6 ulusal CERRAHİ ONKOLOJİ KONGRESİ

24 - 27 Şubat 2022 | Gloria Golf Resort – ANTALYA

DOÇ. DR. GÖKHAN AKKURT

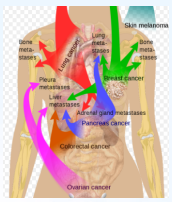
ANKARA ŞEHİR HASTANESİ CERRAHİ ONKOLOJİ KLİNİĞİ

Metastatik karaciğer tümörlerinde lokorejyonel tedavi stratejileri ve sonuçları

Metastatik karaciğer hastalıkları;

- Karaciğerin en sık malign hastalığı
- Kansere bağlı morbidite ve mortalite

- ***Kolon kanseri***
- *Nöroendokrin tümörler*
- *Akciğer kanseri*
- *Meme adenokarsinomları*
- *Over kanseri*
- *Mide kanseri*
- *Pankreas kanseri*
- *Melanom*
- *Sarkom*



- ***Primer tümör tipinden bağımsız olarak;***
  - *İlerlemiş hastalık*
  - *kötü prognoz*
- Hedef → Genellikle palyatif yöntemler

Oligometastaz ★ Yaygın metastaz ⇨ Hastalık prognostik farklılık

Uygun oligometastatik hastalarda ***agresif lokal tedavi*** ⇨ ***Küratif***

Shamimi-Noori S, Gonsalves CF, Shaw CM. Metastatic Liver Disease: Indications for Locoregional Therapy and Supporting Data. Semin Intervent Radiol 2017; 34: 145-166
Griscom JT, Wolf FS. Liver Metastasis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021
Grilley-Olson JE, Webber NP, Demos DS, Christensen JD, Kirsch DG. Multidisciplinary Management of Oligometastatic Soft Tissue Sarcoma. Am Soc Clin Oncol Educ Book 2018; 38: 939-948

Karaciğer metastatik hastalığı → Rezeksiyon / Sistemik kemoterapi

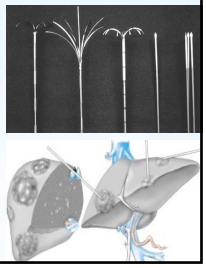
- %10-25 cerrahiye uygun
- Karmaşık karaciğer cerrahisinde önemli gelişmeler
- Majör morbidite ve mortalite
- Balans önemli

Yeni stratejiler ;

- *küratif rezeksiyon için tümörlerin evresini küçültmek*
- *semptomları azaltmak*
- *daha iyi tümör kontrolü sağlamak*

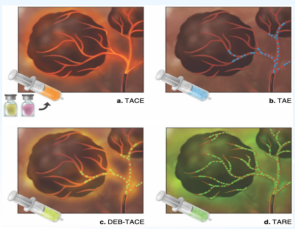
O'Leary C, Soulen MC, Shamimi-Noori S. Interventional Oncology Approach to Hepatic Metastases. Semin Intervent Radiol 2020; 37: 484-491

- Lokorejyonel tedaviler de yeni ***görüntü kılavuzlu tekniklerin gelişmesi***
- Gelişmiş ***hedef farmako-radyoterapötikler***
  - *etkileyici tümör yanıtı*
  - *progresyonsuz sağkalım (PFS)*
  - *genel sağkalım (GS) oranları yüksek*



Lokorejyonel tedavi stratejileri

- ***Transarterial Embolizasyon (TAE)***
- ***Transarterial Kemoembolizasyon (TACE)***
- ***Transarterial Radyoembolizasyon (TARE)***
- ***Ablasyon***

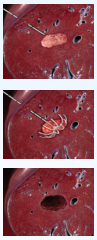


- Kateter tabanlı bölgesel tedaviler

Tümör → Primer hepatik arter

Parankim → Primer portal ven

- ***Normal parankim minimal, tümör maksimal etki***



Makary MS, Khandpur U, Cloyd JM, Mumtaz K, Dowell JD. Locoregional Therapy Approaches for Hepatocellular Carcinoma: Recent Advances and Management Strategies. Cancers (Basel) 2020;12

Summary of locoregional therapy options for metastatic disease to the liver

Modality	Techniques	Risks
TAE	Particulate or liquid embolic agents	PES, liver abscess, liver biloma, liver failure
TACE	Conventional emulsified chemotherapeutic agent (c-TACE) or drug-eluting beads (DEB-TACE)	PES, liver abscess, liver biloma, liver failure
TARE	Yttrium-90 radioisotope loaded on microspheres	REILD, PRS, liver failure, liver abscess, liver biloma
Ablation	Radiofrequency, microwaves, laser, cooling, alternating and direct current	PAS, bleeding, damage to surrounding structures

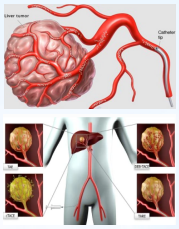
PES: Post-embolization syndrome; REILD: Radioembolization-induced liver disease; PRS: Post-radioembolization syndrome; PAS: Post-ablation syndrome; TAE: Transarterial embolization; TACE: Transarterial chemoembolization; TARE: Transarterial radioembolization.

TAE:
- *partiküler veya sıvı embolik ajanlar*
- *hücresel membran bozulması ve iskemik hücre ölümü*

TACE:
- *lokal kemoterapötik ajanlar + embolizasyon*

c-TACE:
- *lipiodolize kemoterapötik ajan + embolik ajan*

DEB-TACE
- *ilaç salan tanecikler*
- *yüksek standardizasyon ile kemoterapi salınımı*



- ***Postembolizasyon sendromu (PES)***
  - *7-10 gün*
  - *sağ üst kadran ağrısı*
  - *bulantı*
  - *ateş*
  - *karaciğer fonksiyon testlerinde yükselme*
  - *tümör nekrozu ve doku iskemisi*

- ***Hepatik dekompansasyon***
- ***Renal yaralanma***
- ***Biliyer yaralanma***
- ***Enfeksiyon***
- ***Hedef dışı embolizasyon***

Makary MS, Khandpur U, Cloyd JM, Mumtaz K, Dowell JD. Locoregional Therapy Approaches for Hepatocellular Carcinoma: Recent Advances and Management Strategies. Cancers (Basel) 2020;12

TARE; Ytriyumun bir radyoizotopu (*i.e.*, 90Y) ile kaplanmış 30 mikron boyutunda boncuklar

- Beta bozulma sürecinden geçer
- Hücresel DNA onarım mekanizmalarında radyasyona bağ
- Sonuçta hücre ölümü
- *TARE ayakta tedavi imkanı*

Radyoembolizasyon indüklenmiş karaciğer hastalığı (REILD)

Radyasyon Sonrası Sendromu (PRS)
- ateş
- mide bulantısı
- -iştahsızlık
- yorgunluk

Makary MS, Krishnan LS, Wuthrick EJ, Bloomston MP, Dowell JD. Yttrium-90 microsphere selective internal radiation therapy for liver metastases following systemic chemotherapy and surgical resection for metastatic adrenocortical carcinoma. World J Clin Oncol 2018; 9: 20-25

- 4-6 hafta / 3-6 ayda bir tedavi başarısı için ***görüntüleme- laboratuvar***
- ***Response Evaluation Criteria in Solid Tumors (RECIST)***
- ***PET Response Criteria in Solid Tumors (PERCIST)***
- ***BT ve MRG ile boyut değerlendirme***
- ***Modified RECIST (mRECIST)*** → ***HCC***
- ***Modified CT Response Evaluation (Choi)*** → ***Gastrointestinal Stromal Tümör***
- ***European Association for Study of the Liver (EASL) criteria***

Schwartz LH, Litière S, de Vries E, Ford R, Gwyther S, Mandrekar S, Shankar L, Bogaerts J, Chen A, Dancey J, Hayes W, Hodi FS, Hoekstra OS, Huang EP, Lin N, Liu Y, Therasse P, Wolchok JD, Seymour L. RECIST 1.1-Update and clarification: From the RECIST committee. Eur J Cancer 2016; 62: 132-137

RECIST

CR = Disappearance of a… enhancement

PR = At least a 30% dec… meters of viable of target lesions, takin… sions, taking as sum of the diameters… of target lesions

SD = Any cases that do… rial response response or progress…

PD = An increase of at l… the diameters diameters of target le… reference the smallest sum of the d… ancing) target recorded since treatm…

AASLD, American Association for the Study of Liver Diseases; JNCI, Journal of the National Cancer Institute; HCC, hepatocellular carcinoma; mRECIST, modified Response Evaluation Criteria in Solid Tumors; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease.

European Association for the Study of the Liver-EASL criteria

	Response
Complete response	100% necrosis of lesion and no new lesions
Partial response	50–99% necrosis
Stable disease	0–49% necrosis
Progressive disease	≥25% increase in ≥1 lesion or ≥1 new lesion

100% specificity for pathological outcome, imaging correlations with complete histological necrosis were 100% for complete responses, 52% for partial responses and 0% for stable disease

No enhancement, thin rim enhancement, and peripheral nodular enhancement corresponded with 100%, 93%, and 38% complete histologic necrosis, respectively

Ablatif stratejiler

- *Radyofrekans ablasyonu (RFA)*
- *Mikrodalga ablasyonu (MWA)*
- *Kriyoablasyon (CA)*
- *İrreversibl elektroporasyon (IRE)*
- *Lazer kaynaklı interstisyel termoterapi (LITT)*
- *Yüksek yoğunluklu odaklanmış ultrason (HIFU)*

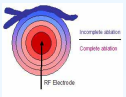
CA da morbidite ve lokal nüks oranları yüksek

- *miyohemoglobinüri*
- *böbrek yetmezliği*
- *kardiyak aritmi*
- *kriyojenik şok*
- *çoklu organ yetmezliği sendromu*
- *şiddetli koagülopati*

Rong G, Bai W, Dong Z, Wang C, Lu Y, Zeng Z, Qu J, Lou M, Wang H, Gao X, Chang X, An L, Li H, Chen Y, Hu KQ. Yang Y. Long-term outcomes of percutaneous cryoablation for patients with hepatocellular carcinoma within Milan criteria. PLoS One 2015; 10

RF:

- *En çok < 3 cm tümörde*
- *Daha az lezyonlu metastazlarda etkili*
- *Hilusta ve büyük kan damarlı bölgelerde ısının emici etkisi*
- *Çok problu stereotaktik RFA (< 8 cm)*



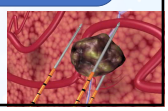
MWA:

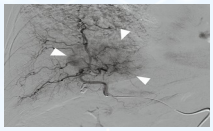
- *Daha hızlı sıcaklık ile daha geniş alan*
- *Daha düzgün ısıtma bölgeleri*
- *Isı emici etkileri daha az*
- *Eş zamanlı ablasyon*

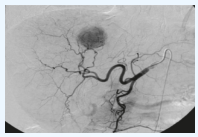
IRE:

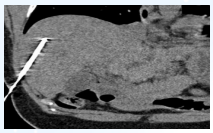
- *En yeni ablasyon*
- *Geri dönüşümsüz elektroporasyon*
- *Yüksek voltaj kullanır*
- *Hücre zarında kalıcı nano gözenekler*
- *Apoptoz*

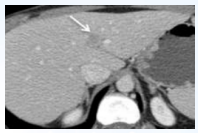
- *Kanama*
- *Diyafram, GI yolu ve safra kesesi gibi çevre organlarda hasar*
- *Self-limiting post-ablation syndrome (PAS)*











KONTRENDİKASYONLAR

KESİN:

- *Ana safra kanalı veya major damar invazyonu*
- *Belirgin ekstrahepatik hastalık*
- *Child C siroz veya aktif KC enfeksiyonu*
- *Dekompanse KC hastalığı*
- *Düzeltilemeyen koagülopati*

GÖRECELİ:

- *Biliyoenterik anastomozlar*
- *Major damar veya organ komşulukları (Kolon, Mide, Safra Kesesi vb)*
- *HCC' nin 5 cm' den büyük olması*
- *Metastatik lezyonların 3 cm' den büyük ve 5 adetten fazla olması*

Livraghi T, Solbiati L, Meloni F, Ierace T, Goldberg SN, Gazelle GS. Percutaneous radiofrequency ablation of liver metastases in potential candidates for resection: the "two-off-time approach". Cancer. 2003 Jun 15;97(12):3027-35.

Kolorektal Karsinom

- Kolorektal karaciğer metastazı (KRKM) karaciğer malignitesinin ***en yaygın türü***
- Kolorektal kanserli hastaların ***yarısından fazlasında*** karaciğer metastazı gelişir
- Cerrahi rezeksiyon ilk seçenek, KRKM da ***%25'i cerrahi aday***

Güncel Guideline → Etkisiz Neoadjuvan- Unrezektabl tm

- Cerrahi tedaviye alternatif???

Engstrand J, Nilsson H, Strömberg C, Jonas E, Freedman J. Colorectal cancer liver metastases – a population-based study on incidence, management and survival. BMC Cancer 2018; 18: 78

TACE (KRKM)

- Doksorubisin kolorektal metastazlarda etkisiz
- ***İrinotekanlı DEB-TACE'ye (DEBIRI) artan ilgi***
- Fiorentini ve ark. DEBIRI ve FOLFIRI üzerine ilk randomize klinik çalışma
- DEBIRI de GS (22 ay/15 ay)
- Progresyonsuz sağkalım (7 ay/4 ay)
- PARAGON II çalışması (DEBIRI × Sistemik kemoterapi → Neoadjuvan olarak)

Jones RP, Malik HZ, Fenwick SW, Terlizzo M, O'Grady E, Stremitzer S, Gruenberger T, Rees M, Plant G, Figueras J, Albiol M, Adam R, Awad S, Poston GJ. PARAGON II - A single arm multicentre phase II study of neoadjuvant therapy using irinotecan bead in patients with resectable liver metastases from colorectal cancer. Eur J Surg Oncol 2016; 42: 1866-1872

TARE (KRKM)

- Unrezektabl KRKM → İtriyum-90 ile transarteriyel radyoembolik tedavi → Artmış Survival

- **SIRFLOX faz III çalışması**
- ***Standart sistemik kemoterapi*** (FOLFOX +/- bevacizumab) × **KT + *TARE***

  - Karşılaştırılabilir sağkalım
  - Daha iyi progresyonsuz sağkalım (PFS)
  - Karaciğerde daha iyi tümör yanıtı
  - Tedaviden sonra daha az canlı tümör dokusu
  - Artmış rezektabilite

Kennedy A, Cohn M, Coldwell DM, Drooz A, Ehrenwald E, Kaiser A, Nutting CW, Rose SC, Wang EA, Savin MA. Updated survival outcomes and analysis of long-term survivors from the MORE study on safety and efficacy of radioembolization in patients with unresectable colorectal cancer liver metastases. J Gastrointest Oncol 2017; 8: 614-624

Ablasyon (KRKM)

COLLISON çalışması (Faz III)

- *Rezektabl KRKM < 3 cm tm*
- ***RFA × Rezeksiyon***
- *Hepatektomi gerektiren küçük fakat derin yerleşimli tümörlerde* ***RFA etkili olabilir***

- Son çalışmalar ... ***ezeksiyona yakın sonuç***

- ***Minimal invaziv***
- ***Azalmış morbidite ve mortalite***
- ***Azalmış hastanede kalış süresi***
- ***Erken iyileşme***

Ruers T, Van Coevorden F, Punt CJ et.al. B; European Organisation for Research and Treatment of Cancer (EORTC); Gastro-Intestinal Tract Cancer Group; Arbeitsgruppe Lebermetastasen und tumoren in der Chirurgischen Arbeitsgemeinschaft Onkologie (ALM-CAO); National Cancer Research Institute Colorectal Clinical Study Group (NCRI CCSG). Local Treatment of Unresectable Colorectal Liver Metastases: Results of a Randomized Phase II Trial. J Natl Cancer Inst 2017; 10

Hof J, Wertenbroek MW, Peeters PM, Widder J, Sieders E, de Jong KP. Outcomes after resection and/or radiofrequency ablation for recurrence after treatment of colorectal liver metastases. Br J Surg 2016; 103: 1055- 1062

Son metaanalizler;

- Rezektabl KRKM da ***MWA > RF***
- Benzer yan etki profili
- Genel ve hastalıksız sağkalım artışı mevcut

- *KT + Ablasyon + DEBIRI ?*
- *NCT02082782 (Faz II, IRE çalışması)*
- *Multidisipliner ekip*

Di Martino M, Rompianesi G, Mora-Guzmán I, Martín-Pérez E, Montalti R, Troisi RI. Systematic review and meta-analysis of local ablative therapies for resectable colorectal liver metastases. Eur J Surg Oncol 2020; 46: 772-781

Nöroendokrin Tümörler (NET)

- Ilımlı, iyi diferansiye ------ Agresif, kötü diferansiye
- En sık KC metastazı (NEKM)

- ***Tedavi***
  - *- Cerrahi*
  - *- Lokorejyonel terapiler*
  - *- Kemoterapi*
  - *- Somatostatin analogları*
  - *- Karaciğer nakli*

- **Küratif rezeksiyon %10-25**
- **Nüks %50-95**
- **Ablasyon**
  - Evre düşürmek
  - Tedavi etmek
  - Karsinoid sendrom kontrolü

Cloyd JM, Ejaz A, Konda B, Makary MS, Pawlik TM. Neuroendocrine liver metastases: a contemporary review of treatment strategies. Hepatobiliary Surg Nutr 2020; 9: 440-451

TAE/TACE (NEKM)

İyi diferansiye
Unrezektabl
Medikal tedaviye dirençli semptomları olan
} **NEKM**

- Benzer sonuçlar, TAE daha az yan etki

Dermine ve ark.

- *NEKM'da TACE uygulanan 25 retrospektif çalışma (1986-2017)*
- *34.5 aylık medyan GS, 18.5 aylık PFS*
- *Morfolojik tepki oranı %49*
- *Ek olarak %27'lik tümör stabilizasyonunu*

Dermine S, Palmieri LJ, Lavolé J et.al. Non-Pharmacological Therapeutic Options for Liver Metastases in Advanced Neuroendocrine Tumors. J Clin Med 2019; 8

TAE/TACE (NEKM)

- **Yakın zamanlı retrospektif çalışmada;**
  - *TACE ile tedavi edilen NEKM'li 197 hasta*
  - *RECIST kriterlerine göre %96 yanıt*
  - *Medyan GS 35.9 ay, PFS 15.9 ay*

- ***c-TACE*** *+ sisplatin, mitomisin C, doksorubisin* × ***DEBTACE*** *+ doksorubisin*
- ***c-TACE daha yüksek semptomatik yanıt ile ilişkilendirildi*** *(%47'ye karşı %30)*
- *Ancak embolizasyon sonrası şikayetler ve KCFT oranı daha yüksek*

- TAE, c-TACE ve DEBTACE yi karşılaştıran devam eden çalışma

Egger ME, Armstrong E, Martin RC 2nd, Scoggins CR, Philips P, Shah M, Konda B, Dillhoff M, Pawlik TM, Cloyd JM. Transarterial Chemoembolization vs Radioembolization for Neuroendocrine Liver Metastases: A Multi-Institutional Analysis. J Am Coll Surg 2020; 230: 363-370
Makary MS, Kapke J, Yildiz V, Pan X, Dowell JD. Conventional versus Drug-Eluting Bead Transarterial Chemoembolization for Neuroendocrine Tumor Liver Metastases. J Vasc Interv Radiol 2016; 27: 1298-1304
Soulen M, White S, Fidelman N, Garcia-Monaco R, Wileyto E, Avritscher R, El-Haddad G. 03:27 PM Abstract No. 105 Randomized Embolization Trial for NeuroEndocrine Tumors (RETNET): first safety report. J Vasc Interv Radiol

TARE (NEKM)

- 2008-2016 TARE ile tedavi edilen 15 NEKM retrospektif çalışma

  - *Medyan semptom yanıtı %89,5 (%55-100)*
  - *RECIST kriterlerine göre medyan yanıt %51 (%12-73)*
  - *10 aylık PFS (9-11 ay)*
  - *Medyan GS 28,5 ay (14-70 ay)*

- **TARE ➡ 148 NEKM hasta**
  - *%70 yanıt oranı, GS 70 ay*

Elf ve ark. 11 hasta randomize kontrollü pilot çalışma
- *TAE ile TARE karşılaştırıldı*
- *6 ayda RECIST kriterlerine göre benzer yanıt oranları*

Dermine S, Palmieri LJ, Lavolé J, Barré A, Dohan A, Abou Ali E, Cottereau AS, Gaujoux S, Brezault C, Chaussade S, Coriat R. Non-Pharmacological Therapeutic Options for Liver Metastases in Advanced Neuroendocrine Tumors. J Clin Med 2019; 8
Kennedy AS, Dezarn WA, McNeillie P, Coldwell D, Nutting C, Carter D, Murthy R, Rose S, Warner RR, Liu D, Palmedo H, Overton C, Jones B, Salem R. Radioembolization for unresectable neuroendocrine hepatic metastases using resin 90Y-microspheres: early results in 148 patients. Am J Clin Oncol 2008; 31: 271-279
Elf AK, Andersson M, Henrikson O, Jalnefjord O, Ljungberg M, Svensson J, Wängberg B, Johanson V. Radioembolization Versus Bland Embolization for Hepatic Metastases from Small Intestinal Neuroendocrine Tumors: Short-Term Results of a Randomized Clinical Trial. World J Surg 2018; 42: 506-513

Ablasyon (NEKM)

- Tek/Kombine kullanılabilir

13 hastalık retrospektif inceleme:
- Ortalama 23 KC metastazı
- Rezeksiyon + RFA ➡ 3 yıllık GS %86

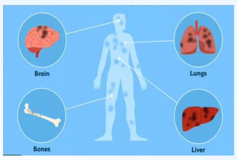
94 hastalık retrospektif çalışma
- Rezeksiyon + RFA ➡ 5 yıllık GS %80, 10 yıllık GS %59

Tek başına RFA ile tedavi edilen NEKM'lı 89 hasta
- *%97 semptomlarda azalma*
- *PFS 16 ay, GS 72 ay*
- *5 yıllık sağkalım %57*

Elias D, Goéré D, Leroux G, Dromain C, Leboulleux S, de Baere T, Ducreux M, Baudin E. Combined liver surgery and RFA for patients with gastroenteropancreatic endocrine tumors presenting with more than 15 metastases to the liver. Eur J Surg Oncol 2009; 35: 1092-1097
Taner T, Atwell TD, Zhang L, Oberg TN, Harmsen WS, Slettedahl SW, Kendrick ML, Nagorney DM, Que FG. Adjunctive radiofrequency ablation of metastatic neuroendocrine cancer to the liver complements surgical resection. HPB (Oxford) 2013; 15: 190-195

Meme Kanseri

- Hastaların 5 de 1 i KC metastazı
- Geç dönemde ortaya çıkar, ***beyin ve kemik metastazından kötü***
- GS 14 ay
- KT + Rezeksiyon?
- Lokorejyonel tedavi
  - *Palyasyon*
  - *Bölgesel kontrol*



Chun YS, Mizuno T, Cloyd JM, Ha MJ, Omichi K, Tzeng CD, Aloia TA, Ueno NT, Kuerer HM, Barcenas CH, Vauthey JN. Hepatic resection for breast cancer liver metastases: Impact of intrinsic subtypes. Eur J Surg Oncol 2020; 46: 1588-1595

TACE (MKKM)

Li ve ark.
- MKKM 48 hasta
- *DEB-TACE (n=28)* × *Sistemik kemoterapi (n=20)*
- 28 aylık medyan GS

Duan ve ark.
- TACE (n=44) × Sistemik kemoterapi (n=43)
- RECIST'e göre iyileştirilmiş yanıt oranları %59,1/%34,9

Vogl ve ark.
- c-TACE + Sistemik kemoterapi ➡ 208 hastada
- 25 aylık medyan GS

Li XP, Meng ZQ, Guo WJ, Li J. Treatment for liver metastases from breast cancer: results and prognostic factors. World J Gastroenterol 2005; 11: 3782-3787
Duan XF, Dong NN, Zhang T, Li Q. Treatment outcome of patients with liver-only metastases from breast cancer after mastectomy: a retrospective analysis. J Cancer Res Clin Oncol 2011; 137: 1363- 1370
Vogl TJ, Nour-Eldin NA, Hammerstingl RM, Panahi B, Naguib NNN. Microwave Ablation (MWA): Basics, Technique and Results in Primary and Metastatic Liver Neoplasms – Review Article. Rofo 2017; 189: 1055-1066

TARE (MKKM)

Deipolyi ve ark.

- *3-5 ayda %75'lik yanıt oranı (PERCIST)*
- *15 aylık GS*

Chang ve ark.

- *TACE (n=32) veya TARE (n=49) uygulama*
- *TACE daha tolere edilebilir*
- *TARE/TACE medyan GS 12.9/4.6 ay*
- *mRECIST kriterlerine göre 3 aylık hastalık kontrolü %47*

Deipolyi AR, England RW, Ridouani F, Riedl CC, Kunin HS, Boas FE, Yarmohammadi H, Sofocleous CT. PET/CT Imaging Characteristics After Radioembolization of Hepatic Metastasis from Breast Cancer. Cardiovasc Intervent Radiol 2020; 43: 488-494
Chang J, Charalel R, Noda C, Ramaswamy R, Kim SK, Darcy M, Foltz G, Akinwande O. Liverdominant Breast Cancer Metastasis: A Comparative Outcomes Study of Chemoembolization Versus Radioembolization. Anticancer Res 2018; 38: 3063-3068

Ablasyon (MKKM)

- **Yakın tarihli retrospektif çalışma;**
  - 33 Oligometastatik meme kanserli hasta
  - 70 aylık medyan GS

  KM olan 14 hastanın alt grup analizi;
  - Ablasyon sonrası PFS 13 ay

Ablasyon;

- *İzole karaciğer metastazlarında* ***tümör kontrolü için uygun bir tedavidir***
- Sistemik kemoterapide zaman ihtiyacını azaltır

Prognostik Faktörler:

- Tümör boyutu

- Östrojen reseptör +

- 5-10 mm ablasyon marjini

Ridouani F, Solomon SB, Bryce Y, Bromberg JF, Sofocleous CT, Deipolyi AR. Predictors of Progression-Free Survival and Local Tumor Control after Percutaneous Thermal Ablation of Oligometastatic Breast Cancer: Retrospective Study. J Vasc Interv Radiol 2020; 31: 1201-1209

Sarkom

- Birçok doku, mezenşimal köken
- Tümör tipi ➡ Prognozu belirler
- Hematojen metastaz (medyan sağkalım 12-19 ay)
- Metastazda sistemik KT standart (%10-25 yanıt)

- ***Unrezektabl tm***
- ***Tekrarlayan,***
- ***Kemo-dirençli hastalık***

➡ **Lokorejiyonel tedavi** ➡

- ***Artan tümör yanıtı***
- ***Genel sağkalım artışı***

Chapiro J, Duran R, Lin M, Mungo B, Schlachter T, Schernthaner R, Gorodetski B, Wang Z, Geschwind JF. Transarterial chemoembolization in soft-tissue sarcoma metastases to the liver – the use of imaging biomarkers as predictors of patient survival. Eur J Radiol 2015; 84: 424-430

TAE (SKM)

Maluccio ve ark.

- *Unrezektabl/tedaviye yanıtsız SKM*
- *15/9 hastada tümör boyutunda %25'ten fazla küçülme*
- *%50'den fazla nekroz*
- *GS 1-, 2-, ve 3 yıllarda* ***62%, 41%, ve 29%***

Diğer çalışma:

- *GIST nedeniyle* ***İmatinib + TAE*** × ***İmatinib + Sunitinib + TAE*** *alan 11 KM hastası*
- *Median sağkalım 15/24 ay*
- *PFS 3.8/3.4 ay*

Maluccio MA, Covey AM, Schubert J, Brody LA, Sofocleous CT, Getrajdman GI, DeMatteo R, Brown KT. Treatment of metastatic sarcoma to the liver with bland embolization. Cancer 2006; 107:1617-1623
Takaki H, Litchman T, Covey A, Cornelis F, Maybody M, Getrajdman GI, Sofocleous CT, Brown KT, Solomon SB, Alago W, Erinjeri JP. Hepatic artery embolization for liver metastasis of gastrointestinal stromal tumor following imatinib and sunitinib therapy. J Gastrointest Cancer 2014; 45: 494-499

TACE (SKM)

- 16 Leiyomyosarkom hastası
- %83 tümör kontrolü veya tedaviye yanıt
- Sisplatin, doksorubisin ve mitomisin-C + Polyvinyl alkol

⬇

20 ay GS

- 30 hasta, retrospektif değerlendirme
- Doksorubisin, sisplatin ve mitomisin + ***c-TACE***
- mRECIST kriterlerine göre %48 yanıt
- PFS 3 ay, medyan ***GS 21 ay***

Rajan DK, Soulen MC, Clark TW, Baum RA, Haskal ZJ, Shlansky-Goldberg RD, Freiman DB. Sarcomas metastatic to the liver: response and survival after cisplatin, doxorubicin, mitomycin-C, Ethiodol, and polyvinyl alcohol chemoembolization. J Vasc Interv Radiol 2001; 12: 187-193
Chapiro J, Duran R, Lin M, Mungo B, Schlachter T, Schernthaner R, Gorodetski B, Wang Z, Geschwind JF. Transarterial chemoembolization in soft-tissue sarcoma metastases to the liver – the use of imaging biomarkers as predictors of patient survival. Eur J Radiol 2015; 84: 424-430

Ablasyon (SKM)

- KM olan ➡ **13 GIST hastası × 12 Diğer sarkom alt tiplerine sahip hasta**

Falk ve ark.

- SKM'lı 281 hastada yaptıkları retrospektif değerlendirmede;
- Unrezektabl metastatik karaciğer hastalığında ***RFA kullanımını desteklemektedir***

Jones RL, McCall J, Adam A, O'Donnell D, Ashley S, Al-Muderis O, Thway K, Fisher C, Judson IR. Radiofrequency ablation is a feasible therapeutic option in the multi modality management of sarcoma. Eur J Surg Oncol 2010; 36: 477-482
Falk AT, Moureau-Zabotto L, Ouali M et.al ; Groupe Sarcome Francais-Groupe D'etude Des Tumeurs Osseuses. Effect on survival of local ablative treatment of metastases from sarcomas: a study of the French sarcoma group. Clin Oncol (R Coll Radiol) 2015; 27: 48-55

Mide Kanseri KC Metastazı

- Dünya çapında en sık teşhis edilen beşinci malignite
- Hastaların yaklaşık %10'u başlangıçta ***karaciğer metastazı*** ile teşhis edilir
- Radikal gastrektomi sonrası ***%37 karaciğer metastazı***
- Ekstrahepatik metastaz olmayanlarda *rezeksiyon ve RFA ile 5 yıllık sağkalım %10-30*

Zhou ve ark.

Palyatif KT (n=16) × Destekleyici Bakım (n=16) × HIFU (n=8)

- HIFU tedavi [illegible] ***görüşündeler.***

- *Ekstrahep*
- *Cerrahi ve*

Sung Jin Oh

- ***İlk olgu:***
  - Ameliyattan 6 ay sonra KM, 2 tümöre ***RFA + Sistemik KT***
- ***İkinci olgu:***
  - Ameliyattan 15 ay sonra KM, 1 tümöre ***RFA + Sistemik KT***
- Nüksüz ***genel sağkalım 108 ay-67 ay***

Bin Zhou, Ning He, Jiaze Wang et.al. HIFU for the treatment of gastric cancer with liver metastases with unsuitable indications for hepatectomy and radiofrequency ablation: a prospective and propensity score-matched study. BMC Surg (2021) 21:208

Sung Jin Oh. Long-Term Survival of Two Patients with Liver Metastases from Advanced Gastric Cancer Treated with Radiofrequency Ablation and Chemotherapy. Case Rep Oncol 2021;14:67–72

Pankreas Kanseri KC Metastazı

cancers MDPI

Systematic Review

Locoregional Treatment of Metastatic Pancreatic Cancer Utilizing Resection, Ablation and Embolization: A Systematic Review

Florentine E. E. Timmer [1,*], Bart Geboers [1], Sanne Nieuwenhuizen [1], Evelien A. C. Schouten [1], Madelon Dijkstra [1], Jan J. J. de Vries [1], M. Petrousjka van den Tol [2], Martijn R. Meijerink [1] and Hester J. Scheffer [1]

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[2] Department of Surgery, Amsterdam University Medical Centers (Location VUmc), De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands; mp.vandentol@amsterdamumc.nl

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- Pankreas duktal adenokarsinomu (PDAC) ***en ölümcül malign tümör***
- 5 yıllık sağkalım oranı %6
- Dördüncü sık ölüm nedeni
- *63.453 hasta*
- *59 çalışma*

Ablation in mPDAC. NS = not specified; R = retrospective; PM = primary + metastatic locoregional treatment; P = primary locoregional treatment; M = metastatic locoregional treatment; res = resection; chemo = chemotherapy; N = neoadjuvant; A = adjuvant; Ac = acute toxicity; L = late toxicity; Sc = synchronous; Mc = metachronous; meta = metastasis; RFA = radiofrequency ablation; IRE = irreversible electroporation; SBRT = stereotactic body radiotherapy; HIFU = high intensity focused ultrasound; LN = lymph nodes; LR = local recurrence; LAPC = locally advanced pancreatic cancer; tox = toxicity; CRT = chemoradiotherapy.

Authors	Year	Design	Nr. of Patients (mPDAC)	Study Details	Synchronous/ Metachronous	Morbidity, Grade 3+	Peri-Procedural Mortality	Chemotherapy, Neoadjuvant/ Adjuvant	Median Overall Survival (Months), mPDAC Only
RFA									
Park	2012	R	34 liver	34 Primary res + liver RFA (PM)	6/28	NS	0%	N: 68% A: 82%	From primary res: -PM: 18 From meta RFA: -PM: 14
Hua	2017	R	102 liver	102 no primary res (unresectable) + liver RFA (M)	102/0	0%	0%	N/A: 100% *Unclear whether prior to or after liver RFA*	From primary/meta diagnosis: -M: T1.4
Lee	2020	R	126 liver	60 Primary res + liver RFA (PM) 66 Primary res + chemo for meta (control, P)	0/126	13%	0%	N: 80% A: NS	From meta RFA: -PM: 12 -Control (P + chemo): 9.1
IRE									
Hong	2018	R	7 liver, peritoneum, omentum	Primary res + meta IRE (PM) or Primary IRE + metastasectomy (PM)	7/0	NS	0%	N: 100% A: 57%	From initial local treatment: -PM: 16

Authors	Year	Design	Nr. of Patients (mPDAC)	Study Details	Synchronous/ Metachronous	Morbidity, Grade 3+	Peri-Procedural Mortality	Chemotherapy, Neoadjuvant/ Adjuvant	Median Overall Survival (Months), mPDAC Only
TACE									
Kim	2010	R	15 liver	15 Primary res + liver TACE (PM)	0/15	13%	0%	N: 13% A: NS	From meta diagnosis: -PM: 9.6 From meta TACE: -PM: 7.5
Azizi	2011	R	32 liver	32 Primary res + liver TACE (PM)	NS	0%	0%	N: 100% A: NS	From meta TACE: -PM: 16
Kotoyan	2012	Pro	6 liver (± EHD)	6 Primary NS + liver TACE (M ± P)	NS	30%	0%	N: 100% A: NS Concomitant: 100%	From unknown: -M ± P: 9.3
Sun	2017	R	18 liver (± EHD)	18 liver TACE ± primary res (M ± P)	NS	0%	0%	N: 44% A: NS	NS
Vogl	2018	R	112 liver	112 Primary res + liver TACE (PM)	NS	0%	0%	N: 100% A: NS	From TACE: -PM: 19
Das	2019	R	182 liver	-84 RFA/ISI + TACE -59 TACE -123 matched control: syst chemo *All groups include MI and MO disease*	NS	RFA/ISI + TACE: 13 in 75 pts TACE only: 16 in 143 pts Controls: 28 in 123 pts	0%	N: NS A: NS Control: 100%	NS
TARE/TACE									
Ouyang	2018	R	184 liver (± EHD)	*No primary resection, some pts may have received primary SIRT* -64 LDT + systemic chemo (M): ○ 20 × TARE ○ 14 × TACE ○ 17 × TARE + TACE ○ 13 × other combinations -120 Systemic chemo -NO control!	184/0	M: 30% Control (chemo): 18%	TACE: 1 pt	N: 100% A: NS	From primary/meta diagnosis: -M: 8.7 -Control (chemo): 6.3

Embolization in mPDAC. NS = not specified; R = retrospective; Pro = prospective; TARE = transarterial radioembolization; SIRT = selective internal radiation therapy (same as TARE); TACE = transarterial chemoembolization; PM = primary + metastatic locoregional treatment; P = primary locoregional treatment; M = metastatic locoregional treatment; res = resection; RFA = radiofrequency ablation; ISI = iodine-125 seed implantation; LDT = liver-directed therapy; N = neoadjuvant; A = adjuvant; EHD = extrahepatic disease; Sc = synchronous; Mc = metachronous.

Authors	Year	Design	Nr. of Patients (mPDAC)	Study Details	Synchronous/ Metachronous	Morbidity, Grade 3+	Peri-Procedural Mortality	Chemotherapy, Neoadjuvant/ Adjuvant	Median Overall Survival (Months), mPDAC Only
SIRT/TARE									
Cao	2010	Pro	7 liver (±EHD)	3 Primary res + liver SIRT (PM) 4 liver SIRT only (M)	6/1	Ac: 0% L: 0%	0%	N: 100% A: NS	NS
Michl	2014	R	19 liver (±EHD)	15 Primary res + liver SIRT (PM) 4 liver SIRT only (M)	9/10	Ac: 9% L: 43-64%	16% (likely TARE-related)	N: 84% A: 47%	From meta SIRT: -M ± P: 9
Gibbs	2015	Pro	14 liver (±EHD)	4 Primary res + liver SIRT (PM) 10 liver SIRT only (M)	Sc + Mc *Numbers not specified*	Ac: 36% L: 50%	14%	Concomitant: 100%	From enrolment/SIRT: -PM: 13.6 -M: 4.2
Kim	2016	R	16 liver (±EHD)	6 Primary res/SBRT + liver SIRT (PM) 10 liver SIRT only (M)	NS	6%	0%	Concomitant: 94%	From meta diagnosis: -M ± P: 22 From meta SIRT: -M ± P: 12.5
Kim	2019	R	33 liver (±EHD)	23 Primary res/SBRT + liver SIRT (PM) 10 liver SIRT only (M)	NS	Clinical: 15% Lab: 9%	3% (likely TARE related)	N: 82% A: 30%	From primary diagnosis: -M ± P: 20.8 From meta SIRT: -M ± P: 8.1
Nezami	2019	Pro	3 liver	3 Primary treatment NS + liver SIRT (M ± P)	NS	Clinical: 36.5% Lab: 36.5%	0%	Concomitant: 100%	NS
Kayaleh	2020	R	26 liver (±EHD)	8 Primary res + liver SIRT (PM) 18 no primary res + liver SIRT (M)	13/13	Clinical: 3 in 77 pts Lab: 9 in 77 pts	0%	N: 100% A: 73%	From primary diagnosis: -M ± P: 33 From meta diagnosis: -M ± P: 21.8 From meta SIRT: -M ± P: 7

Melanom KC Metastazı

- Tüm cilt kanserlerinin %2'si
- Cilt kanserine bağlı ölümlerin %75
- %10 karaciğer metastazı
- Medyan sağkalım 2-8 ay

- ***Radyofrekans Ablasyon***
- ***Mikrodalga Ablasyon***
- ***Cryoablation***
- ***İrreverzıbl elektroporasyon***
- ***TACE***

Daniel Putzer, Peter Schullian & Reto Bale. Locoregional ablative treatment of melanoma metastases. INTERNATIONAL JOURNAL OF HYPERTHERMIA 2019, VOL. 36, NO. 2, 59–63

> Int J Clin Oncol. 2017 Jun;22(3):577-584. doi: 10.1007/s10147-017-1095-0. Epub 2017 Jan 31.

Efficacy and toxicity of transarterial chemoembolization therapy using cisplatin and gelatin sponge in patients with liver metastases from uveal melanoma in an Asian population

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Affiliations + expand

PMID: 28144882 DOI: 10.1007/s10147-017-1095-0

Abstract

Background: Although both immune-checkpoint inhibitors and targeted therapies such as MEK inhibitors have been evaluated in metastatic uveal melanoma, the efficacy of these therapies is modest to date. The purpose of this study was to evaluate the efficacy and toxicity of transarterial chemoembolization (TACE) therapy for liver metastasis from uveal melanoma in an Asian population.

Methods: We retrospectively assessed the clinical data of patients with liver metastases from uveal melanoma who received TACE therapy using cisplatin (70 mg/m^2) and gelatin sponge between 1997 and 2008.

Results: We identified 29 eligible patients. The overall response rate was 21%. The median survival time was 23 months, and the 1-, 2-, and 5-year survival rates were 72.4, 39.4, and 0%, respectively. The favorable prognostic factors were partial response and stable disease, <25% of the tumor volume within the liver at baseline, and normal serum lactate dehydrogenase (LDH) and normal alkaline phosphatase at baseline. Among them, normal LDH at baseline was the only independent prognostic factor in multivariate analysis. The common adverse events (AEs) were liver enzyme elevation (100%), nausea (72.4%), abdominal pain (65.5%), vomiting (55.2%), post-embolization syndrome (34.5% of patients, 9.6% of TACE procedures), and pyrexia (24.1%). Grade ≥3 AEs consisted of aspartate aminotransferase elevation (34.5%), alanine aminotransferase elevation (51.7%), and serum creatinine elevation (3.4%).

> Acta Oncol. 2018 Oct;57(10):1373-1380. doi: 10.1080/0284186X.2018.1465587. Epub 2018 Apr 23.

Selective internal radiation therapy (SIRT) as treatment for hepatic metastases of uveal melanoma: a Finnish nation-wide retrospective experience

Sanni Tulokas [1], Hanna Mäenpää [1], Erno Peltola [2], Tero Kivelä [3], Pia Vihinen [4], Aku Virta [4], Siru Mäkelä [1], Raija Kallio [5], Micaela Hernberg [1]

Affiliations + expand

PMID: 29683787 DOI: 10.1080/0284186X.2018.1465587

Abstract

Background: In Finland, selective internal radiation therapy (SIRT) is at present the preferred first-line loco-regional therapy for uveal melanoma patients with hepatic metastases not suitable for surgery. We retrospectively evaluate the outcome and safety of SIRT in this group of patients.

Material and methods: Yttrium-90 microspheres were delivered via the hepatic artery into the circulation of metastases from uveal melanoma in 18 patients with a predicted life expectancy of more than three months in three Finnish tertiary referral centers between November 2010 and December 2015. Progression-free survival (PFS), toxicity and overall survival (OS) were evaluated. Patients with historical uveal melanoma without extrahepatic metastases, who had received systemic chemotherapy as first-line treatment for their hepatic metastases at the Helsinki University Hospital between January 2006 and May 2010, were used as a historical control group.

Results: Partial response and stable disease were observed in three (17%) and eight (44%) patients, respectively; one patient was not evaluable for response. Median PFS after SIRT was 5.6 (range, 1.3-40.8) months. Median OS after SIRT was 13.5 (range, 3.6-44.8) months compared with 10.5 (range, 3.0-16.5; p = .047) months for the historical chemotherapy group. Among patients who received SIRT as first-line treatment, the median OS was 18.7 (range, 8.2-44.8) months, significantly longer than that of the chemotherapy group (10.5 months, p = .017). There were no treatment-related deaths. Toxicity was mainly WHO grade 1-2 and self-limited.

> Cardiovasc Intervent Radiol. 2016 Aug;39(8):1128-35. doi: 10.1007/s00270-016-1336-z. Epub 2016 Apr 7.

Stereotactic Radiofrequency Ablation for Metastatic Melanoma to the Liver

Reto Bale [1], Peter Schullian [2], Matthias Schmuth [3], Gerlig Widmann [2], Werner Jaschke [2], Georg Weinlich [3]

Affiliations + expand

PMID: 27055850 DOI: 10.1007/s00270-016-1336-z

Abstract

Purpose: To evaluate the outcome of patients with melanoma liver metastasis treated with stereotactic radiofrequency ablation (SRFA).

Material and method: Following IRB approval, a retrospective evaluation of the treatment of 20 patients with 75 melanoma liver metastases was performed.

Results: A median number of 2 lesions (range 1-14) per patient with a median size of 1.7 cm (range 0.5-14.5 cm) were treated. 67 lesions were <3 cm (89.3 %) and 8 lesions were >3 cm (10.7 %). Per patient a median of 1 ablation session was performed (range: 1-4) totaling 34 sessions. There were no procedure-related deaths and all major complications (n = 3) could be easily treated by pleural drainages. The primary and secondary success rates were 89.3 and 93.3 %, respectively. The overall local recurrence rate was 13.3 %. Four of ten local recurrences were re-treated successfully by SRFA. During follow-up, 9/20 patients developed extrahepatic metastatic disease and 10/20 had liver recurrence at any location. The median OS from the date of SRFA was 19.3 months, with an OS of 64, 41, and 17 % at 1, 3, and 5 years, with no significant difference for patients with cutaneous and ocular melanoma. The median DFS after SRFA for all 20 patients was 9.5 months, with 37, 9, and 0 % at 1, 3, and 5 years.

Conclusions: Due to the high local curative potential and the promising long-term survival rates associated with minimal morbidity and mortality, radiofrequency ablation seems to be an attractive alternative to resection in patients with melanoma liver metastases.

Sonuç

- Metastatik karaciğer hastalığı ***karaciğerin en sık görülen malign tümörleridir.***
- Kansere bağlı ***morbidite*** ve ***mortalitenin*** başlıca nedeni

Küratif amaçlı | *Semptom kontrolü*

Tümör kontrolü | *Palyasyon*

Evrelemenin rezeksiyona indirgenmesi

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teşekkürler…