NEOADJUVAN TEDAVİ SONRASI MEMEYE VE AKSİLLAYA CERRAHİ YAKLAŞIM

Dr.CEMALETTİN TOPUZLU BAŞKENT TIP FAKÜLTESİ GENEL CERRAHİ ANABİLİM DALI

Ankara Meme Hastalıkları Derneği 7 Nisan 2018











HALSTED'İN PERMEASYON PARADİGMASI 'HİPOTEZİ'



Meme kanseri lokal bir hastalıktır. Önce bölgesel lenfatiklere Bundan sonra kan yoluyla yayılır.

ÇÖZÜM : RADİKAL MASTEKTOMİ

İlk ameliyat1882İlk seri (50 hasta)1894



POST AXILLARY DISSECTION LYMPHEDEMA



Her şey yoruma açıktır, ancak belirli bir tarih diliminde hangi yorumun öne çıkacağı, gerçeğin ne olduğundan çok o tarihte geçerli güce tabidir

FRIEDRICH NIETZSCHE

"SİSTEMİK HASTALIK" PARADİGMASI (HİPOTEZ) 1967

BERNARD FISHER

Meme hastalığı sistemik bir hastalıktır, bu nedenle çeşitli etkin yerel ve bölgesel tedavi yöntemlerden hiçbirinin sağkalımı etkilemesi beklenmemelidir!

NSABP B-04 ÇALIŞMASI (1971)



Aksillası klinik negatif 1765 hastayı kapsayan randomize ve prospektif NSABP B-04 çalışmasının 25 yıl sonraki sonuçları:

RM, TM-RT ve sadece TM yapılan hastalarda tüm sağkalım açısından hiçbir fark yoktur.

Sadece TM yapılan hastalarda çok az sayıda gelişen aksilladaki nüksler , ALND ile etkin şekilde kontrol edilmiştir.

NASBP B6 TRIAL (20 years)



DÜNYADA İKİ FARKLI **INSAN VARDIR: BILMEK İSTEYENLER** VE **INANMAK ISTEYENLER**

F.W.NİETZSCHE (1844-1900)

Lokal nüks ve yaş ilişkisi



al relapse by about 50%. In all, I defend the position with clinically node negative breast cancer (possibly negative ultrasound of the axillary nodes) and an mastectomy, SN should be performed and full ation of the sentinel node (s) and primary cancer ed. Based on this information, the policy regarding strment should be discussed and decided: no further in SNB ITC and micrometastes only), radiotherapy vall (in larger tumors and macrometastases) or ALND 3 involvement; in our experience very rare). Those shes immediate breast reconstruction, our team will the patients about the extra risks of side effects and strome, in case post mastectomy radiotherapy is doning intra-operative assessment of the SN, many pared a full ALND.

ents where intra-operative assessment of the SN can ose with proven lymph node metastases at primary ho have been treated with up front chemotherapy. Natients with triple negative and HER2 positive plete remission of the SN's can be achieved in patients, ALND is still considered standard of care. N (and or clipped node) after up front chemotherapy ode) is free of disease [5,6], one could refrain from on the radiotherapy, since this in general indicated

en the results from randomised trials, the guidelines an Society of Clinical Oncology, and the alternative e for patients with diseased nodes, it seems patients to have intraoperative axillary lymph node mperative that decisions about how to treat axillary re made with knowledge of tumour biology, the in the sentinel nodes, and any planned radiotherapy rapy. Most importantly, patients need to participate andoned long ago because it denied patients the ontribute to their treatment planning. It is now time ith intraoperative sentinel lymph node assessment.

Sentinel lymph node biopsy for patients with reast cancer: American Society of Clinical Oncology tice Guideline Update. J Clin Oncol. 2016 Dec 12: 47. [Epub ahead of print]

erghese ET, Nair A, Pathak S, Kim B, White J, et al. eview and meta-analysis of cytokeratin 19-based

SA 7.2

Age and molecular subtype: Impact on surgical decisions

T. King*. Dana Farber/Brigham and Women's Cancer Center, Boston, USA

The relationship between age and breast cancer subtype is complex. Both impact risk of LRR and survival; however, the increased risk imparted by young age appears to differ among breast cancer subtypes, and as more is learned about the heterogeneity of breast cancer, the absolute risk from young age alone will likely continue to lessen. At the other end of the age spectrum, there is a growing body of evidence demonstrating a favorable interaction between older age and molecular subtype such that many older women with estrogen receptor positive breast cancer may be spared axillary staging and/or adjuvant radiation therapy without a detrimental impact on survival.

It is clear that young breast cancer patients experience higher rates of local recurrence and contralateral breast cancer (CBC). They also frequently present with more aggressive clinic-pathologic features, including hormone receptor negative and HER2/neu overexpressing disease, and are more likely to be categorized in the high-risk group by molecular subtyping when compared to their older counterparts. However, the increased risk of local recurrence attributed to age alone has decreased in more recent years and is likely attributable to improved local therapy strategies, improvements in adjuvant therapies and the implementation of subtypespecific targeted therapies.

Although earlier studies comparing rates of local recurrence following breast-conserving therapy (BCT) versus mastectomy in young women reported conflicting results, more recent data demonstrate dramatic improvements in local control among young women over time, and no difference in local recurrence or survival between BCT and mastectomy. Similarly, rates of CBC remain low, less than 1% per year, for almost all age groups and are also influenced by treatment of the primary tumor. Thus, while the use of contralateral prophylactic mastectomy has dramatically increased there is no evidence that CPM improves survival in women of any age. Additionally, an increased risk of LRR in triple-negative cancers is apparent; yet this increased risk of LRR is present following surgical treatment with both BCT and mastectomy and does not significantly differ by age.

Thus for both age and subtype, it appears that the intrinsic biology is the strongest predictor of outcome. In young women, appropriate use of standard local therapy strategies remains important; yet bigger surgery is not better, and in the context of multi-disciplinary care, deescalation of local therapy can be safely considered in appropriately selected older women.

Disclosure of interest: No significant relationships.

NAK ve MKC DEN SONRA NÜKS

LUMİNAL A%5.2LUMİNAL B%7.88LUMİNAL B HER2(+)%6.61NONLUMİNAL HER2 (+)%13.10ÜÇLÜ (-)%16.76

Shim et al.

Alt tiplere göre nüks



Arvold et al, J Clin Oncol, 2011

pCR SAĞLANAN HASTALARDA LUMİNAL A 'YA GÖRE DİĞER TİPLERDE LOKOREJYONAL NÜKS HR ORANI (CI %95)

ÜÇLÜ (-) HER2 (+) Trans (-) HER2 (+) Trans (+)

HR 6.44 (2.83-14.0) HR 6.26 (2.81-13.93) HR 3.37 (1.10-10.34)

MOLEKÜLE	R SUBTIPLE	RE GÖRE NAC ve			
MKC' DEN SONA LRR SİZ VE IBTR SİZ					
5 YILLIK SAĞKALIM					
	LRR siz (%)	IBR'siz (%)			
Luminal A	96.6	97.8			
Luminal B1	93.9	93.9			
Luminal HER2+	90.8	92.8			
HER2 (Tx.+)	92.9	92.9			
HER2 (Tx)	78.3	89.1			
Üçlü (-)	79.6	84.6			
pCR (+) hastal	arda LRR ve IB	TR daha iyi			

Jwa E et al .Res Treat. 2016;48(4):1363-1372

Campbell J et al 2017 Aug;165(1):181-191. doi: 10.1007/s10549-017-4303-8. Epub 2017 Jun 2. Comparison of residual cancer burden, American Joint Committee on Cancer staging and pathologic complete response in breast cancer after neoadjuvant chemotherapy: results from the I-SPY 1 TRIAL (CALGB 150007/150012; ACRIN 6657).

Several pathologic staging systems characterize residual tumor in patients

undergoing neoadjuvant chemotherapy for breast cancer. Pathologic complete response (pCR) is now accepted by the Food and Drug Administration as an endpoint for granting accelerated drug approval. Two other systems of post-neoadjuvant pathologic tumor staging-residual cancer burden (RCB) and the American Joint Committee on Cancer post-neoadjuvant therapy staging system (yAJCC)-have been developed to characterize residual tumors when patients do not achieve pCR. The optimal system and the ways in which these systems complement each other have not been fully determined. **METHODS:**

Using data from the I-SPY 1 TRIAL, we compared pCR, RCB, and yAJCC as predictors of early recurrencefree survival (RFS) to identify ways to improve post-neoadjuvant pathologic evaluation. **RESULTS:**

Among 162 patients assessed, pCR identified patients at lowest risk of recurrence, while RCB and yAJCC identified patients at highest risk. Hormone-receptor (HR) and HER2 subtypes further improved risk prediction. Recursive partitioning indicated that triple-negative or HER2+ patients with yAJCC III or RCB 3 have the highest recurrence risk, with an RFS of 27%. Our analysis also highlighted discrepancies between RCB and yAJCC stratification: 31% of patients had discrepant RCB and yAJCC scores. We identified differential treatment of lymph node involvement and tumor cellularity as drivers of these discrepancies. **CONCLUSIONS:**

These data indicate that there is benefit to reporting both RCB and yAJCC for patients in order to identify those at highest risk of relapse.





enefit ?

15 / 35

Quantification of the residual disease as continuous variak post-treatment staging

Bresidual Cancer Burden Calculator

(1) Primary Tumor Bed

Primary Tumor Bed Area: Overall Cancer Cellularity (as percentage of area): Percentage of Cancer That Is *in situ* Disease:

(2) Lymph Nodes

Number of Positive Lymph Nodes:

Diameter of Largest Metastasis:

Residual Cancer Burden: Residual Cancer Burden Class:

	8	(mm) X 6	(mm)
'area):	20	(%)	
ie:	1	(%)	
	0	-	
	0	(mm)	
Reset	Calo	culate	
	1.47	7	
	RCB	-II	

Comparison of breast-conserving surgery with mastectomy in locally advanced breast cancer after good response to neoadjuvant chemotherapy: A PRISMA-compliant systematic review and meta-analysis.

Sun Y et al Baltimore Medicine 2017 Oct;96(43):e8367. doi:

10.1097/MD.00000000008367.

.METHODS:

We searched the electronic databases of Medline (Pubmed) and Cochrane Library for reports on local recurrence (LR), regional recurrence (RR), distant recurrence (DR), 5-year disease-free survival (DFS) or 5-year overall survival (OS) in patients with LABC receiving BCS or mastectomy (MT) and with good response to NACT. Based on the research results, we conducted a meta-analysis using Review Manager 5.3.

RESULTS:

Our study showed that 16 studies with a combined total of **3531 patients**, of whom 1465 patients underwent BCS, whereas 2066 patients underwent MT. There was no significant heterogeneity among these studies (Q statistic: P = .88; I = 0%). Patients with good response to NACT showed no significant difference in LR and RR [odd ratio (OR) = 0.83; 95% confidence interval (CI): 0.60-1.15; P = .26; OR = 0.56; 95% CI: 0.33-0.93; P = .03], while we figured out a lower DR (OR = 0.51; 95% CI: 0.42-0.63; P < .01), a higher DFS (OR = 2.35; 95% CI: 1.84 to 3.01, P < .01) and a higher OS (OR = 2.12; 95% CI: 1.51 to 2.98, P < .01) in BCS compared with MT.

CONCLUSION:

This meta-analysis concluded that BCS was a safe surgery for patients with LABC and had good response to NACT

Smith BL et all Journal of the American College of Surgeons [05 Jul 2017, 225(3): 361-365]

Nipple-sparing mastectomy (NSM) has gained popularity for breast cancer treatment and prevention. There are limited data about long-term oncologic safety of this procedure. We reviewed oncologic outcomes of consecutive therapeutic NSM at a single institution. Nipple-sparing mastectomy was offered to patients with no radiologic or clinical evidence of nipple involvement. There were 2,182 NSM performed from 2007 to 2016. Long-term outcomes were assessed in the 311 NSM performed in 2007 to 2012 for Stages 0 to 3 breast cancer; 240 (77%) NSM were for invasive cancer and 71 (23%) were for ductal carcinoma in situ. At 51 months median follow-up, 17 patients developed a recurrence of their cancer. Estimated disease-free survival was 95.7% at 3 years and 92.3% at 5 years. There were 11 (3.7%) locoregional recurrences and 8 (2.7%) distant recurrences; 2 patients had simultaneous locoregional and distant recurrences. There were 2 breast cancer-related deaths in patients with isolated distant recurrences. No patient in the entire 2,182 NSM cohort has had a recurrence in the retained nipple-areola complex.Rates of locoregional and distant recurrence are acceptably low after nipple-sparing mastectomy in patients with breast cancer. No patient in our series has had a recurrence involving the retained nipple areola complex.







Periareolar mammaplasty



Lateral mammaplasty



J-plasty



L-plasty



Inferior pedicle mammaplasty







Inferior Mammary Fold plasty



Omega mammaplasty



Medial mammaplasty



Vertical mammaplasty



Inverted-T mammaplasty







Breast Lift

Discarded tissue

Breast Reduction



YAP,YAPMA!

- 1-Memesinde yaygın mikro-kalsifikasyonları olan hastalar NAKT den yarar görmezler.
- 2-Hastaları MG,USG,MR yöntemlerini kullanarak değerlendirin.Meme görüntülenmesinde uzmanlaşmış görüntülme uzmanlarıyla çalışınız.! USG nin duyarlılık ve özgüllüğü çok artmıştır (duyarlılık %91). MR da yanlış pozitif sonuçların olabileceğini aklınıza getiriniz.
- 3-NAKT başlamadan önce memedeki tümörün ve aksilladaki metastatik olarak değerlendirilen LAP lara metalik klip konulmasını isteyiniz!
- 4-NACT den üç haftadan sonra cerrahi planlanabilir ancak bir yan etki oluşmuş ise acele etmeyiniz ! (Özellikle kardiyolojik).
- 5-Güvenilir çalışmalar MKC ile mastektomi arasında sağkalım ve yerel nüks açısından fark olmadığını göstermektedir.
- 6-NAKT den sonra primer tümör, %70 konsentrik ,%30 yamalı (patch) küçülür.
- 7-Eksizyondan sonra ,memede reziüel tümör kalması,lokal nüksü artırır. Çıkarılan tümör kitlesinin sınırlarını iyi değerlendirecek ,meme konusunda uzmanlaşmış patologlarla çalışınız.
- 8-Lokal nüks gelişme olasılığının tümörün genomik yapısıyla yakın ilişkili olduğunu hatırlayınız !. En çok "üçlü negatif" ve "nonluminal ER(+)" ler.
- 9-Onkoplastik teknikleri iyi kavrayın ve yaygın olarak kullanın.
- 10-Meme derisi ve meme başı korunarak yapılan mastektomi (SSM) ameliyatının sonuçları lokal nüks gelişimi ve sağ kalım açısından diğer ameliyatlarla eş değerdir. Bu konuda deneyim kazanmaya ve ekip oluşturmaya gayret ediniz.

11-

AKSİLLER DİSSEKSİYON SONRASI LENFÖDEM



ALND' DA MORBIDITE

	ALND(%)	<u>SLNB(%)</u>
LENF ÖDEM	27 - 46	2,6 - 5
OMUZ AĞRISI	68	36
KOLDA UYUŞMA	19,3	4
HAREKET KISITLIĞI	* 1	
ANKSIYETE INDEKSI		

Zavagno G.Ann Surg: 2008 ;247:207213 Peintinger F. Br J Cancer: 2003; 89: 648-652

Lymphedema: clinical observation and/or treatment



BCC 2017

EORTC

Donker, Lancet Oncol 2014 Nov;15(12)

st gallenoncology



CELL TRAPPING IN IMMUNOLOGICALLY SENSITIZED LYMPH NODES

E. DOUGLAS MCSWEENEY., M.D., CEMALETTIN TOPUZLU, M.D., AND WILLIAM M. STAHL, M.D., F.A.C.S.

THE MORPHOLOGIC characteristics of sensitized lymph nodes are well documented but the functional significance of these changes is largely unknown. The purpose of this study was to investigate whether the demonstrable phenomena of lymph node cell trapping could be enhanced by immunologic stimulation of specific regional lymph nodes.

In 8 dogs the hind paw lymphatic vessels, running to a single popliteal lymph node, were cannulated using microsurgical technique. Previous studies (1) have shown that erythrocytes tagged with Cr51 and infused in this lymphatic vessel can be counted by external scintillation counting over the popliteal node. Three sequential injections of 0.2 ml. of tagged erythrocytes were

From the Department of Surgery, University of Vermont Medical School, Burlington. Supported by American Cancer Society Grant T -309 Fund. The assistance of C. Janney, B.S., Ph.D., is gratefully acknowledged.

Reprint from Vol. XVI, Surgical Forum, American College of Surgeons, 1965

Reprinted Joses THE AMERICAN SURGEON DECEMBER, 1969, VOL. 35, NO. 12

The Importance of Biological Factors in the Barrier Function of Lymph Nodes

CEMALETTIN TOPUZLU,* M.D., KENNETH HUNT, B.A., CARLSTON HAINES, M.D., A. G. MACKAY, M.D.

From the Departments of Surgery, University of Vermont College of Medicine, Burlington, Vermont and Hacettepe University College of Medicine, Ankera, Turkey

DESPITE their clinical significance in the prognosis and treatment of neoplastic diseases, the functional aspects of lymph nodes were not well elucidated until recently.

One of several lymph node actions is the barrier function, the ability to filter and trap cellular and noncellular elements and, since regional lymph nodes provide the first line defense against lymphatic tumor spread, they deserve good understanding. It has been speculated, though never conclusively demonstrated, that the barrier function of the lymph node consists of two main components, namely, mechanical and biological filtration. Mechanical filtration is simple passive entrapment which is the natural result of the lymph node structural makeup. On the other hand, biological filtration is the result of active cellular function such as phagocytosis. This study was undertaken to investigate the role of biological factors in the barrier function of the lymph node.

Materials and Methods

The principles of laboratory animal care propagated by the National Society for Med-

ical Research were followed. Randomized mongrel dogs weighing 10-20 Kg, were an esthetized with sodium pentobarbital (30 mg. /Kg.) and the airway intubated with an endotracheal tube. The animals were permitted to ventilate spontaneously on room air. The dorsal hind paw lymphatics were visualized with Sky blue and were cannulated utilizing microsurgical techniques. The catheters placed into the lymphatics were kept open with a continuous perfusion of 0.9% normal saline at a rate of 0.2 ml./minute using a Harva d Constant Infusion Pump. Approximately 0.2 ml. of blood was drawn from another animal and the allogeneic red blood cells (RBC) were tagged with ACD solution and 100 ac of Chromium-51 in 10 ml. of normal saline. Three successive blood cell washings with 0.9% sodium chloride solution removed all the free radioactivity in the supernate. In the final concentration, 0.2 ml. contained 40 × 10⁶ RBC's. Lymphocyte suspensions were prepared from allogeneic lymphocytes obtained from dog retrocecal and mesenteric lymph nodes and tagged with 100 uc. of Chromium-51. After three washings with 0.9% of sodium chloride solution, their viability was determined with Trypan blue. The final lymphocyte suspension contained 400,000 cells per 0.2 ml. The amount of radioactivity present in 0.2 ml. of RBC, lymphocyte suspensions and in the popliteal lymph nodes was determined with external scintillation counting by using a Nuclear-

^{*} Present address: Hacettepe University College of Madicine, Department of Surgery, Ankare, Turkey.

This study was supported by American Cancer Seciety, Vermont Division grant 6E-66 #2 and in part by HE 11493.

Gold Medil Paper, Fortan on Progress in Surgery, Presented at the Meeting of the Southrastern Surgicel Congress, April 28-May 1, 1969.



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Science, 1966 Jun 3;152(3727):1397-8.	

Transmigration of lymph nodes by tumor cells.

Fisher B, Fisher ER.

Abstract

When either V2, Brown-Pearce, or Walker tumor cells were perfused at low pressure into the afferent lymphatic of popliteal lymph nodes or were injected into the foot pads of rabbits, they rapidly appeared in lymph draining from the node. This finding indicates that lymph nodes are not the effective barrier to dissemination of tumor cells they had previously been assumed to be.

PMID: 5949244 [PubMed - indexed for MEDLINE]

Transmigration of Lymph Nodes by Tumor Cells

vestigation to substantiate this concept. Zeidman and Buss noted in 1954 that when V2 or Brown-Pearce carcinoma cells were injected into the afferent lymphatic of the rabbit popliteal lymph node and the nodes were removed 1 to 42 days later, only 2 of 30 animals demonstrated growth of tumor in pelvic nodes. This suggested to them that the popliteals as well as other lymph nodes were an effective, albeit temporary barrier to the further spread of cancer. The failure to observe tumor growth at sites other than in the injected node is, in our opinion, not conclusive evidence that transnodal passage of tumor cells failed to occur. Consequently, we have reinvestigated this aspect of tumor spread.

The afferent and efferent lymphatics of the popliteal lymph nodes of anesthetized rabbits were identified with or without the use of Evans Blue dye previously injected into the foot pad. With minimal trauma and no manipulation of the node, these vessels were cannulated with polyethylene tubing (PE-50). The cannula in the afferent lymphatic was connected by a Y connection to a 1-ml syringe which, by means of constant perfusion with a Harvard pump, deined for cells. Tumor cells morphologically identical with those of the parent tumors were observed in one or more of the lymph samples collected from 15 such preparations. They were present in the efferent lymph following perfusion of as few as 500,000 cells and at pressures as low as 10 mm-Hg. All three types of tumor cells were found in efferent lymph.

To eliminate the possibility that results were an artifact of the perfusion, Brown-Pearce and V2 rabbit tumor cell suspensions (1 to 5 $\times 10^6$ cells in 2 ml of saline) were injected into the foot pad after the efferent lymphatic of the popliteal node had been cannulated. Lymph was collected and treated in a manner similar to that described above. Tumor cells were evident in all of ten such preparations within 60 minutes after inoculation: not infrequently tumor cells were observed in lymph collected 10 minutes after inoculation. In many, cells appeared not only singly, but in clumps

Extensive investigation is under way to quantitate the transnodal passage of such cells, to evaluate the effect of nodal alteration, and to equate cell viability following its egress from the node. The data obtained from these experiments prompts the conclusion that while tumor cells *may* be sequestrated in the lymph node, they also traverse that structure.

> BERNARD FISHER EDWIN R. FISHER

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References and Notes

- R. Virchow, Cellular Pathology, F. Chance, trans. (Lippincott, Philadelphia, 1863).
 R. K. Gilchrist and V. C. David, Ann. Surg.
- R. K. Gilchrist and V. C. David, Ann. Surg 108, 621 (1938).
- C. E. Drinker, M. E. Field, H. K. Ward, J. Exp. Med. 62, 849 (1934).
- J. M. Yoffey and E. R. Sullivan, *ibid.* 69, 133 (1939).
- C. A. Buckman and W. M. Stahl, Jr., Surg. Forum 14, 116 (1963); A. Engeset, Lancet 1962-1, 324 (1962); C. F. Silvester, Amer. J. Anat. 12, 447 (1912).
- E. Goldman, Proc. Roy. Soc. Med. Surg. Sec. No. 1, 1, 1 (1907); J. M. Yoffey, Brit. Med. J. 2, 1052 (1932).
- J. M. Yoffey and F. C. Courtice, Lymphatics, Lymph and Lymphoid Tissue (Harvard Univ. Press, Cambridge, Mass., 1956), pp. 94-110.
- S. Rusznyák, M. Földi, G. Szabó, Lymphatics and Lymph Circulation (Permagon New York, 1960), p. 35.
- R. A. Willis, Pathology of Tumours (Butterworth, London, ed. 3, 1960), pp. 167-172; The Spread of Tumours in the Human Body (Butterworth, London, 1960).
- I. Zeidman and J. M. Buss, *Cancer Res.* 14, 403, (1954).
 I. Supported by PHS grants CA-05716, CA-
- Supported by PHS grants CA-05716, CA-06670, HE-07822, and American Cancer Society grant P-142. The technical assistance of Joyce Mitchell, E. Rodis, and R. Pellegrini is acknowledged.

23 February 1966

SPEKTRUM (TAYF) PARADİGMASI (HİPOTEZİ) 1994

SAMUEL HELLMANN UMBERTO VERONESI

Meme kanseri heterojen bir hastalıktır, başından itibaren lokal bir hastalıktır ve hep öyle kalır

veya

tanısı konduğu andan itibaren sistemik karakterdedir ve hep öyle seyreder



Axillary treatment for operable primary breast cancer

Bromham N, SchmidtHansen M, Astin M, Hasler E, Reed MW Cochrane Database Syst Rev. 2017 Jan 4;1:CD004561. do: 10.1002/14651858.D004561.pub3. (26 randomize kontrollu çalışma)

ALND yapılmayan hastalarda Uzak met.olasılık : HR 1.06, %95 CI 0.87-1.30 Tüm sağkalım : HR 1.06, %95 CI 0.96-1.17 Lokal nüks olasılık : HR 1.53, %95 CI 1.31-1.78 Lenfödem olasılık : OR 0.37, %95 CI 0.29-0.46

AKSİLLADA HİÇBİR GİRİŞİM YAPILMAYAN HASTALAR

Calışma süresi:1995-2006 Median takip: 10.4 yıl Hasta sayısı: 194 (postmen, Tm <2cm, ER+, LVI-) 5yil(%) **10yıl(%) Aksiller nüks** 0.8 1.9 Uzak hastalıksız SK 99.2 97.0 Hastalıksız SK 96.6 91.2 Tüm SK 90.3 75.5

Axillary Lymph Node Dissection versus Axillary Radiotherapy in Patients with a Positive Sentinel Node: The AMAROS Trial

The AMAROS trial showed that substituting axillary lymph node dissection by radiotherapy of the axillary and periclavicular nodes (ART) in patients with sentinel node (SN) metastases results in less lymphoedema, without a significant difference in the 5-year axillary recurrence rate (ARR).

Three surgical studies showed no increase in ARR after omitting axillary treatment in cases of limited SN metastases, provided that adjuvant systemic therapy and tangential breast radiotherapy were applied.

On the other hand, several recent radiotherapy trials, including a metaanalysis by the Early Breast Cancer Trialists' Collaborative Group, showed that regional radiotherapy improves disease-free survival where there are positive axillary nodes. In view of the low ARR and good overall survival with contemporary breast cancer treatments, limiting axillary treatment and its associated morbidity is a logical development.

However, it is too early to omit axillary treatment in all SN positive patients. ART is a safe next step in reducing axillary treatment.

Boersma L, van der Sangen MJ. Ned Tijdschr Geneeskd. 2015

Effect of Axillary Dissection vs No Axillary Dissection on 10-Year Overall Survival Among Women With Invasive Breast Cancer and Sentinel Node MetastasisThe ACOSOG Z0011 (Alliance) Randomized Clinical Trial

Armando E. Giuliano, MD; Karla V Ballman, PhD; Linda McCall, MS; Peter D. Beitsch, MD; Meghan B. Brennan, RN, ONP, PhD; Pond R. Kelemen, MD; David W. Ollila, MD; Nora M. Hansen, MD; Pat W. Whitworth, MD; Peter W. Blumencranz, MD; A. Marilyn Leitch, MD; Sukamal Saha, MD; Kelly K. Hunt, MD; Monica Morrow, MD.

JAMA 2017;318(10):918-926. doi:10.1001/jama.2017.11470 September 12, 2017

A long term results of treatment of breast cancer without axillary surgery - Predicting a SOUND approach?

Traditionally axillary surgery has been used to provide staging information and until recently was thought to improve loco-regional control. However, a more minimal approach to the axilla is now being adopted. The aim of this study was to assess long term outcomes of patients with 'low-risk' breast cancers who did not undergo any axillary surgery. 'Low-risk' criteria were: postmenopausal, <20 mm grade 1 or <15 mm grade 2, LVI-ve, ER +ve.

METHODS:

Women with invasive breast cancer that did not undergo any axillary surgery were identified. Patients were censored when an event or death occurred or at last follow-up at breast clinic or with their General Practitioner.

RESULTS:

Between 05/01/1995-20/11/2006, 194 patients (199 tumors) were operated upon without axillary surgery. Median follow-up was 10.4 years. 128 patients met low-risk criteria and 71 did not (patient choice = 42, medical fitness = 29). In the 'low risk' cohort there were two axillary recurrences, with a cumulative incidence of 0.8% and 1.9% at 5 and 10 years respectively.

	<u>5years</u>	<u> 10 years</u>
DDFS	99.2% (95% CI: 94.1-99.9%)	97.0% (95% CI: 90.0-99%)
DFS	96.6% (95% CI: 91.1-98.7%)	91.2% (95% CI: 82.6-95.6%)
OS	90.3% (95% CI: 83.6-94.4)	75.5% (95% CI: 65.9-82.8)

CONCLUSION:

Axillary recurrence and DDFS in this low-risk cohort is favourable. In the modern era of breast cancer management it is possible to define a group of women in whom axillary surgery can be omitted

O'Connell RL, RusbyJE, Stamp GF, Conway A, Roche N, Barry P, Khabra K, Bonomi R, Rapisarda IF, Della Rovere GQ. Eur J Surg Oncol 2016 Jul;42(7):942-8



st galleroncology

CC 2017

Lenf düğümü metastazları; uzak metastazların

"işareti, indicator" üdür

"yöneticisi,governor"ü değildir.

INSANIN İNANCI ASLA ZİNCİRİ OLMAMALIDIR

Ernest Renan 1823-1892



Axilla cN+ after chemo? Targeted Axillary Dissection (TAD)

Identification and Resection of Clipped Node Decreases the False-negative Rate of Sentinel Lymph Node Surgery in Patients Presenting With Node-positive Breast Cancer (T0-T4, N1-N2) Who Receive Neoadjuvant Chemotherapy Results From ACOSOG Z1071 (Alliance)

n = 141	
FNR when clipped node within SLN specimen (76%)	6.8%
FNR when clipped node within ALND specimen (19%)	19%

BCC 2017

Boughey, Ann Surg 2016;263:802-807



st gallenong



Moleküler subtiplere göre aksillanın negatif ve pozitif olma olasılığı

	<u>(-)%</u>	<u> (+)%</u>
Triple (-)	77.4	22.6
Luminal A	73.4	26.6
Luminal B	45.3	54.7
HER-2 +	40.0	60.0



How should the results of sentinel node biopsy (SNB) be used in clinical practice? What is the role of SNB in special circumstances in clinical practice? What are the potential benefits and harms associated with SNB? ASCO Clinical update Quide lines December 2016

Recommendation 1. Clinicians should not recommend axillary lymph node dissection (ALND) for women with early-stage breast cancer who do not have nodal metastases (Type: evidence based; benefits outweigh harms. Evidence quality: high. Strength of recommendation: strong).

Recommendation 2.1. Clinicians should not recommend ALND for women with earlystage breast cancer who have one or two sentinel lymph node metastases and will receive breast-conserving surgery with conventionally fractionated whole-breast radiotherapy (Type: evidence based; benefits outweigh harms. Evidence quality: high. Strength of recommendation: strong).

Recommendation 2.2. Clinicians may offer ALND for women with early-stage breast cancer with nodal metastases found in SNB specimens who will receive mastectomy (Type: evidence based; benefits outweigh harms. Evidence quality: low. Strength of recommendation: weak).

Recommendation 3. Clinicians may offer SNB for women who have operable breast cancer who have the following circumstances:

3.1. Multicentric tumors (Type: evidence based; benefits outweigh harms. Evidence quality: intermediate. Strength of recommendation: moderate).

3.2. Ductal carcinoma in situ when mastectomy is performed. (Type: informal consensus; benefits outweigh harms. Evidence quality: insufficient. Strength of recommendation: weak).

3.3. Prior breast and/or axillary surgery (Type: evidence based; benefits outweigh harms. Evidence quality: intermediate. Strength of recommendation: strong).

3.4. Preoperative/neoadjuvant systemic therapy (Type: evidence based; benefits outweigh harms. Evidence quality: intermediate. Strength of recommendation: moderate).

Conclusions and Relevance: Among women with T1 or T2 invasive primary breast cancer, no palpable axillary adenopathy, and 1 or 2 sentinel lymph nodes containing metastases; 10-year overall survival for patients treated with sentinel lymph node dissection alone was noninferior to overall survival for those treated with axillary lymph node dissection. These findings do not support routine use of axillary lymph node dissection in this patient population based on 10year outcomes.

Wednesday, 15 March 2017 15.30–17.00 Session 1:

News since St.Gallen 2015: De-escalating and escalating treatment according to stage and breast cancer subtype

SA 1.1 De-escalating and escalating surgery in the management of early breast cancer

M. Morrow*. Memorial Sloan-Kettering Cancer Center, New York, USA

The recognition that breast cancer subtypes differ in the risk of both local and systemic recurrence, coupled with the beneficial impact of systemic therapy on local control, offers the opportunity to better individualize the surgical approach to breast cancer management in order to minimize the morbidity of treatment. An increasing body of evidence demonstrates that individualization of the approach to axillary management is both safe and effective. The ACOSOG Z0011trial demonstrating that patients with cT1-2,N0 tumor undergoing BCT and found to have metastases in 1 or 2 sentinel nodes could be safely be treated without axillary dissection was initially published with a median follow-up of 6.3 years, raising concerns that late recurrences might occur in the ER+ population. With further follow-up, the 10 year cumulative rate of nodal recurrence in the sentinel node only group (1.5%) does not differ significantly from that in the axillary dissection group (0.5%), and no differences in DFS or OS on the basis of axillary surgery assignment have been observed.

Alt tiplere göre LRR



Arvold et al. J Clin Oncol, 2011

NAC sonrası SLNB Meta-analiz

- Metaanaliz
- 24 çalışma
- 1779 hasta
- Bulunma oranı %63-100
 Pooled estimate: %89.6
- Yanlış negatiflik: %0-33 — Pooled estimate: %8.4

Kelly A, Acad Radiol, 2009

ACOSOG Z1071 ÇALIŞMASI cN(+) bx (+) hastaların NACT sonra cN0 olması cN1 %83.9 cN2 %68.4 Ameliyattan sonra: % 41.0 pCR **SLN (+)** % 20.6 ALND (+) **%** 7.4 Her ikisinde (+) % 31.0

JAMA.2013;310(14):1455-1461.doi:10.1001/jama.2013.278932

Axillary Ultrasound Accurately Excludes Clinically Significant Lymph Node Disease in Patients with Early Stage Breast Cancer

Tucker NS , Cyr AE, Ademuywa FO, Tabchy A, George K, Sharma PK, Jn LX, Sanat S, Aft R, Gao F, Margenthaler JA, Gllanders WE. Ann Surg. 2016 Dec;264(6):10981102.

*Department of Surgery †Department of Internal Medicine ‡Divison of Biostatistcs §Department of Pathology, Washington Universty School of Medicine, St. Louis, MO.

Abstract assess the performance characteristics of axillary ultrasound (AUS) for accurate exclusion of clincally significant axillary lymph node (ALN) disease. Sentinel lymph node biopsy (SLNB) is currently the standard of care for staging the axilla in patients with clinical T1T2, N0 breast cancer. AUS is a noninvasive alternative to SLNB for staging the axilla. Patients were identified using a prospectively mantaned database. Senstivity, specifity, and negative predictive value (NPV) were calculated by comparing AUS findings to pathology results. Multivariate analyses were performed to identfy patient and/or tumor characteristics associated with false negative (FN) AUS. A blinded review of FN and matched true negative cases was performed by 2 independent medical oncologists to compare treatment recommendations and actual treatment received. Recurrence-free survival was described using KaplanMeer product Imt methods. A total of 647 patients with clinical T1T2, N0 breast cancer underwent AUS between January 2008 and March 2013.

AUS had a sensitivity of 70%, NPV of 84%, and PPV of 56% for the detection of ALN disease. For detection of clinically significant disease (>2.0mm), AUS had a sensitivity of 76% and NPV of 89%.

FN AUS did not significantly impact adjuvant medical decison making. Patients with FN AUS had recurrencefree survival equivalent to patients with pathologic N0 disease. AUS accurately excludes clinically significant ALN disease in patients with clinical T1T2, N0 breast cancer. AUS may be an alternative to SLNB in these patients, where axillary surgery is no longer considered therapeutic, and predictors of tumor biology are increasingly used to make adjuvant therapy decisions.

PMID: 26779976 PMCID: PMC4947031 [Available on 20171201] DOI: 10.1097/SLA. 0000000000015

Accuracy of axillary ultrasound after different neoadjuvant chemotherapy cycles in breast cancer patients

This study determined whether axillary ultrasound (AUS) accurately predicted the status of axillary lymph nodes of patients who received different number of cycles of neoadjuvant chemotherapy (NAC).

MATERIALS AND METHODS:

From 2008 to 2015, 656 cases of patients with breast cancers who received NAC and had subsequent axillary lymph node dissection were included in this study. The findings of preoperative AUS were tested by pathological examination. We evaluated the sensitivity, specificity and accuracy of AUS for patients who received two-, four-, and six-cycle NAC.

RESULTS:

In the two-cycle subgroup, the sensitivity (Sn), specificity (Sp) and diagnostic odds ratio (DOR) were 80.2% (95% CI: 74.3%-86.2%), 61.4% (95% CI: 48.8%-74.0%) and 6.64 (95% CI: 3.36-12.4) respectively. In the four-cycle subgroup, the Sn, Sp and DOR were 69.7% (95% CI: 62.2%-77.1%), 66.1% (95% CI: 53.7%-78.5%) and 4.47 (95% CI: 2.32-8.62), respectively. In the six-cycle subgroup, the Sn, Sp and DOR were 56.7% (95% CI: 49.5%-64.0%), 74.5% (95% CI: 62.8%-87.2%) and 3.83 (95% CI: 1.863-7.86), respectively. Furthermore, the patients with normal AUS findings after six cycles of NAC have few positive nodes than patients with suspicious findings (p < 0.001).

CONCLUSION:

The Preoperative AUS is a potentially useful imaging modality to predict the pathologic status of axilla within four cycles of NAC. Although the accuracy is lower for patients who completed six cycles of NAC than that who received four- and two-cycles, the number of positive lymph nodes for patients with normal findings on AUS is low.

Ye BB, Zhao HM, Yu Y, Ge J, Wana X, Cao XC. ONCOTARGET Nov 11, 2016. doi: 10.18632/oncotarget.13313. [Epub ahead of print]



MEME KANSERİNİN CERRAHİ TEDAVİSİNDE AKSİLLA DİSSEKSİYON YAPMAYI, KOLLARDA LENFÖDEM VE DİĞER KOMPLİKASYONLARI AZALTMAYI AMAÇLAYAN YENİ BİR ALGORİMA ÖNERİSİ:

1- NSAB B-04,NSABP B-6,ACOSOG Z0011,AMOROS çalışmaları (Meme kanserinde pozitif aksiller lenf düğümleri, uzak metastazların ve kısa sağkalımın YÖNETİCİSİ DEĞİL SADECE İŞARETİ' dirler)

2- Gelişmiş aksiller US yöntemlerinin pozitif aksilla lenf düğümlerini belirlemedeki duyarlılığı (79%), özgüllüğü (99%) ve PPV (%100) yüksektir.

3- Yeni NACT protokolleri, pozitif lenf düğümlerini negatife çevirmede çok yüksek oranda etkin (80-90%) olmaktadır.

KISALTMALAR: cNOAx = klinik negatif aksilla, cN+Ax= klinik pozitif aksilla AxUS= aksiller ultrason tetkiki, cNO SLNB %86.6 (-) Makrometastaz %5.4 Mikrometastaz %2.7 İzole Tm hücreleri %2.7

Noordea M : Netherlands Cancer Institute 2018





Din ve bilim arasında temel bir fark var ! Din otoriteye dayanıyor, Bilim ise gözlem ve mantığa. Sonunda bilim kazanacak , çünkü işe yarıyor.'' Stephan Hawking

Teşekkür Ederim

Aksillanın (+) olma olasılığı %13.4 makrometastaz %5.4, mikrometastaz %2.7 HR+(HR2)- %0 HR- HER 2(+) %12 üçlü negatif %1.5

Davenport L 11.European Cancer Meeting ,Mart 22 2018 Barcelona Netherlands Cancer Institute