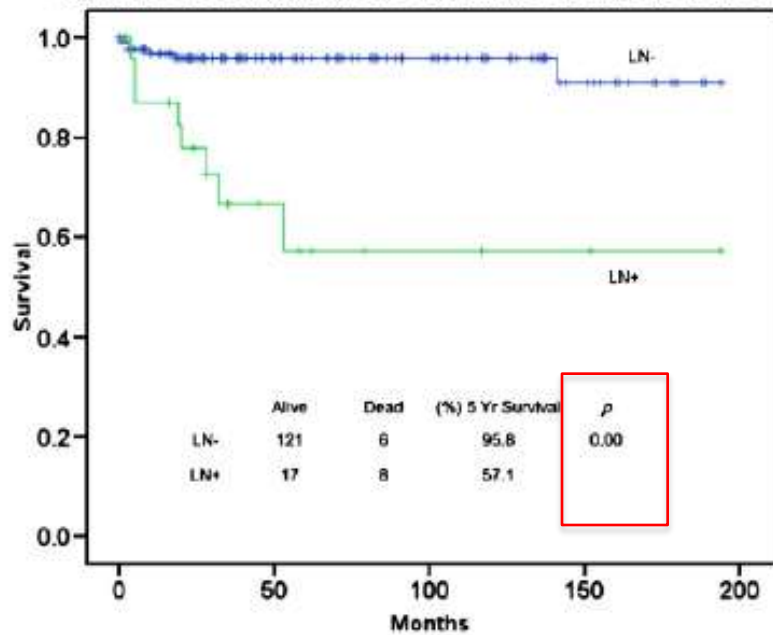
Lenf nodu sayısı	LN metastaz oranı
1-10 (n=327)	%16.8
11-20 (n=126)	%17.5
21-97 (n=86)	%23

Survival: lymph node metastasis and stage in malignant germ cell tumors of the ovary

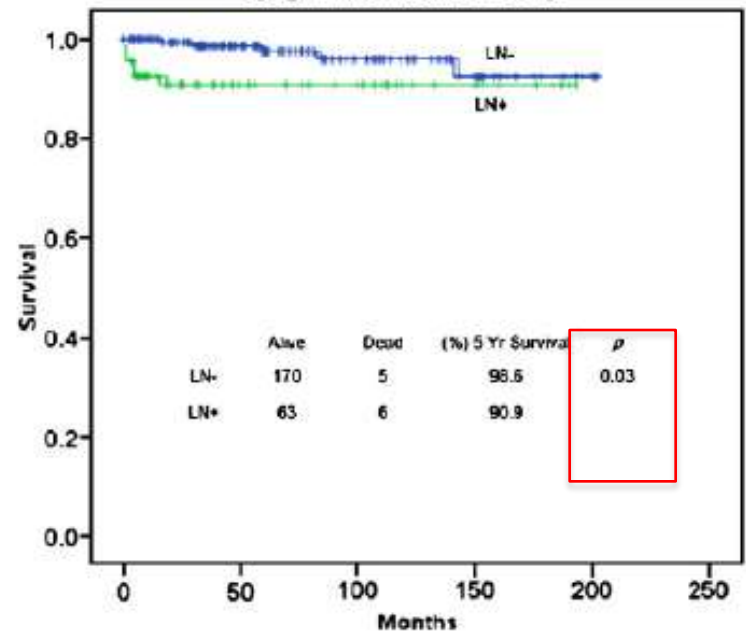
Variable		Hazard ratio	95% CI	<i>p</i> value
Lymph node metastasis	Yes	2.87	1.439–5.725	0.003
	No	1.0	–	
Stage	Advanced stage (FIGO III and IV)	2.41	1.213–4.789	0.012
	Early stage (FIGO I and II)	1.0	–	

Multivariate analysis using Cox proportional hazards model in a forward stepwise (conditional LR) method revealed lymphnode involvement and FIGO stage as the only independent predictors of survival in germ cell tumors of the ovary. Reference group for the respective variables have a hazards ratio of 1 U. All other variables in the model (age, race, histology, grade) were eliminated due to $p > 0.05$.

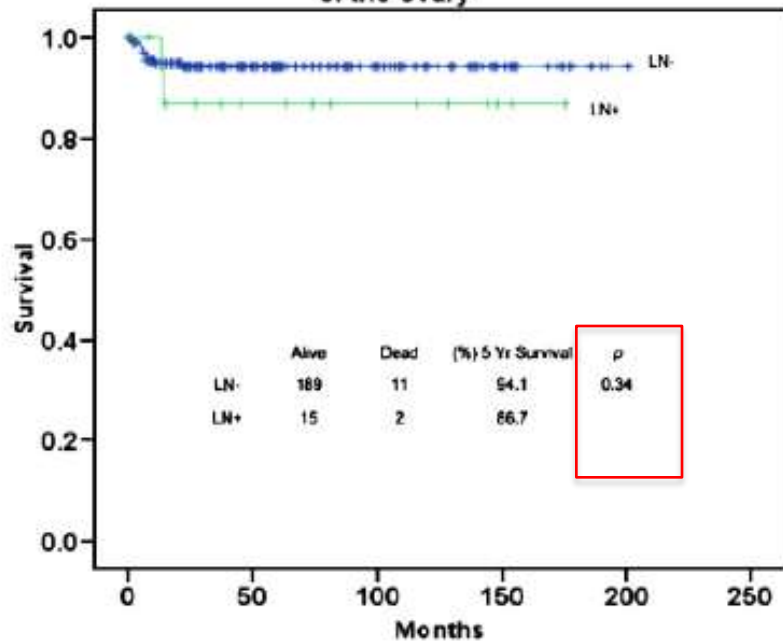
A Survival based on lymphnode status in MGCT/PNDCT of the ovary



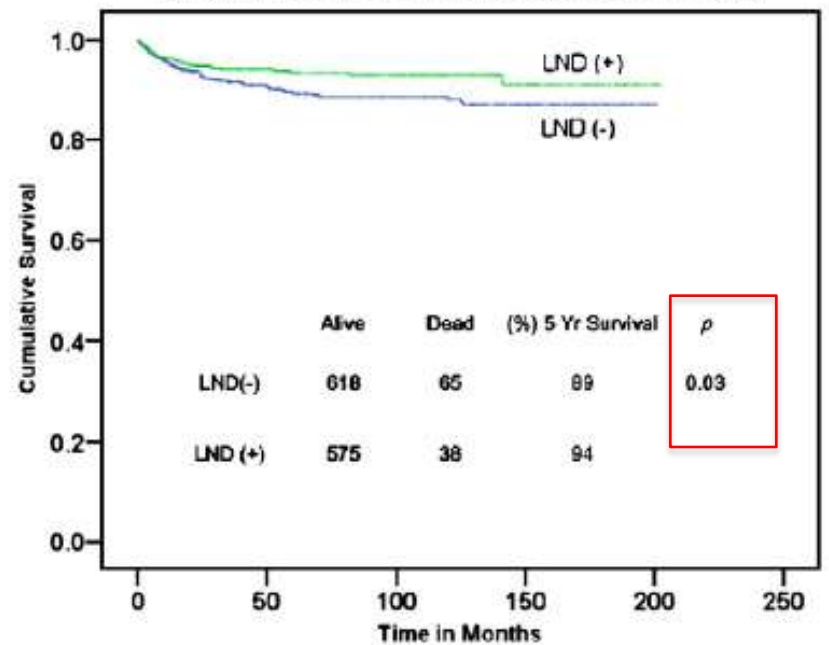
B Survival based on lymphnode status in malignant dysgerminoma of the ovary



C Survival based on lymphnode status in malignant teratoma of the ovary



D Survival curves for OGCT with (+) and without (-) lymphadnectomy in SEER 1988-2004 cohort ($p=0.03$)



Prognostic impact of lymphadenectomy in clinically early stage malignant germ cell tumour of the ovary

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SEER data, 1988-2006; 1083 stage I olgu
590 LND -
493 LND + (%10.5 upstage)

Survival in clinical stage I ovarian malignant germ cell tumour

Survival in clinical stage I ovarian dysgerminoma

Table 2 5-Year survivals in clinical stage I OGCT patients by stage and histology

Variable	N	LND-I (%)	LND+I (%)	LND+3C (%)	P-value
Overall	1083	96.9	97.7	93.4	0.5

Clinical stage

Lenfadenektomi overe sınırlı germ hücreli tümörlerde bağımsız prediktör değildir

Histology

Dysgerminoma	354	97.9	97.5	97.5	0.99
MT	516	98.3	98.6	83.3	0.10
MGCT/PNDCT	213	92.4	96.3	75	0.38
MT+MGCT/PNDCT	729	96.6	97.8	79.5	0.053

Abbreviations: MGCT/PNDCT = mixed germ cell tumour with pure nondysgerminoma cell tumour; MT = malignant teratoma; OGCT = ovarian germ cell tumour.

Months

Months

lymphadenectomy
ve nodes
ive nodes

lymphadenectomy
tive nodes

250

FIGO stage III with positive nodes

FIGO stage III with positive nodes

Endodermal sinus tumor of the ovary: The Hacettepe University experience

Ali Ayhan*, Cagatay Taskiran, Gurkan Bozdog,
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Received 21 November 2004; accepted 18 April 2005

Table 2

Comparison of 5-year overall survival (OS) rates by prognostic variables and treatment regimens

Variables	5-year OS rate (%)	P
Age (<20 vs. ≥20)	(41 vs. 57)	0.37
Histology (pure vs. mixed)	(50 vs. 43)	0.87
Stage (I vs. II–IV)	(81 vs. 8)	<0.001
Size, cm (<10 vs. 10–19 vs. ≥20)	(50 vs. 51 vs. 38)	0.55
Type of surgery (conservative vs. complementary)	(67 vs. 27)	0.03
Lymphadenectomy (performed vs. not performed)	(62 vs. 43)	0.41
Adjuvant therapy (platin based vs. others)	(78 vs. 0)	<0.001



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Review

Lymph-node metastasis in stage I and II sex cord stromal and malignant germ cell tumours of the ovary: A systematic review



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Klinik evre I-II Sex Cord Stromal Tümörlerde LN metastazı yok

Evre I-II Germ hücreli tümörlerde LN metastazı yak. %11
(En yüksek disgerminomda %18)

Table 1
Incidence of positive lymph nodes in FIGO stage I-II sex cord stromal cell tumours.

Reference	Patients	FIGO stage I + II	FIGO stage I + II with removed lymph nodes	Number of removed lymph nodes per patient				Patients with positive lymph nodes
	n			n	n	Locations	Mean	Median
Abu-Rustum et al. [5]	68	60	NS	Pelvic Para-aortic	11.6 6	10 4	0-36 0-19	0
Ayhan et al. [6]	60	38	12	-	-	-	-	0
Brown et al. [4]	257	86	49	Pelvic and/or para-aortic	-	9	3-28	0
Park et al. [7]	106 ^a	93	25	Pelvic and/or para-aortic	28.8	29	5-53	0
Thrall et al. [8]	87	56	NS	Pelvic and para-aortic	-	14	3-80	0
Total	578	333	-	-	-	-	-	0

Abbreviations: FIGO: International Federation of Gynaecology and Obstetrics, NS: not specified.

^a Only adult granulosa cell tumours.

Table 2
Incidence of positive lymph nodes in FIGO stage I-II malignant germ cell tumours.

Reference	Patients	FIGO stage I + II	FIGO stage I + II with removed lymph nodes	Number of removed lymph nodes per patient				Patients with positive lymph nodes
	n			n	n	Locations	Mean	Median
Kumar et al. [9]	1296	NS	432	-	12 ^a 14 ^b	-	1-96 ^a 1-96 ^b	51 (11.8)
Mahdi et al. [3]	1083	1083	493	-	11 ^a 2 ^b	8 ^a 1 ^b	1-47 ^a 1-15 ^b	52 (10.5)
Rogers et al. [10]	57	57	21	Pelvic/para-aortic; Perirenal chains	-	-	-	0
Total	2436	-	946	-	-	-	-	103 (10.9%)

Abbreviations: FIGO: International Federation of Gynaecology and Obstetrics, NS: not specified.

^a Cohort of patients with negative nodes.

^b Cohort of patients with positive nodes.

Evrelemede LN (Özet)

- Lenfadenektomide konsensus yoktur
- Bulky ya da şüpheli lenf nodları çıkarılmalıdır
- Klinik erken evre germ hücreli tümörlerde yapılmalıdır
 - Stage Ia disgerminom,
 - Stage Ia, grade 1 immatür teratom

Karşı Over

- Normal görünen bir over varsa biyopsi, wedge rezeksiyon yapılmamalıdır
- Fertilité isteyen ancak bilateral tutulumu olan ve postoperatif kemoterapiye aday olan hastalarda yaklaşım güçtür
 - Over korunursa kemoterapi etki etmeyebilir, relaps riski fazladır
 - Over dokusu veya oosit dondurma seçenekleri düşünülebilir
- Disgenetik gonad varsa BSO
- Yoğun metastatik hastalıkta bile karşı over normale fertilité koruyucu cerrahi düşünülebilir

Yetersiz evreleme varsa...

- Histopatolojik bulgular gözden geçirilir
- İlk operasyon kayıtları değerlendirilir
- Postoperatif abdomen CT yapılmalıdır
- Kemoterapi alacaksa yeniden evrelendirme cerrahisine gerek yoktur
- Kemoterapi gerekmiyeyekse ve sadece izlem yeterli ise yeniden evrelendirme yapılmalıdır.

Germ Hücreli Tümörlerin Yönetimi

Management of Germ Cell Tumors of the ovary

Stage	Surgery (fertility-sparing surgery when indicated)	Chemotherapy	Surveillance policy
Dysgerminoma			
Stage IA	X	-	X
Stage IB-IC	X	X	(X)
Stage IIA-IV	X	X	
Immature teratoma			
Stage IA G1	X	-	X
Stage IA G2-G3	X	X	(X)*
Stage IB-IC	X	X	(X)
Stage IIA-IV	X	X	
Yolk sac tumor			
Stage IA-IB	X	X	X
other stages	X	X	

X=suggested

(X) = suggested by some authors

- = no therapy

* Properly surgical staged

Seks Kord-Stromal Tm Yönetimi

Management of Sex Cord Stromal Tumor of the ovary

Stage	Surgery	Chemotherapy	Surveillance policy
Granulosa cell tumor			
Stage IA-IC	X	-	X
Stage IIA-IV	X	X	
Sertoli-Leydig cell tumors			
Stage IA	X	-	X
All Stages with poorly differentiated or heterologous elements	X	X	

X = suggested

- = no therapy

Kemoterapi

Table 12-4. VAC, VBP, AND BEP REGIMENS

REGIMEN	DOSAGE SCHEDULE
VAC	
Vincristine, 1.5 mg/m ² (maximum dose 2.5 mg)	Weekly IV administration for 12 weeks
Dactinomycin, 0.5 mg Cyclophosphamide, 5–7 mg/kg	5-day IV course every 4 weeks
VBP	
Vinblastine, 12 mg/m ²	IV every 3 weeks for 4 courses
Bleomycin, 20 U/m ² (maximum dose 30 U/m ²)	IV weekly for 7 courses; eighth course given in week 10
Cisplatin, 20 mg/m ²	Daily × 5 every 3 weeks for 3–4 courses
BEP	
Bleomycin, 20 U/m ² (maximum dose 30 U)	IV weekly × 9
Etoposide, 100 mg/m ²	IV days 1–5 q 3 weeks × 3
Cisplatin, 20 mg/m ²	IV days 1–5 q 3 weeks × 3

BEP, bleomycin, etoposide, cisplatin; VAC, vincristine, actinomycin D (dactinomycin), cyclophosphamide; VBP, vinblastine, bleomycin, cisplatin.

3-4 kür

Carboplatin+Etoposid

izlem

- Relapsların %90' ı ilk 2 yıl içinde
- İlk 2 yıl 3 ayda, sonra 6 ayda bir muayene
- Gerekirse görüntüleme (USG, CT, MR, PET)
- Uzun süre izlem gerekir (genellikle 5 yıl)
 - Disgerminoma için 10 yıl
- En sık rekürrens yeri
 - Üst batın (%55-70)
 - Pelvis (%30-45), retroperitoneal lenf nodları

Fertilite ve teratojenite

- Fertilite korunan olgularda tedavi sonrası normal menstrüel fonksiyonler geri döner
- Gebelik sağlanabilir
- Tedavi erken gebelik kaybı ya da malformasyona yol açtığıın gösteren kanıt yoktur.

Sonuç

- Non-epitelyal over tümörleri adölesan ve genç yetişkinlerde daha sıktır
- Sağkalım oranları yüksektir
- Kemoterapötik ajanlara duyarlıdır (özellikle cisplatin temelli)
- Cerrahi evreleme, özellikle klinik erken evre germ hücreli tümörlerde yapılmalıdır

Sonuç

- Evrelemede komplet lenfadenektomi tartışmalıdır, bulky lenf nodları çıkarılmalıdır
- Erken evrede fertilitite koruyucu cerrahi etkin ve güvenlidir
- Optimal sitoredüksiyon kararı kişisel olmalı
- Geç dönemde rekürrensler ortaya çıkabilir, yakın izlem zorunludur (en az 5 yıl)



2017

Sağlık
Mutluluk
Barış