

COVID-19 ile iliřkili Mukormikozis (CAM)

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Enfeksiyon Hast. ve Klinik Mikr. AD

25.05 2021

- Mukormikoz tüm dünyada kandidiyazis ve aspergillozis'den sonra en sık üçüncü invaziv fungal enfeksiyon
 - İnvaziv küf enfeksiyonlarında en yaygın ikinci etken
 - İnsidansı giderek artmakta!
 - 1.2 (1988-2006) -3.3 (2007-2015) /100.000 hastane başvurusu
 - Yüksek mortalite !
 - Mortalite altta yatan hastalık, tutulum yeri ve tedaviye bağlı değişmekte (20% - 80%)
-
- Bitar D *et al. Emerg Infect Dis* 2009
 - Rees JR *et al. Clin Infect Dis* 1998
 - Guinea J. *et al. PLoS One* 2017

Mukormikoz İçin Genel Risk Faktörleri

- Hematolojik malignite (AML) / HSCT
- Uzamış/ciddi nötropeni
- Kontrolsüz diabet
 - Ketoasidoz
- Solid organ malignitesi/transplantasyon
- Aşırı demir yüklenmesi, deferoxamin tedavisi
- Kemoterapi
- Biyolojik ajan kullanımı

- Major travma
 - Yanık, penetran travma, cerrahi yara
- Uzamış kortikosteroid kullanımı
- Hemodiyaliz
- İV ilaç alışkanlığı
- Malnutrisyon
- Prematurite

- Jeong, W., et al. *CMI* 2019
- Petrikos et al. *CID* 2012

COVID ilişkili mukormikoz (CAM)

Risk Faktörleri-1

- COVID-19, pulmoner ve ekstrapulmoner vasküler yataklarda endoteliyalite ve mikrovasküler tromboza neden olur ve mukormikozun anjiyoinvaziv etkilerini şiddetlendirebilir
- COVID-19 ayrıca immün disregulasyonu indükleyerek (örn: lenfopeniye neden olarak) mukormikoz dahil olmak üzere fırsatçı enfeksiyonlara yatkınlık oluşturabilir.

COVID ilişkili mukormikoz (CAM)

Risk Faktörleri-2

- **Sistemik kortikosteroid tedavisi:** Kortikosteroidlerin bazı COVID-19 hasta gruplarında faydalı olduğunu kanıtlamış olsa da, kortikosteroidler invaziv küf enfeksiyonları gelişme riskini artırabilir.
- **Diyabet:** COVID-19 yönetimini zorlaştıran önemli bir komorbiditedir. Hiperglisemi, kortikosteroidler tarafından da indüklenebilir.
- **Monoklonal antikorlar ve geniş spektrumlu antibiyotikler** mantar enfeksiyonunun oluşumuna veya kötüleşmesine neden olabilir.

Mukormikozda Klinik Formlar

- Rino/orbito/serebral (en sık)
 - lokalize sinüs
 - lokalize orbital
 - lokalize sereral
 - sino-orbital
 - sino-serebral
 - rino-orbito-serebral
- Pulmoner
- Kutanöz
- Dissemine
- Diğer (Gastrointestinal, renal, hepatik, endokardit, peritonit)



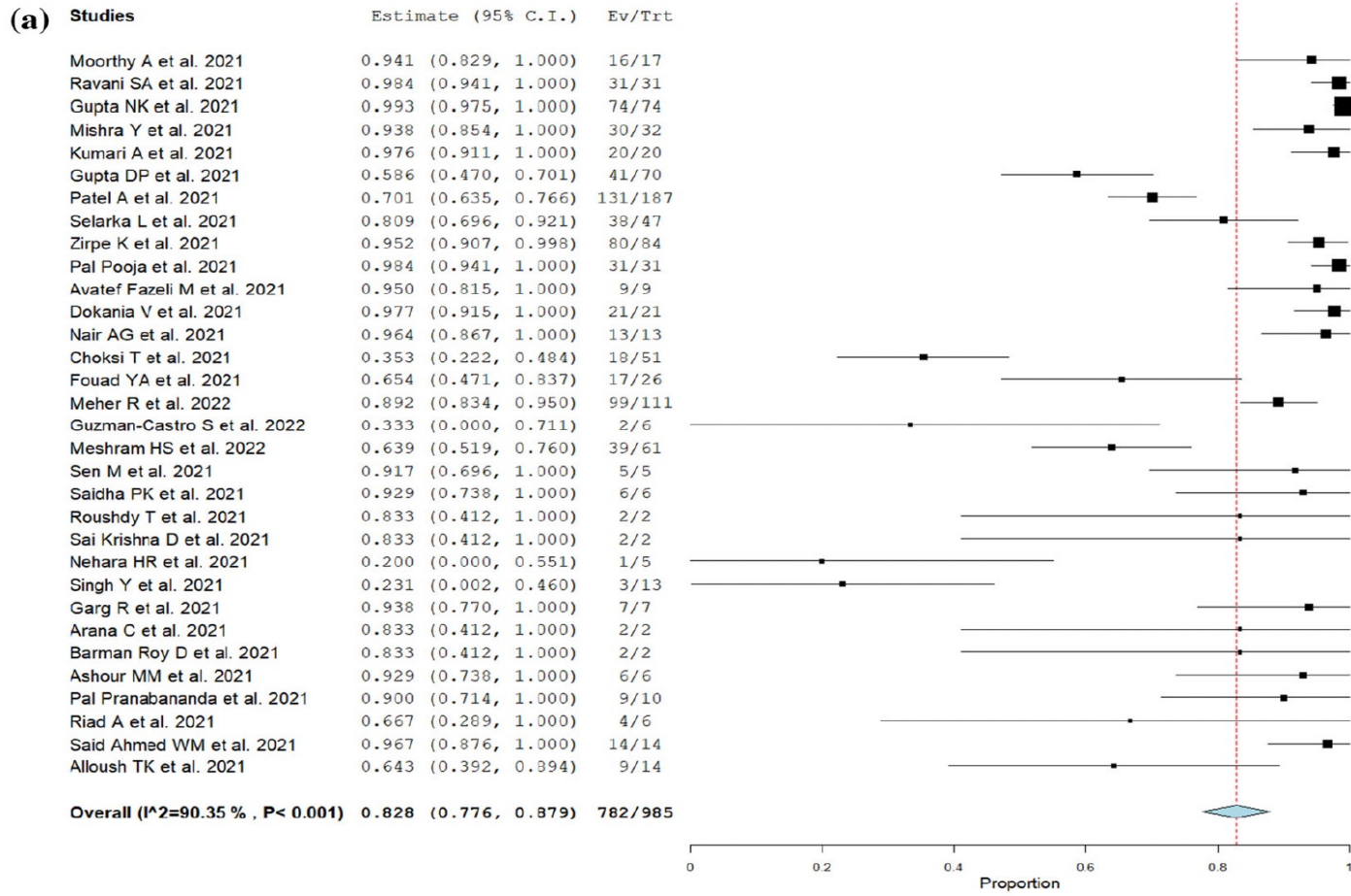
**Sıralama
CAM'da
değişmedi**

Clinical Features and Mortality of COVID-19-Associated Mucormycosis: A Systematic Review and Meta-Analysis

Atsuyuki Watanabe ^{# 1}, Matsuo So ^{# 2}, Hayato Mitaka ², Yoshiko Ishisaka ², Hisato Takagi ³,

Abstract

The recent increase of COVID-19-associated mucormycosis (CAM) has been commanding global attention. However, basic epidemiologic characteristics have not firmly been established. In this systematic review and meta-analysis, we sought to determine the clinical manifestations, potential risk factors, and outcomes of CAM. Observational studies reporting CAM were searched with PubMed and EMBASE databases in January 2022. We collected data on comorbidities and treatment for COVID-19, and performed a one-group meta-analysis on the frequency of orbital exenteration procedure and mortality of CAM using a random-effect model. Fifty-one observational studies, including a total of 2,312 patients with proven CAM, were identified. Among the 51 studies, 37 were conducted in India, 8 in Egypt, and 6 in other countries. The most common comorbidity was diabetes mellitus (82%). While 57% required oxygenation, 77% received systemic corticosteroids. Among CAM, 97% were rhino-orbital-cerebral (ROCM), and 2.7% were pulmonary mucormycosis. Usual presentations were headache (54%), periorbital swelling/pain (53%), facial swelling/pain (43%), ophthalmoplegia (42%), proptosis (41%), and nasal discharge/congestion (36%). Regarding the outcomes, orbital exenteration was performed in 17% (95% CI: 12-21%, $I^2 = 83%$) of the COVID-19-associated ROCM patients. The mortality of CAM was 29% (95% CI; 22-36%, $I^2 = 92%$). In conclusion, this systematic review and meta-analysis indicated that the most prevalent type of CAM was ROCM, and most CAM patients had diabetes mellitus and received systemic glucocorticoids. Clinicians in the endemic areas should have a high index of suspicion for this invasive fungal complication of COVID-19 when a diabetic patient who received high-dose systemic glucocorticoids developed rhino-orbital symptoms.



CAM hastalarında uygulanan endoskopik veya cerrahi işlem sıklığı

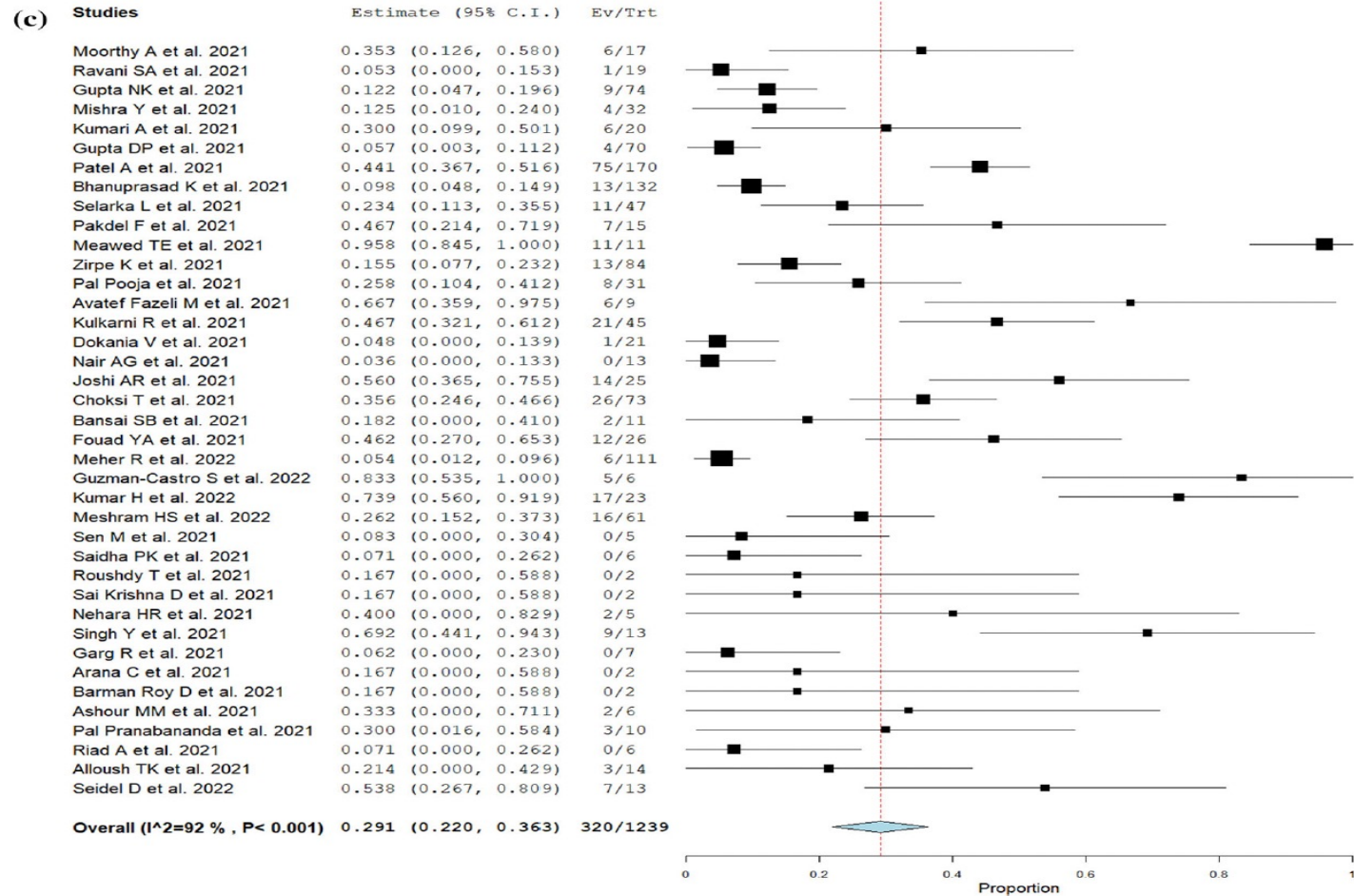


Fig. 2 continued

CAM gene mortality

Definition, diagnosis, and management of COVID-19-associated pulmonary mucormycosis: Delphi consensus statement from the Fungal Infection Study Forum and Academy of Pulmonary Sciences, India

COVID-19-associated pulmonary mucormycosis (CAPM) remains an underdiagnosed entity. Using a modified Delphi method, we have formulated a consensus statement for the diagnosis and management of CAPM. We selected 26 experts from various disciplines who are involved in managing CAPM. Three rounds of the Delphi process were held to reach consensus ($\geq 70\%$ agreement or disagreement) or dissensus. A consensus was achieved for 84 of the 89 statements. Pulmonary mucormycosis occurring within 3 months of COVID-19 diagnosis was labelled CAPM and classified further as proven, probable, and possible. We recommend flexible bronchoscopy to enable early diagnosis. The experts proposed definitions to categorise dual infections with aspergillosis and mucormycosis in patients with COVID-19. We recommend liposomal amphotericin B (5 mg/kg per day) and early surgery as central to the management of mucormycosis in patients with COVID-19. We recommend response assessment at 4–6 weeks using clinical and imaging parameters. Posaconazole or isavuconazole was recommended as maintenance therapy following initial response, but no consensus was reached for the duration of treatment. In patients with stable or progressive disease, the experts recommended salvage therapy with posaconazole or isavuconazole. CAPM is a rare but under-reported complication of COVID-19. Although we have proposed recommendations for defining, diagnosing, and managing CAPM, more extensive research is required.

Panel 1: Definitions of COVID-19 associated pulmonary mucormycosis

COVID-19-associated pulmonary mucormycosis (CAPM) is diagnosed either simultaneously with or within 3 months of virologically confirmed COVID-19.

Proven CAPM

Histopathology or cytology showing aseptate hyphae or culture obtained by a sterile procedure from a usually sterile site (pleural fluid or lung) showing growth of Mucorales.

Probable CAPM

Presence of all the following: compatible clinical features, risk factors, and suggestive imaging (thick-walled cavity, large consolidation, reversed halo sign, or multiple large nodules) and demonstration of aseptate hyphae (with or without growth of Mucorales) in a sample representative of the lower respiratory tract (including bronchoalveolar lavage, non-bronchoscopic bronchial lavage, bronchial washings, bronchial brushing, endotracheal aspirates, and sputum).

Possible CAPM

Presence of all the following: compatible clinical features; uncontrolled diabetes, prolonged or inappropriate glucocorticoid therapy (dose, duration, or indication deviating from the current evidence-based practice for glucocorticoids in COVID-19); and highly suggestive radiology (reversed halo sign, mycotic aneurysm, or thick-walled cavity), in the absence of a definite alternative diagnosis.

CAM Tanı

- Risk faktörleri + klinik veya radyolojik şüphe
- Mukormikoz hızla ilerleyen ve yıkıcı bir enfeksiyon olduğundan hastalıktan şüphe durumunda acil müdahale gerektirir.
- Kesin tanı için klinik örnek gerekli (Biyopsi, BAL, balgam, BOS)
 - Direk mikroskopi
 - Kültür
 - Histopatoloji
 - Moleküler yöntemler

Klinik Şüphe !!!

Risk faktörleri olan hastada

- İmmun supresif ve kontrolsüz diyabet
- Yüzde veya sino-orbital bölgede hızlı ilerleyen enfeksiyon
- Yüzde tek taraflı ağrı
- Eşlik eden ani gelişen diplopi
- Nekrotik siyah renkli skar (geç dönem bulgusu)

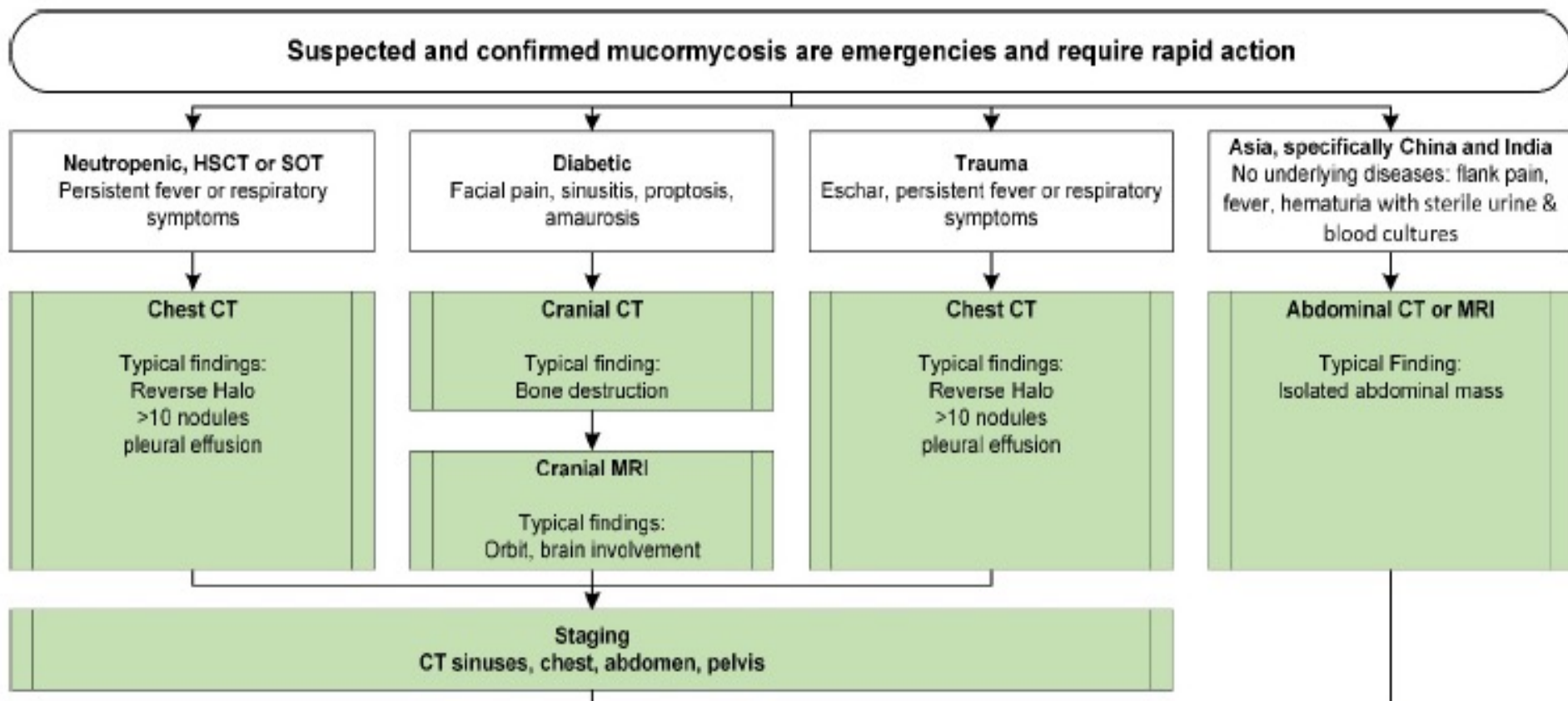
Rino-orbito-serebral tutulum düşünülmeli



Cornely, Oliver A., et al. "*The Lancet infectious diseases* 2019

Global guideline for the diagnosis and management of mucormycosis: An initiative of the ECMM in cooperation with ESCMID/EFISG and MSG ERC

Figure 6. Optimum diagnostic pathway for mucormycosis, when all imaging and assay techniques are available



CASE REPORT

Coronavirus Disease (Covid-19) Associated Mucormycosis (CAM): Case Report and Systematic Review of Literature

Deepak Garg · Valliappan Muthu · Inderpaul Singh Sehgal · Raja Ramachandran ·
Harish Kumar · Akhila Bhalla · Chandan D. Das · Anandika Chakrabarti

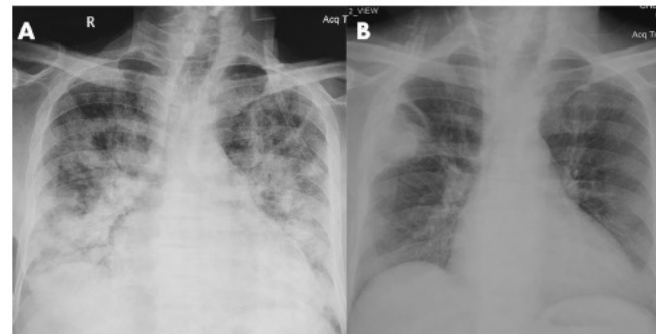


Fig. 1 Chest radiograph at admission **a** showing bilateral diffuse infiltrates and cardiomegaly. In the third week of hospitalization, a cavity with intracavitary content **b** can be seen in the right upper zone

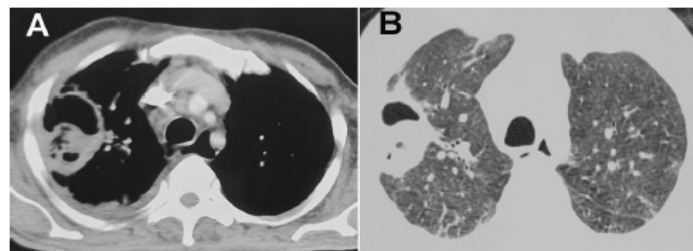


Fig. 2 Computed tomography showing thick-walled cavity in the right upper lobe in the corresponding mediastinal **A** and lung window **B** sections

Mukormikozda Görüntüleme

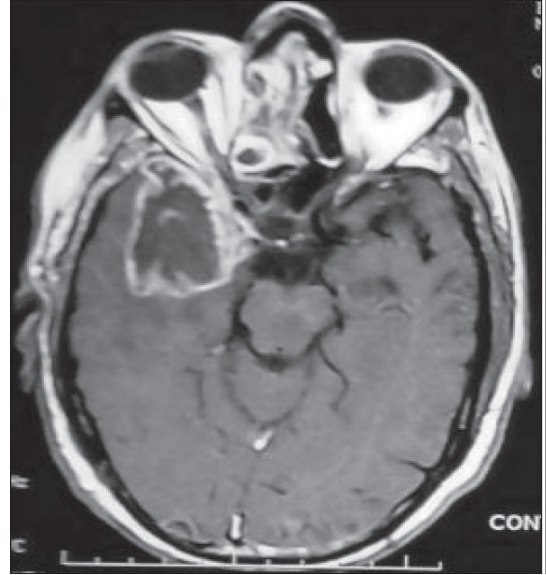
- Akciğer: Hematolojik maligniteli hastalarda mucor'un en sık tutulduğu alan
 - Ters halo (%10) (tuberküloz, Aspergillus)
 - >10 nodüler infiltrat
 - >3 cm nodül
 - Plevral efüzyon
 - Halo (Aspergillus, tuberküloz, CMV, Nocardia.....)

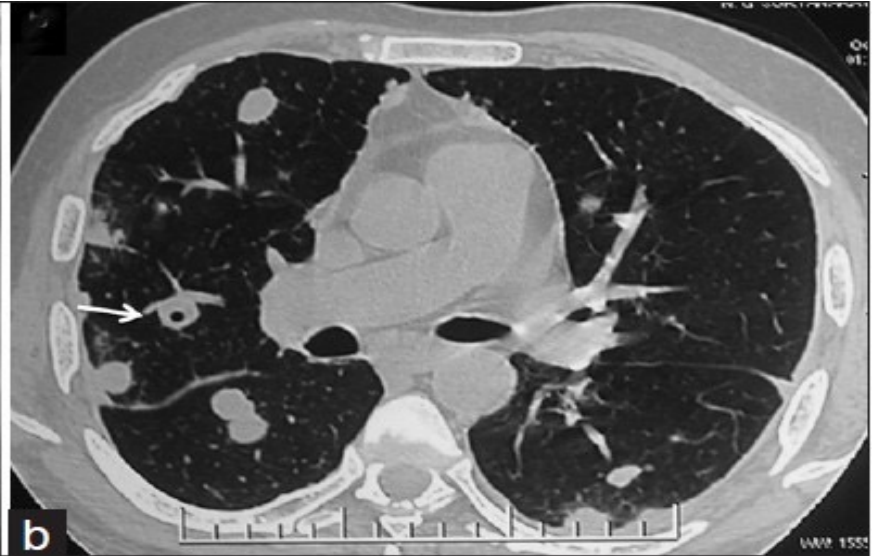
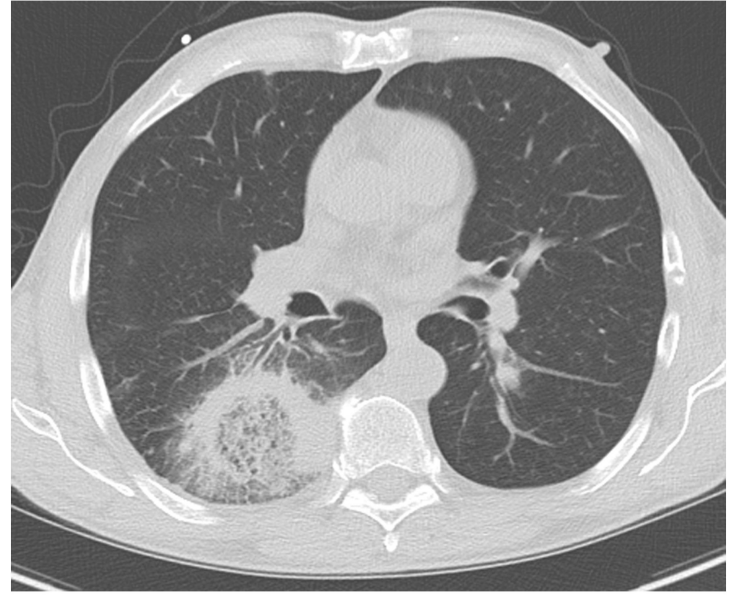
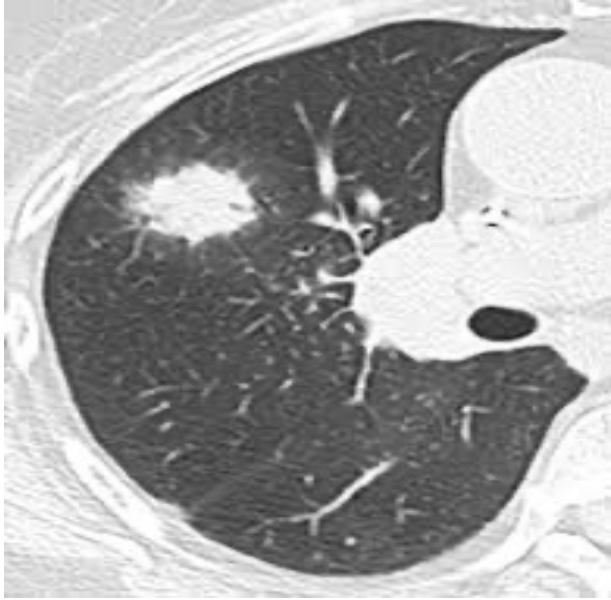
Bu bulgular mukormikozu destekleyen bulgular ancak spesifik bulgular değil

Görüntüleme

- Akciğer:
 - Ters halo (%10) (Non spesifik: Tuberküloz, Aspergilloz'da da görülür)
 - >10 nodüler infiltrat
 - >3 cm nodül
 - Plevral efüzyon
 - Halo (Aspergillus, Tuberküloz, CMV, Nocardiyoz'da da görülür)
- Rhino-orbita-cerebral :
 - Kemik yıkımı
 - Mukozal kalınlaşma
 - İntrakranial yayılım

Bu bulgular mukormikozu destekleyen bulgular ancak spesifik bulgular değil





CAM'da Görüntüleme

- Pulmoner ve dissemine mukormikozun klinik ve radyolojik özellikleri nonspesifik olduğundan ve COVID-19 ile ilişkili olduğu düşünülen bulgularla örtüşebileceğinden COVID-19 ile ilişkili mukormikoz tanısı zordur, bu da atlanmış veya gecikmiş tanılara neden olabilir.
- Akciğerin periferik bölgelerindeki ters halo işareti, immün yetmezliği olan hastalarda pulmoner mukormikoz için önemli bir bulgu olarak kabul edilmesine rağmen COVID-19'lu hastalarda, COVID-19'un potansiyel radyolojik özelliklerinden biri olarak da tanımlandığı için daha az spesifiktir.
- Kaviter akciğer lezyonları COVID-19'da küf enfeksiyonlarına ters halo işaretinden daha spesifik olabilse de, bu lezyonlar hem COVID-19 ile ilişkili pulmoner aspergillozda hem de pulmoner COVID-19 ile ilişkili mukormikozda sıklıkla gözlenir.

Panel 2: CT findings of COVID-19-associated pulmonary mucormycosis

Highly suggestive

- Thick-walled cavity
- Reversed halo sign
- Large consolidation or necrotising pneumonia
- Mycotic aneurysm
- Bird's nest sign
- Multiple large nodules (nodules >1 cm)
- Serial imaging showing cavity with an air-fluid level

Suggestive

- Pleural effusion

Non-specific

- Pneumothorax

Not suggestive

- Enlarged mediastinal lymph nodes
- Centrilobular nodules or tree-in-bud appearance (could be seen in patients with haemoptysis or in patients with coexisting COVID-19-associated pulmonary aspergillosis)

COVID-19 ile ilişkili Mukormikoz pulmoner BT bulguları

Kuvvetli düşündürür

- Kalın duvarlı kavite
- Ters halo işareti
- Büyük konsolidasyon veya nekrotizan pnömoni
- Mikotik anevrizma
- Kuş yuvası işareti
- Çoklu büyük nodüller (nodüller >1 cm)
- Hava-sıvı seviyesi içeren kaviteyi gösteren seri görüntüleme

Düşündürür

- Plevral efüzyon

Spesifik değil

- Pnömotoraks

Düşündürücü değil

- Büyümüş mediastinal lenf düğümleri
- Sentrilobüler nodüller veya tomurcuk içinde ağaç görünümü (hemoptizisi olan veya COVID-19 ile ilişkili pulmoner aspergillozun eşlik ettiği hastalarda görülebilir)

Mikrobiyolojik İnceleme

- Direk mikroskopi: Hızlı, yol gösterici, kültürle doğrulanmalı
- KOH ile muamele, kalkoflor beyazı veya Gomori methamine- silver ile boyama
 - Hiyalen
 - Septasız, veya seyrek septalı
 - Serit benzeri dik açı ile dallanan
 - Geniş (6-16 μm) çaplı
 - Düzensiz, hifler



Fig. 3 Lactophenol cotton blue (LCB) mount from the growth revealed aseptate hyphae with nodal rhizoids and short sporangiophores with terminal spherical sporangia filled with brownish sporangiospores, suggestive of *Rhizopus microsporus*

Kültür

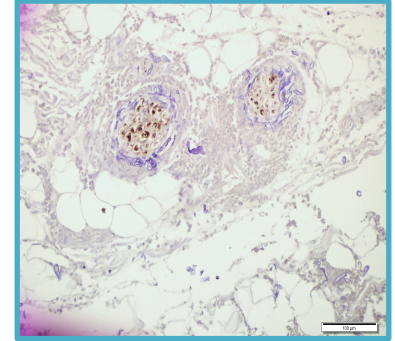
- 30-37C⁰ de, genellikle 24-48 saatte ürer
- Petri kutusunu dolduran yünümsü örgüde koloni (3-5 gün)
- Biyopsi materyali ezilmemeli
- Cins ve tür düzeyinde tanımlama imkanı



Histopatoloji

Tür ve cins ayırımı yapılamaz

- **Nekrotik doku içinde Mucorales takımına ait fungal hifler**
- **Perinöral invazyon**
- İnfarkt (Hemorajik)
- Damar invazyonu
- Nötrofilik infiltratlar
- Granülom



Serolojik Testler

- Galaktomannan: Negatif
- 1,3 Beta-D Glukan: Negatif

Yeni Tanısal Yaklaşımlar

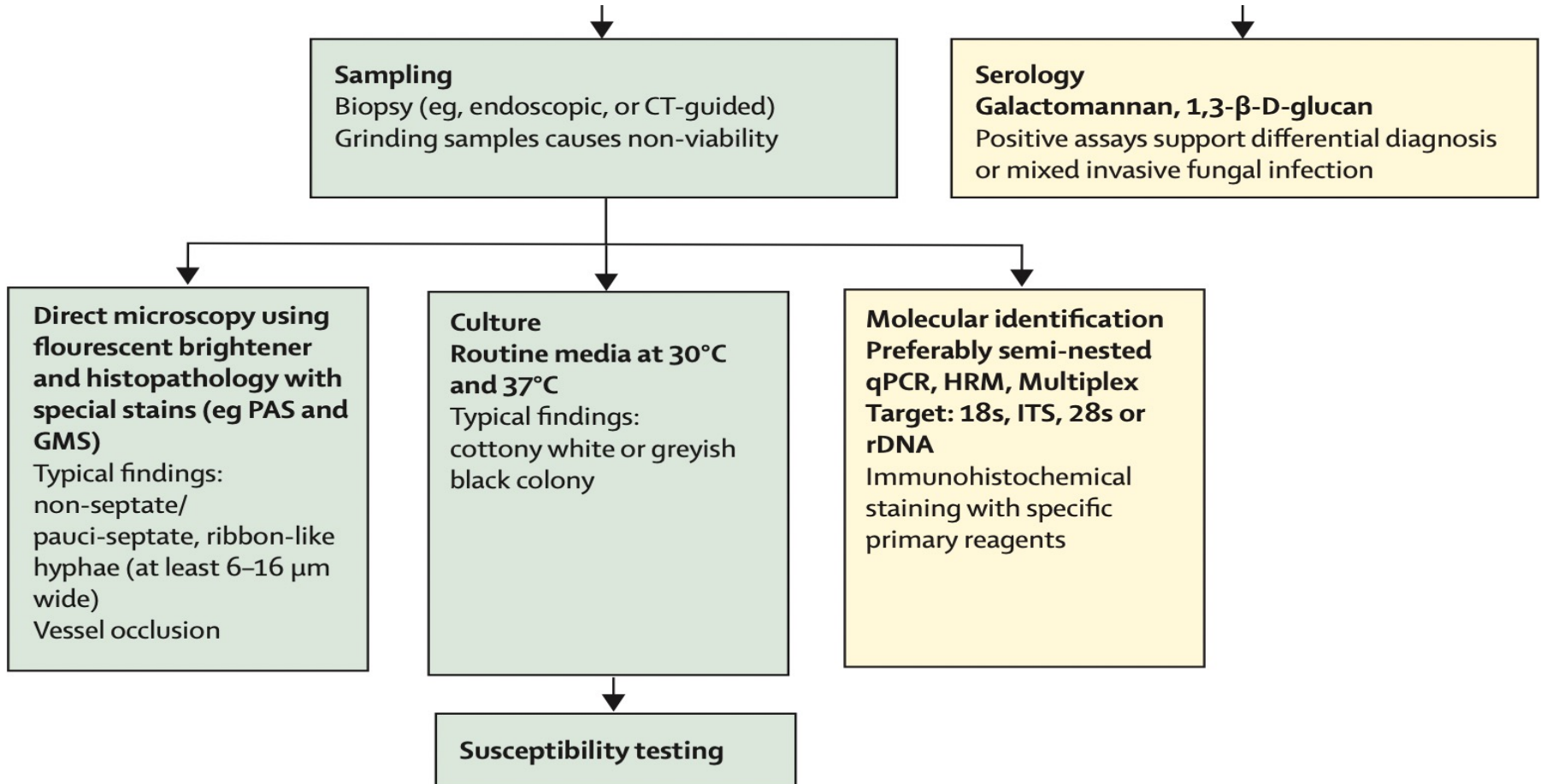
- ELISPOT (Mucorales-specific T cells saptanması)
- Molecular testler (PCR)
 - Taze klinik materyal
 - Parafinli örnek
 - Serum
 - Kültür
- MALDI-TOF

Henüz standardize edilememiştir

Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium



Oliver A Cornely, Ana Alastruey-Izquierdo, Dorothee Arenz, Sharon C A Chen, Eric Dannaoui, Bruno Hochhegger, Martin Hoenigl, Henrik E Jensen, Katrien Lagrou, Russell E Lewis, Sibylle C Mellinghoff, Mervyn Mer, Zoi D Pana, Danila Seidel, Donald C Sheppard, Roger Wahba, Murat Akova, Alexandre Alanio, Abdullah M S Al-Hatmi, Sevtap Arikian-Akdagli, Hamid Badali, Ronen Ben-Ami, Alexandro Bonifaz, Stéphane Bretagne, Elio Costantini, Muthu Chandrasekaran, Amal K Chhabra, Ross F Compton, Lutz Guder, Lutz Hees, Andrew H Groll, James Gubbins, Chris Hatfield



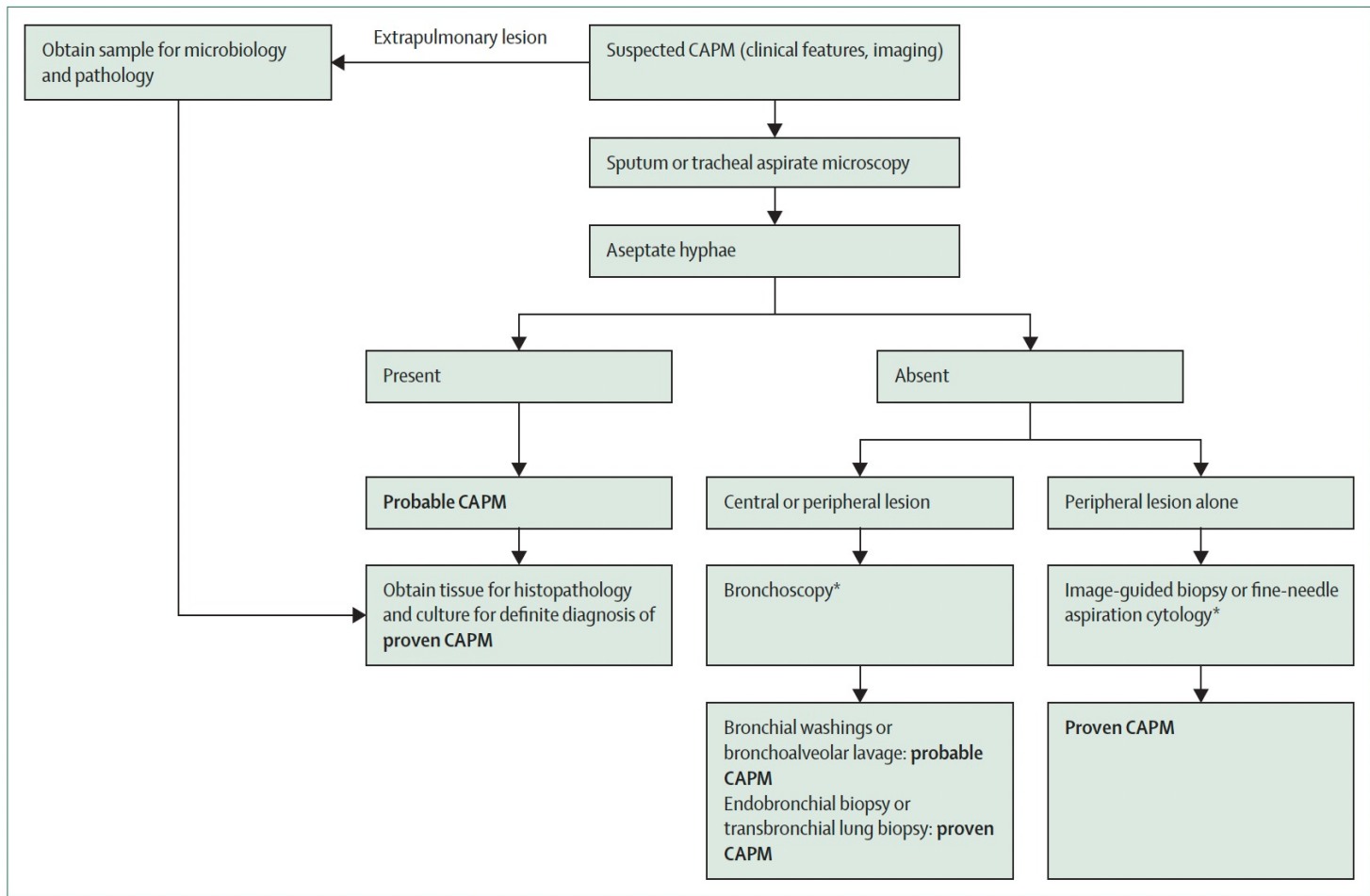


Figure 1: Diagnostic algorithm for evaluating suspected CAPM
 CAPM=COVID-19-associated pulmonary mucormycosis. *Direct microscopy or histopathology showing broad aseptate hyphae.

Tedavi

- Antifungal tedavi
- Uygun ve erken cerrahi debritleme
- Altta yatan koşulların kontrolü/tedavisi

Delaying amphotericin B-based frontline therapy significantly increases mortality among patients with hematologic malignancy who have zygomycosis.

Chamilos G¹, Lewis RE, Kontoyiannis DP.

⊕ Author information

Abstract

BACKGROUND: Zygomycosis is an emerging opportunistic mycosis among immunocompromised patients with a particularly poor prognosis.

METHODS: We analyzed the impact of delaying effective amphotericin B-based therapy on outcome among 70 consecutive patients with hematologic malignancy who had zygomycosis in our institution during the period 1989-2006. We used classification and regression tree analysis to identify the mortality breakpoint between early and delayed treatment.

RESULTS: Delayed amphotericin B-based therapy (i.e., initiating treatment ≥ 6 days after diagnosis) resulted in a 2-fold increase in mortality rate at 12 weeks after diagnosis, compared with early treatment (82.9% vs. 48.6%); this remained constant across the years of the study and was an independent predictor of poor outcome (odds ratio, 8.1; 95% confidence interval, 1.7-38.2; $P = .008$) in multivariate analysis. Active malignancy ($P = .003$) and monocytopenia ($P = .01$) at the time of diagnosis of infection were also independently associated with a poor

Tedaviye erken başlanması mortaliteyi 2 kat azaltmış

hematological malignancy who are at an increased risk for zygomycosis.

In Vitro Activities of Posaconazole, Itraconazole, Voriconazole, Amphotericin B, and Fluconazole against 37 Clinical Isolates of Zygomycetes

Qiu N. Sun,^{1,2} Annette W. Fothergill,^{3*} Dora I. McCarthy,³
Michael G. Rinaldi,^{3,4} and John R. Graybill^{1,4}

Int J Antimicrob Agents. 2019 Jan 9. pii: S0924-8579(19)30002-0. doi: 10.1016/j.ijantimicag.2019.01.002. [Epub ahead of print]

The contemporary management and clinical outcomes of mucormycosis: a systematic review and meta-analysis of case reports.

Jeong W¹, Keighley C², Wolfe R³, Lee WL¹, Slavin MA⁴, Chen SC², Kong DCM⁵.

- İnvitro çalışmalarda amfoterisin B ve posakonazol mucorales takımına en etkili ajanlar
- İsavukonazol mukorales takımına etkili (*M. circinelloides* hariç), ancak MİK değerleri posakonazolden 2-3 adım daha yüksek

Isavuconazole treatment for mucormycosis: a single-arm open-label trial and case-control analysis



Francisco M Marty, Luis Ostrosky-Zeichner, Oliver A Cornely, Kathleen M Mullane, John R Perfect, George R Thompson III, George J Alangaden, Janice M Brown, David N Fredricks, Werner J Heinz, Raoul Herbrecht, Nikolai Klimko, Galina Klyasova, Johan A Maertens, Sameer R Melinkeri, Ilana Oren, Peter G Pappas, Zdeněk Ráčil, Galia Rahav, Rodrigo Santos, Stefan Schwartz, J Janne Vehreschild, Jo-Anne H Young, Ploenchan Chetchotisakd, Sutep Jaruratanasirikul, Souha S Kanj, Marc Engelhardt, Achim Kaufhold, Masanori Ito, Misun Lee, Carolyn Sasse, Rochelle M Maher, Bernhardt Zeiher, Maria J G T Vehreschild, for the VITAL and FungiScope Mucormycosis Investigators*

Summary

Background Mucormycosis is an uncommon invasive fungal disease with high mortality and few treatment options. Isavuconazole is a triazole active in vitro and in animal models against moulds of the order Mucorales. We assessed the efficacy and safety of isavuconazole for treatment of mucormycosis and compared its efficacy with amphotericin B in a matched case-control analysis.

Methods In a single-arm open-label trial (VITAL study), adult patients (≥ 18 years) with invasive fungal disease caused by rare fungi, including mucormycosis, were recruited from 34 centres worldwide. Patients were given isavuconazole

Lancet Infect Dis 2016

Published Online

March 8, 2016

[http://dx.doi.org/10.1016/S1473-3099\(16\)00071-2](http://dx.doi.org/10.1016/S1473-3099(16)00071-2)

See Online/Comment

[http://dx.doi.org/10.1016/S1473-3099\(16\)00127-4](http://dx.doi.org/10.1016/S1473-3099(16)00127-4)

Isavukonazol

- İkinci kuşak triazol
- Oral ve IV formları mevcut
- Mart 2015 mukormikoz için FDA onayı

Isavuconazole treatment for mucormycosis: a single-arm open-label trial and case-control analysis



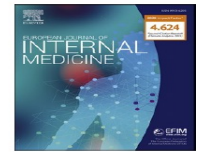
Francisco M Marty, Luis Ostrosky-Zeichner, Oliver A Cornely, Kathleen M Mullane, John R Perfect, George R Thompson III, George J Alangaden, Janice M Brown, David N Fredricks, Werner J Heinz, Raoul Herbrecht, Nikolai Klimko, Galina Klyasova, Johan A Maertens, Sameer R Melinkeri, et al.

	Isavuconazole	Amphotericin B	p value
Crude all-cause mortality, n/N (%; 95% CI)*	7/21 (33%; 14.6–57.0)	13/33 (39%; 22.9–57.9)	p=0.775†
Weighted all-cause mortality (%; ‡ 95% CI)*	33%; 13.2–53.5	41%; 20.2–62.3	p=0.595§
Crude mortality by matching covariates, n/N (%)			
Haematological malignancy	5/11 (45%)	7/18 (39%)	NA
Severe disease¶	6/12 (50%)	8/13 (62%)	NA
Surgical treatment	4/9 (44%)	3/13 (23%)	NA

Primary treatment with isavuconazole-treated cases (VITAL) versus amphotericin B-treated controls (FungiScope).
 *95% CI are based on an exact binomial distribution (crude) or normal approximation (weighted). †Calculated from Fisher's exact test. ‡Weights were applied according to the ratio of the number of controls matched to each case.
 §Calculated from a χ^2 test. ¶CNS involvement or disseminated disease (defined as disease involving >1 non-contiguous organ). ||Resection or debridement at the site of infection at treatment start (SD 7 days).

Table 5: All-cause mortality through day 42 for a matched case-control analysis of patients with mucormycosis

İsavukonazol ve AmB etkinlik açısından benzer bulunmuş



Original article

Survival in rhino-orbito-cerebral mucormycosis: An international, multicenter ID-IRI study

Yasemin Cag^{a,*}, Hakan Erdem^b, Mehmet Gunduz^c, Suheyra Komur^d, Handan Ankarali^e,

Abstract

Background: Mucormycosis is an emerging aggressive mold infection. This study aimed to assess the outcome of hospitalized adults with rhino-orbito-cerebral mucormycosis (ROCM). The secondary objective was to identify prognostic factors in this setting.

Methods: This study was an international, retrospective, multicenter study. Patients' data were collected from 29 referral centers in 6 countries. All qualified as "proven cases" according to the EORTC/MSGERC criteria.

Results: We included 74 consecutive adult patients hospitalized with ROCM. Rhino-orbito-cerebral type infection was the most common presentation ($n = 43$; 58.1%) followed by rhino-orbital type ($n = 31$; 41.9%). Twenty (27%) had acquired nosocomial bacterial infections. A total of 59 (79.7%) patients (16 in combination) received appropriate antifungal treatment with high-doses of liposomal amphotericin B. Fifty-six patients (75.7%) underwent curative surgery. Thirty-five (47.3%) required intensive care unit admission (27; 36.5% under mechanical ventilation). Hospital survival was 56.8%, being reduced to 7.4% in patients with invasive mechanical ventilation. A multivariate binary backward logistic regression model identified confusion at admission (OR 11.48), overlapping hospital-acquired infection (OR 10.27), use of antifungal treatment before diagnosis (OR 10.20), no surgical debridement (OR 5.92), and the absence of prior sinusitis (OR 6.32) were independently associated with increased risk for death.

Conclusion: Today, ROCM still has high mortality rate. Improving source control, rational therapy, and preventing nosocomial infections may improve survival in this severe infection.

Keywords: Debridement; Hospital-acquired infection; Mucormycosis; Neutropenia; Rhino-orbito-cerebral mucormycosis; Risk Factors.

Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium



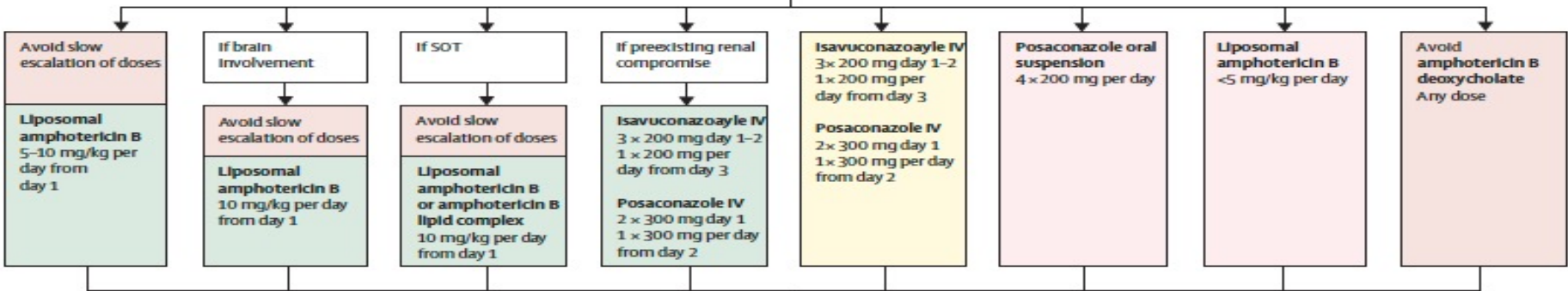
Oliver A Cornely, Ana Alastruey-Izquierdo, Dorothee Arenz, Sharon C A Chen, Eric Dannaoui, Bruno Hochhegger, Martin Hoenigl, Henrik E Jensen, Katrien Lagrou, Russell E Lewis, Sibylle C Mellinghoff, Mervyn Mer, Zoi D Pana, Danila Seidel, Donald C Sheppard, Roger Wahba, Murat Akova, Alexandre Alario, Abdullah M S Al-Hatmi, Sevtap Arikian-Akdagli, Hamid Badali, Ronen Ben-Ami, Alexandro Bonifaz, Stéphane Bretagne, Elio...

Strongly recommended
 Moderately recommended
 Marginally recommended
 Recommended against

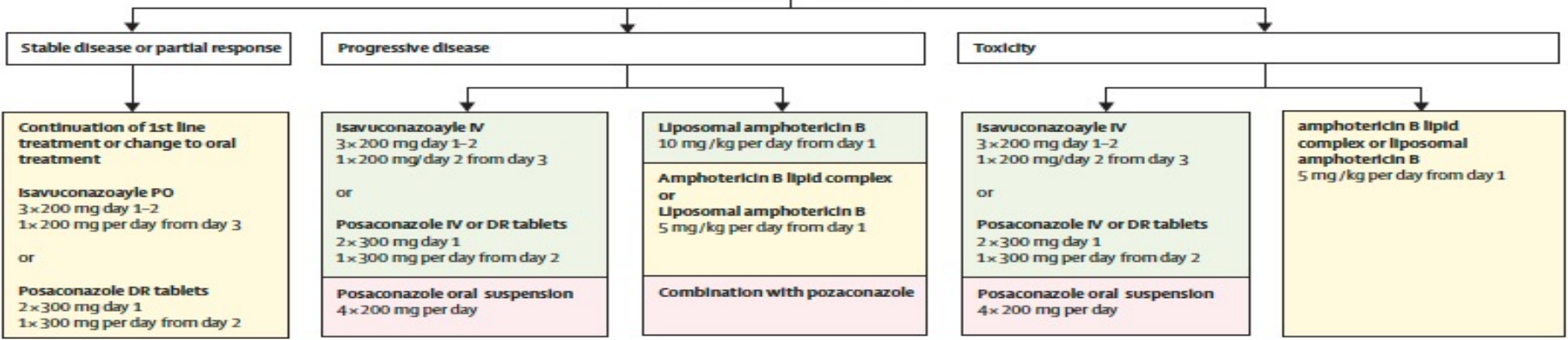
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Suspected and confirmed mucormycosis are emergencies and require rapid action

Surgical debridement with clean margins for 3 purposes: (1) disease control, (2) histopathology, (3) microbiological diagnostics
 Plus
 Immediate treatment initiation



Response assesment (eg weekly imaging)



Pulmoner CAM Tedavi

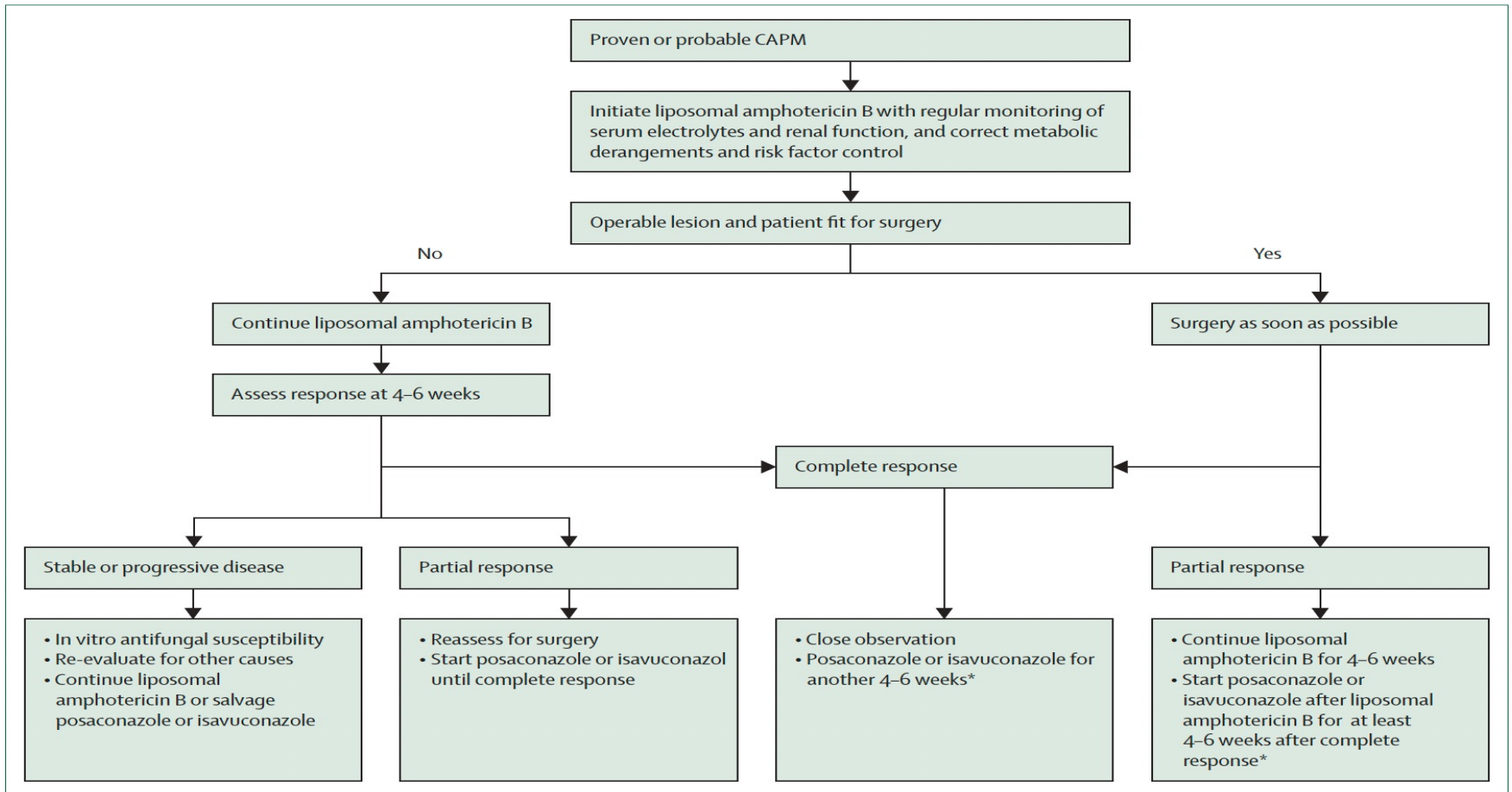


Figure 2: Proposed algorithm for treating CAPM

CAPM=COVID-19-associated pulmonary mucormycosis. *Treatment duration should be individualised and could be extended up to 12 weeks after complete response.

Pulmoner CAM Tedavi Yanıtı

Definition

Success

Complete response	Survival and resolution of all attributable clinical features (symptoms and signs) of disease, and resolution of the radiological lesion (or lesions) or persistence of only a scar or postoperative changes that can be equated with a complete radiological response
Partial response	Survival and resolution of all attributable clinical features (symptoms and signs) of disease, and a 25% or higher reduction in the diameter of radiological lesion (or lesions); or radiological stabilisation (<25% reduction in the diameter of the lesion), and resolution of all attributable symptoms and signs of fungal disease

Failure

Stable disease	Survival and minor or no improvement in all attributable clinical features (symptoms and signs) of disease and radiological stabilisation (<25% reduction in the diameter of the lesion)
Progressive disease	Worsening clinical symptoms or signs of disease, and new sites of disease or radiological worsening of pre-existing lesions or persistent isolation of Mucorales
Death	Death due to any cause during the period of assessment

The criteria have been adapted from the Mycoses Study Group and European Organisation for Research and Treatment of Cancer consensus criteria for response assessment in invasive mould disease.¹⁰⁶

Table 2: Response assessment criteria in COVID-19 associated pulmonary mucormycosis

Altta Yatan Koşulların Kontrolü

- Diyabetin kontrolü
- Hasta nötropenikse hemopoietik growth faktör verilmesi
- Steroidin kesilmesi veya azaltılması
- Deferoxamin tedavisinin kesilmesi
- İmmun supresyonun azaltılması

Tedavi Süresi

- Hasta bazında değerlendirilmeli
- Klinik ve radyolojik tam iyileşme
- Altta yatan risk faktörleri düzelene kadar

Tedaviye devam edilmeli

Sonuç

- Ciddi COVID hastalarında özellikle yüksek doz steroid kullanımı ve immun module edici tedaviler CAM için risk oluşturmakta
- Özellikle YBÜ yatışı gerektiren ciddi COVID hastalarında; antibiyotik tedavisine yanıt vermeyen ateş, klinik ve radyolojik kötüleşme durumunda IFI olasılığı düşünölmeli
- Klinisyenler COVID-19 hastalarında ciddi bağışıklık sistemi baskılayıcı koşullar olmasa bile COVID-19 ile ilişkili mukormikozu mutlaka akılda tutmalıdır.

