VII CONGRESO SEICAV
Sociedad Española de Infecciones Cardiovasculares
SEVILLA 16 Y 17 DE NOVIEMBRE DE 2018

MESA 1

Novedades en el diagnóstico y tratamiento de la Endocarditis.

Paciente con EI por SAMS en válvula protésica biológica

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Hospital Universitario Virgen de las Nieves, Granada

16 DE NOV 2018

SEVILLA

Caso

- Paciente 71 con AP FA, DM-2, válvula protésica biológica aórtica (Heteroinjerto porcino con stent) desde hacia unos 3 años por una valvulopatia reumática (estenosis aórtica), hiperlipidemia en tratamiento con Bisoprolol, Metformina, sintrom, y Atorvastatina.
- Acude a urgencias por un síndrome febril de 12 h de evolución de hasta 38,4ºC, intensos escalofríos, tos irritativa, sensación disneica y malestar general.
- Exploración física:
  - Fr 24rpm, SO2 92%, Fc 120lpm, Tª 38,5ºC, TA 100/50mmhg, sensación de enfermedad.
  - No tolera el decúbito.
  - ACR soplo sistólico polifocal 2/6. Crepitantes bibasales gruesos.
  - Abdomen globuloso, blando, depresible, RI conservados, no se palpan masas, megalias.
  - MMII: edemas de +/+++.

¿Qué harías con el paciente?

- 1-Sacar hemocultivos, analítica y esperar resultados.
- 2-Sacar hemocultivos, analítica, Rx tórax, ECG y pautar tratamiento antibiótico empírico puesto que el paciente tiene qSOFA 2.
- 3-Sacar hemocultivos, analítica, Rx tórax, ECG y pautar tratamiento antibiótico empírico puesto que el paciente tiene qSOFA2 y pedir ECOcardio de urgencias.
- 4- Lo dejaría en sillones le pondría paracetamol para ver evolución porque estamos en época de gripe, y alta.

- Analítica:
  - Hb 12g/dL. Leucocitos 13000 leuc/mm3 (90%PMN), plaquetas 270.000 cél/mm3.
  - PCR 170 mg/dL;PCT 4; láctico 2. BNP 500 pg/mL.
  - Creatinina 1.7mg/dL; urea 70 mg/dL; K 3,5 meq; Na 134 meq.
  - GOT 40 UI; GPT 45UI; FA 105 mg/dL; GGT 75 mg/dL, Bt 1.
  - Coagulación INR 2,5; fibrinógeno 700.
- Se extrajeron Hemocultivos.
- ECG: FA, eje normal, 120 lpm, no hay alteraciones en QRS ni en ST.
- Rx de tórax: pinzamiento de ambos senos costo-frénicos, hilios congestivos, ICT en el límite, aurícula izquierda aumentada.

- ECOcardio TT: imagen en cara ventricular de Valva aórtica anterior un eco áspero e irregular, oscilante sugerente de vegetación. I. Ao leve-moderada. AI dilatada. VI ligeramente dilatado. FE 50%.
- Se ingresa se pone tto antibiótico Daptomicina 10mg/kg/24h + cloxacilina 2g/iv/4h.
- A las 12h del ingreso nos avisan por Hemocultivos positivos cocos gram positivos en racimo (estafilococos) en las 4 tomas.

- A las 48h nos informan de que es SAMS se le deja en tto con cloxacilina 2g/iv/4h y se asocia rifampicina 600mg/iv/24h.
- En 96 h el paciente queda afebril y los reactantes de fase aguda están prácticamente normalizados, PCR 50, PCT normal, leucocitos, plaquetas normales y función renal normales.
- Al 7º día se hace ETE: no hay datos de absceso en el anillo de la válvula aórtica, insuficiencia aortica leve-moderada, y una imagen de 1,1 cm de aspecto irregular adherida a la valva anterior de V Ao sugerente de vegetación, oscilante, FE 50%. AI dilatada. No se puede medir presión pulmonar.

- El paciente al 8º día de ingreso presentó un episodio de apraxia, acalculia, disfasia, alexia, desorientación, amaurosis izquierda que le duró unos 20 minutos, recuperándose sin secuelas.
- Se le administró 300mg de AAS.
- Se extrajo: Hemocultivos sin fiebre.
  - Hemograma: Hb 10g/dL, plaquetas 250; leucocitos 10500 cél/uL.
  - Bioquímica: Urea 40, creatinina 1.1 mg/dL, Na 135, K 3,2, Ca 9,7; BT 1;
- ECG: FA, 80lpm, eje izquierdo, no datos de isquemia.
- Coagulación: fibrinógeno 200, INR 3; TP 60%
- TAC cerebral de urgencias: lesiones antiguas isquémicas lacunares, leve atrofia cortical, pero sin datos actuales de hemorragia, ni isquemia, no se observan émbolos.

- Al 10 día el paciente se encontraba práctimente asintomático, andando por la planta, y se le hizo una ECO-ETT sin empeoramiento valvular y sin imágenes sugerentes de vegetación.

¿Qué haría usted en este momento?

- 1- Contactaría con Cirugía cardiovascular para explantación e implantación nueva válvula
- 2- Contactaría con C Cardiovascular para valoración y solicitaría PET cardiaco.
- 3- Extraería hemocultivos incluso sin fiebre, lo presentaría en grupo multidisciplinar (Endocarditis "Team") y propondría PET/TAC Cardiaco.
- 4- Sacaría hemocultivos, y seguiría tratamiento antibiótico hasta completar 4-6 semanas si los Hemos fueran negativos.

Management Strategies and Outcome for Prosthetic Valve Endocarditis

Fabio Chirillo, MD[a,*], Piergiorgio Scotton, MD[b], Francesco Rocco, MD[c], Roberto Rigoli, MD[d], Alessandra Pedrocco, MD[a], Paola Martire, MD[a], Alessandro Daniotti, MD[a], Giuseppe Minniti, MD[c], Elvio Polesel, MD[c], and Zoran Olivari, MD[a]

The aim of this study was to assess the impact of an operative protocol with a multidisciplinary approach on the outcome of patients with prosthetic valve endocarditis (PVE). A formal policy for the care of PVE was introduced at our hospital in 2003 in which patients were referred to and managed by a preexisting team involving a cardiologist, a specialist in infectious diseases, and a cardiac surgeon. All patients underwent transesophageal echocardiography as soon as clinical suspicion of PVE arose. If high-risk conditions such as heart failure, ring abscess, conditions associated with impending malfunctioning of the prosthesis, or vegetations at high risk for systemic embolization were found during the initial multidisciplinary evaluation (performed within 12 hours of admission), patients were operated on within 48 hours. Stable patients were evaluated weekly by the multidisciplinary team, and on-treatment surgery was performed whenever high-risk conditions developed or when there was persistent fever/bacteremia after 1 week of adequate antibiotic therapy. Comparing the period 2003 through 2009 with 1996 through 2002 (when a multidisciplinary policy was not followed), patients with PVE were more numerous (61 vs 38), older (mean age 68.3 vs 63.1, $p = 0.01$), and had more comorbidities (mean Charlson index 3.15 vs 2.42, $p = 0.03$). The most frequent causative organisms were *Staphylococci* in both periods. In the second period, fewer patients had delayed diagnosis (39% vs 71%, $p = 0.03$), heart failure (20% vs 45%, $p = 0.01$), abscess (20% vs 39%, $p = 0.04$), culture-negative infective endocarditis (11% vs 29%, $p = 0.03$), and worsened renal function (21% vs 42%, $p = 0.04$). A significant reduction in in-hospital mortality (53% to 23%, $p = 0.04$) and 3-year mortality (60% to 28%, $p = 0.001$) was observed, driven by the increased number of patients successfully treated with medical therapy alone (44% vs 16%, $p = 0.04$). In conclusion, formalized, collaborative management led to significant improvement in PVE-related mortality. © 2013 Elsevier Inc. All rights reserved. (Am J Cardiol 2013;112:1177–1181)

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Demographic, clinical, microbiological, and echocardiographic characteristics of 99 patients with prosthetic valve endocarditis during the 2 periods

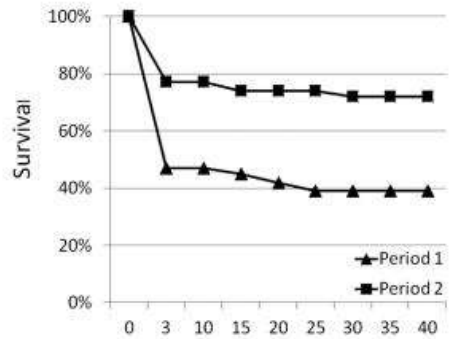
Variable	Period 1	Period 2	p Value
Mitral	14 (37%)	21 (34%)	0.83
Aortic and mitral	2 (5%)	3 (5%)	1
Initial regurgitation 2+/4+	20 (52%)	26 (43%)	0.41
High-risk vegetations	10 (26%)	12 (20%)	0.46
Abscess	15 (39%)	12 (20%)	0.04
Left ventricular ejection fraction <0.45	14 (37%)	32 (52%)	0.15
Causative agents			
Oral *Streptococci*	2 (10%)	3 (5%)	1
Group D *Streptococci*	2 (10%)	7 (11%)	0.47
Staphylococcus aureus	11 (34%)	24 (39%)	0.39

Table 2
Outcome data of 99 patients with prosthetic valve endocarditis according to the period of observation and treatment

Variable	Period 1	Period 2	p Value
Mechanical prosthetic valve	2 (17%)	0	0.13

Table 3
Multivariate analysis of 3-year mortality (Cox multivariate analysis)

Diabetes mellitus	2.3	0.9–13	0.32
Renal failure	2.1	0.7–3.8	0.10
Immunosuppression	15.3	0.9–12	0.17
Charlson co-morbidity index	11	0.5–22	0.33
Charlson co-morbidity index >2	1.9	0.9–5.2	0.10



an Journal of Cardiology 2013;
112(8):1177-81.

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Rev Bras Cir Cardiovasc. 2014 Jan-Mar;29(1):16-24.

Surgical treatment of aortic valve endocarditis: a 26-year experience.

Adademir T[1], Tuncer EY[1], Tas S[1], Donmez AA[1], Polat EB[2], Tuncer A[1].

Author information

Abstract

OBJECTIVE: We have retrospe
years.

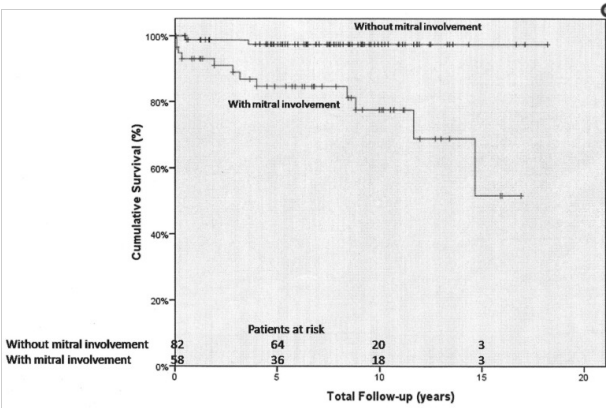
METHODS: From June 1985 to
(79.3%) patients were male an
endocarditis. The mean durati

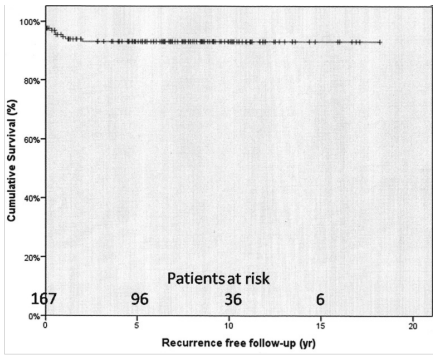
RESULTS: Two hundred and e
replacement with mechanical p
patients had low cardiac outpu
61.1±10.3%, respectively. In-h
renal failure and low cardiac o
was found to be a significant ri

- 283 EI intervenidas (1985-2011).
- 15.5% de mortalidad intra-hospitalaria lo que se asociaba a:

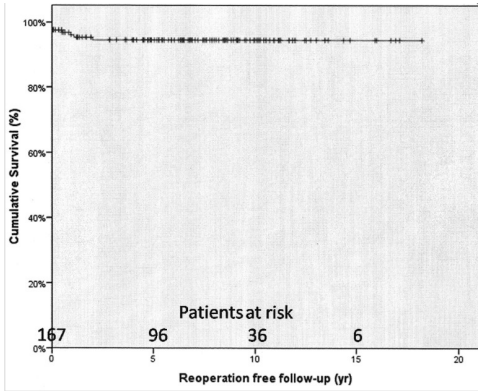
-Género femenino.
-Intervención de emergencia
-Insuficiencia renal post-operaratoria
-Bajo gasto cardiaco.

CONCLUSION: Surgery for aortic valve endocarditis has significant mortality. Emergency operation, female gender, postoperative renal failure and low cardiac output are significant risk factors. Risk for recurrence and need for reoperation is low.





Survival free from recurrence



Survival free from reoperation

Interactive Cardiovascular and Thoracic Surgery 15 (2012) 1057–1062
doi:10.1093/icvts/ivs372 Advance Access publication 24 August 2012

BEST EVIDENCE TOPIC - ADULT CARDIAC

Do all patients with prosthetic valve endocarditis need surgery?

Saina Attaran*, Andrew Chukwuemeka, Prakash P. Punjabi and Jon Anderson

Department of Cardiothoracic Surgery, Hammersmith Hospital, Imperial College, London, UK

- Tan pronto como la EIVP es diagnosticada hay que contactar con el cirujano.
- La cirugía debería realizarse tan pronto como sea posible en caso de:
  - **Insuficiencia cardiaca.**
  - **disfunción valvular.**
  - **regurgitación/obstrucción severa.**
  - **dehiscencia y absceso anular.**
  - ***S. aureus* en EIVP.**
- La cirugía debería hacerse antes de la aparición de complicaciones como émbolos cerebrales.
- En pacientes con EIVP estables, con otros micirooganismo no SA, sin complicaciones valvulares ni cardiacas, la cirugía puede posponerse.

BMC Res Notes. 2017 Nov 9;10(1):580. doi: 10.1186/s13104-017-2907-z.

A complicated prosthetic valve endocarditis due to methicillin resistant Staphylococci treated with linezolid and ciprofloxacin: a case report.

Amiyangoda CGK[1], Wimalaratna H[2], Bowatte S[2].

Heart Lung. 2005 Jan-Feb;34(1):69-71.

Methicillin-resistant Staphylococcus aureus prosthetic aortic valve endocarditis with paravalvular abscess treated with daptomycin.

Mohan SS[1], McDermott BP, Cunha BA.

Open Forum Infect Dis. 2015 Oct 29;2(4):ofv156. doi: 10.1093/ofid/ofv156. eCollection 2015 Dec.

Prolonged Use of Oritavancin for Vancomycin-Resistant Enterococcus faecium Prosthetic Valve Endocarditis.

Johnson JA[1], Feeney ER[2], Kubiak DW[3], Corey GR[4].

⊕ Author information

Abstract

Oritavancin is a novel lipoglycopeptide with activity against Gram-positive organisms including streptococci, methicillin-resistant Staphylococcus aureus, vancomycin-resistant S aureus (VRSA), and vancomycin-resistant enterococci (VRE) [1-3]. The US Food and Drug Administration approved oritavancin as a single intravenous dose of 1200 mg for the treatment of acute bacterial skin and skin structure infections on the basis of 2 clinical trials demonstrating noninferiority compared with vancomycin [4, 5]. There are limited options for treatment of serious VRE infections. Monotherapy with daptomycin or tigecycline or linezolid may be sufficient in some cases, but combination therapy is often indicated for severe or complicated infections such as endocarditis. Several antibiotic combinations have been used in isolated case reports with some efficacy, including the following: high-dose ampicillin with an aminoglycoside [6], ampicillin with ceftriaxone or imipenem [7, 8], high-dose daptomycin with ampicillin and gentamicin [9] or with gentamicin and rifampin [10], daptomycin with tigecycline [11, 12], quinupristin-dalfopristin with high-dose ampicillin [13] or doxycycline and rifampin [14], and linezolid with tigecycline [15]. The limited efficacy, limited susceptibility, and extensive toxicities with many of these agents and combinations present barriers to effective treatment. Additional treatment options for VRE endocarditis would be valuable. Although oritavancin has been shown to have in vitro activity against some isolates of VRE, clinical data are lacking. We describe the first use of a prolonged course of oritavancin in the treatment of a serious VRE infection, prosthetic valve endocarditis.

J Am Heart Assoc. 2018 Sep 4;7(17):e010027. doi: 10.1161/JAHA.118.010027.

Cardiac Surgery Compared With Antibiotics Only in Patients Developing Infective Endocarditis After Transcatheter Aortic Valve Replacement.

Mangner N[1], Leontyev S[2], Woitek FJ[1], Kiefer P[2], Haussig S[1], Binner C[2], Mende M[3], Schlotter F[4], Stachel G[4], Höllriegel R[1], Hommel J[1], Binner-Oussenek K[5], Misfeld M[2], Thiele H[4,6], Borger MA[2], Holzhey D[2], Linke A[1].

⊕ Author information

- Comparar (Cirugia+AB vs AB+tto médico)de EI tras TAVI
- 22 Cirugia+ ab vs 44 Ab+tto médico (más mayores p=0,006; score STS p =0,029 y más IR crónica (p=0,037).
- No había diferencias de mortalidad al año 65% (cirugía) vs 68.2 (ab); p=0.802.
- Los FR de mortalidad al año: cualquier indicación de cirugía HR 6.20 (1.8-21.4); sepsis (HR 4.03 (1.97-8.24); I. mitral > o igual 2 (HR 2.91 (1.33-6.37).
- Debe de hacerse decisión individualizada en el contexto de un Endocarditis team.

most reasonable treatment option.

Clin Infect Dis. 2015 Mar 1;60(5):741-9. doi: 10.1093/cid/ciu871. Epub 2014 Nov 10.

Impact of early valve surgery on outcome of Staphylococcus aureus prosthetic valve infective endocarditis: analysis in the International Collaboration of Endocarditis-Prospective Cohort Study.

Chirouze C[1], Alla F[2], Fowler VG Jr[3], Sexton DJ[3], Corey GR[3], Chu VH[3], Wang A[3], Erpelding ML[4], Durante-Mangoni E[5], Fernández-Hidalgo N[6], Giannitsioti E[7], Hannan MM[8], Lejko-Zupanc T[9], Miró JM[10], Muñoz P[11], Murdoch DR[12], Tattevin P[13], Tribouilloy C[14], Hoen B[15]; ICE Prospective Investigators.

⊕ Collaborators (318)

⊕ Author information

Abstract

BACKGROUND: The impact of early valve surgery (EVS) on the outcome of Staphylococcus aureus (SA) prosthetic valve infective endocarditis (PVIE) is unresolved. The objective of this study was to evaluate the association between EVS, performed within the first 60 days of hospitalization, and outcome of SA PVIE within the International Collaboration on Endocarditis-Prospective Cohort Study.

METHODS: Participants were enrolled between June 2000 and December 2006. Cox proportional hazards modeling that included surgery as a time-dependent covariate and propensity adjustment for likelihood to receive cardiac surgery was used to evaluate the impact of EVS and 1-year all-cause mortality on patients with definite left-sided S. aureus PVIE and no history of injection drug use.

RESULTS: EVS was performed in 74 of the 168 (44.3%) patients. One-year mortality was significantly higher among patients with S. aureus PVIE than in patients with non-S. aureus PVIE (48.2% vs 32.9%; P = .003). Staphylococcus aureus PVIE patients who underwent EVS had a significantly lower 1-year mortality rate (33.8% vs 59.1%; P = .001). In multivariate, propensity-adjusted models, EVS was not associated with 1-year mortality (risk ratio, 0.67 [95% confidence interval, .39-1.15]; P = .15).

CONCLUSIONS: In this prospective, multinational cohort of patients with S. aureus PVIE, EVS was not associated with reduced 1-year mortality. The decision to pursue EVS should be individualized for each patient, based upon infection-specific characteristics rather than solely upon the microbiology of the infection causing PVIE.

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Table 2. Factors Associated With the Performance of Early Valve Surgery in *Staphylococcus aureus* Prosthetic Valve Infective Endocarditis Patients (Propensity Analysis)

	SA PVIE (n = 167)	EVS (n = 74)		Univariate Analysis			Multivariate Analysis	
Characteristic	No.	No.	%	OR	95% CI	*P* Value	OR	95% CI
Male sex	98	42	42.9	1		.65		
Female sex	69	32	46.4	1.2	.6–2.1			
Age ≤ 65 y	84	42	50.0	1		.14		
Age >65 y	83	32	38.6	0.6	.3–1.2			
Duration of symptoms >1 mo prior to presentation	17	12	70.6	3.3	1.1–9.8	.04		
Chronic hemodialysis	15	3	20.0	0.3	.1–1.0	.03		
Diabetes mellitus	31	9	29.0	0.4	.2–1.0	.05		
Cancer	12	7	58.3	1.9	.6–6.1	.30		
Charlson index, per 1 unit	79	33	41.8	1.1	.8–1.4	.58		
Nosocomial IE	72	33	45.8	1.2	.7–2.3	.53		
Prior history of IE	32	14	43.8	1.0	.4–2.1	.95		
Intracardiac device	27	9	33.3	0.6	.2–1.4	.22		
Evidence of new regurgitation	73	36	49.3	1.4	.8–2.6	.28		
Paravalvular complications	54	36	66.7	3.9	2.0–7.7	<.0001	4.1	1.9–8.6
Prosthetic valve dehiscence	15	12	80.0	5.8	1.6–21.3	.003		
CHF (NYHA class III or IV)	43	17	39.5	0.8	.4–1.6	.46		
Stroke	57	27	47.4	1.2	.6–2.3	.59		
Embolic event	26	14	53.8	1.6	.7–3.6	.29		
Intracardiac abscess	44	29	65.9	3.4	1.6–7.0	.0008		

Abbreviations: CHF, congestive heart failure; CI, confidence interval; EVS, early valve surgery; IE, infective endocarditis; NYHA, New York Heart Association; OR, odds ratio; PVIE, prosthetic valve infective endocarditis; SA, *Staphylococcus aureus*.

Table 3. Prognostic Multivariate Model Adjusted on Age, Sex, Stroke, Heart Failure, Paravalvular Complications, and Early Valve Surgery—Endpoint: In-Hospital Mortality

Variable	RR	95% CI	*P* Value
Age (per 1-year increment)	1.03	1.01–1.05	.0075
Female sex	1.17	.68–2.01	.58
Stroke (time-dependent)	2.94	1.68–5.14	<.0002
Cardiac failure (NYHA class III or IV)	2.00	1.13–3.50	.0163
Early valve surgery (time-dependent)	0.82	.41–1.62	.5645

Model is based on 166 patients, after exclusion of 2 cases due to missing data.

Abbreviations: CI, confidence interval; NYHA, New York Heart Association; RR, risk ratio.

Table 4. Prognostic Multivariate Model Adjusted on Age, Sex, Stroke, Heart Failure, Paravalvular Complications, and Early Valve Surgery—Endpoint: 1-Year Mortality

Variable	RR	95% CI	*P* Value
Age (per 1-year increment)	1.03	1.01–1.05	.002
Female sex	1.43	.91–2.40	.12
Stroke (time-dependent)	2.54	1.58–4.09	<.0001
Cardiac failure (NYHA class III or IV)	2.02	1.25–3.26	.004
Paravalvular complications	1.20	.74–1.96	.46
Early valve surgery (time-dependent)	0.67	.39–1.15	.15

Model is based on 150 patients, after exclusion of 18 cases due to missing data.

Abbreviations: CI, confidence interval; NYHA, New York Heart Association; RR, risk ratio.

En consecuencia, los autores recomendaban individualizar la cirugía y no basar la decisión en el hecho de que el microorganismo implicado fuese un SA.

Clin Infect Dis. 2018 Oct 22. doi: 10.1093/cid/ciy908. [Epub ahead of print]

Investigating the impact of early valve surgery on survival in Staphylococcus aureus infective endocarditis using a marginal structural model approach - results of a large prospectively evaluated cohort.

Rieg S[1], von Cube M[2], Kaasch A[3], Bonaventura B[1], Bothe W[4], Wolkewitz M[2], Peyerl-Hoffmann G[1], Deppe AC[5], Wahlers T[5], Beyersdorf F[4], Seifert H[6,7], Kern WV[1].

- Analizan el impacto de una cirugía precoz en una EI por SA (dentro de 60 días)
- N=203 con EI, 50 se les hizo cirugía precoz.
- La mortalidad a los 30 días del 26%
- No encontraron que la cirugía precoz mejorara la supervivencia
- La cirugía en EI por SA debería ser individualizada.

RESULTS: 203 patients were included in the analysis, fifty patients underwent EVS. All-cause mortality at day 30 was 26%. In the conventional multivariable Cox regression model the effect of EVS on the death hazard was 0.85 (95% CI 0.47-1.52). Using the weighted cox model the death hazard rate of EVS was 0.71 (95% CI 0.34-1.49. In subgroup analyses no survival benefit was observed in patients with septic shock (HR 0.80 [CI 0.26-2.46]), in NVIE (HR 0.76 [CI 0.33-1.71]) or PVIE (HR 1.02 [CI 0.29-3.54]) or in patients with EVS within 14 days (HR 0.97 [CI 0.46-2.07]).

CONCLUSIONS: Using both a conventional Cox regression model and a weighted Cox model (MSM), we did not find a survival benefit for patients who underwent EVS in our cohort. Until results of randomized controlled trials are available, EVS in SAIE should be based on individualized decisions of an experienced multidisciplinary team.

- Endocarditis Team valoró al paciente y de forma conjunta actitud expectante en función de resultados de PET/TAC.
- PET/TAC no mostraba captación sugerente de infección.

Los beneficios del PET/TC(A) se relacionan mayoritariamente con la identificación temprana de la implicación endocárdica, una mejor evaluación de las lesiones perivalvulares, y la documentación de complicaciones extracardiacas (episodios embólicos silentes o episodios infecciosos metastásicos).

	Sensibilidad	Especificidad	Valor predictivo positivo	Valor predictivo negativo
Criterios de Duke (CD)	52%	94,7%	92,9%	59,7%
PET/TC	87%	92,1%	93,6%	84,3%
CD + PET/TC	90,7%	89,5%	92%	87,9%

	Sensibilidad	Especificidad	Valor predictivo positivo	Valor predictivo negativo
PET/TCA	91%	90,6%	92,8%	88,3%
PET/TC sin contraste	86,4%	87,5%	90,2%	82,9%

Pizzi MN. Circulation 2015, 132: 113-1126

Diapositiva 20

cHT1 carmen Hidalgo Tenorio; 04/11/2018

Int J Cardiovasc Imaging. 2018 Oct 31. doi: 10.1007/s10554-018-1487-x. [Epub ahead of print]

99mTc-HMPAO-labeled leukocyte SPECT/CT and transthoracic echocardiography diagnostic value in infective endocarditis.

Holcman K[1], Szot W[2,3], Rubiś P[4], Leśniak-Sobelga A[4], Hlawaty M[4], Wiśniowska-Śmiałek S[4], Małecka B[5], Ząbek A[5], Boczar K[5], Stępień A[4], Podolec P[4], Kostkiewicz M[4,2].

⊕ Auth

N=40 (pacientes con sospecha EI 2015-2016) comparan ETE vs PET/TC
PET encontró menor tasa de FP, mayor exactitud diagnóstica, especificidad y VPP que la ETE

Abstrac
Infective dy
was to e d
tomogra acic
echocar ± 18)
with suspected IE in the years 2015-2016. All patients underwent clinical evaluation, TTE and 99mTc-HMPAO-SPECT/CT for the assessment of lesions typical for IE. Scans were evaluated for the presence and location of increased radioactivity foci, corresponding to the accumulation of radiolabeled leukocytes in inflammatory lesions. After 6 months, the patients were re-evaluated clinically and with TTE. Final IE diagnosis was established in 14 (35%) patients. Lesions typical for IE were shown in 28 (70%) TTEs and 16 (40%) 99mTc-HMPAO-SPECT/CTs. The latter tests were characterized by 90% accuracy, 93% sensitivity, 88% specificity, 96% negative predictive value (NPV), 81% positive predictive value (PPV). TTE demonstrated 60% accuracy, 93% sensitivity, 42% specificity, 92% NPV, and 46% PPV. 99mTc-HMPAO-SPECT/CT was characterized by a lower number of false-positive results compared to TTE (3 vs. 15). In patients with suspected IE, 99mTc-HMPAO-SPECT/CT yields a smaller number of false-positive results, significantly higher diagnostic accuracy, specificity and PPV than TTE. It helps to differentiate IE infectious and sterile echocardiographic lesions and reduces by 27% the number of misdiagnosed IE classified in the 'possible IE' category by modified Duke Criteria.

- **La sensibilidad diagnóstica de la PET combinada con un angio-TC (PET/aTC) oscila entre el 91 y el 97%**, siendo su principal indicación las sospechas de EI valvular protésica posibles/rechazadas según los criterios de Duke modi cados en las cuales persiste una alta sospecha clínica.
- Desde 2015, las guías europeas de manejo de EI han incluido tanto a la PET/TC como a la angio-TC cardíaca individualmente como criterios mayores de diagnós co de EI protésica
- **En el caso de infección de disposi vos, si bien la técnica aún no ene una fuerte recomendación en las guías de prác ca clínica, existe ya una aceptable evidencia de su utilidad en dicho contexto.**
- **La sensibilidad diagnós ca de la PET/TAC es prác camente del 100% para el diagnós co de infección del generador y/o cables extra- vasculares**, mientras que es más limitada para evaluar el trayecto intravascular y/o intracardíaco de los electrodos

Rev Esp Med Nucl Imagen Mol. 2018 Feb 26. pii: S2253-654X(18)30011-8. doi: 10.1016/j.remn.2018.01.002. [Epub ahead of print]

Methodology of the 18F-FDG PET/TC cardiac for the diagnosis of prosthetic endocarditis and intracardiac devices.

[Article in English, Spanish]

Aguadé Bruix S[1], Roque Pérez A[2], Cuéllar Calabria H[2], Pizzi MN[3].

Author information

Abstract

Infective **endocarditis** (IE) is a serious pathology with a poor prognosis, whose mortality has no changed significantly despite advances in its diagnosis and treatment in the last 30years. The diagnostic capacity of the modified Duke criteria in prosthetic **endocarditis** and/or devices does not exceed 50%, so new tools are necessary for the diagnosis of this entity in this context. The ^{18}F-FDG **PET**/CTA combines a highly sensitive technique to detect inflammatory-infectious activity and a technique with high anatomical resolution to assess the structural lesions associated with **endocarditis**. With a diagnostic sensitivity between 91-97%, this hybrid technique has become a useful diagnostic tool in the suspicion of IE of patients with prosthetic valves or devices, becoming a major criterion in the diagnostic algorithm of current guidelines. This excellent diagnostic capacity depends directly on the quality of the obtained exploration anc the knowledge at the time of interpreting the images. The aim of this review is to describe and standardize the methodology of cardiac ^{18}F-FDG **PET**/CTA in the diagnosis of **endocarditis** in prosthetic valves and intracardiac devices, with special emphasis on the particularities of the patient's preparation, the **PET** and CT acquisition procedures, and the subsequent imaging

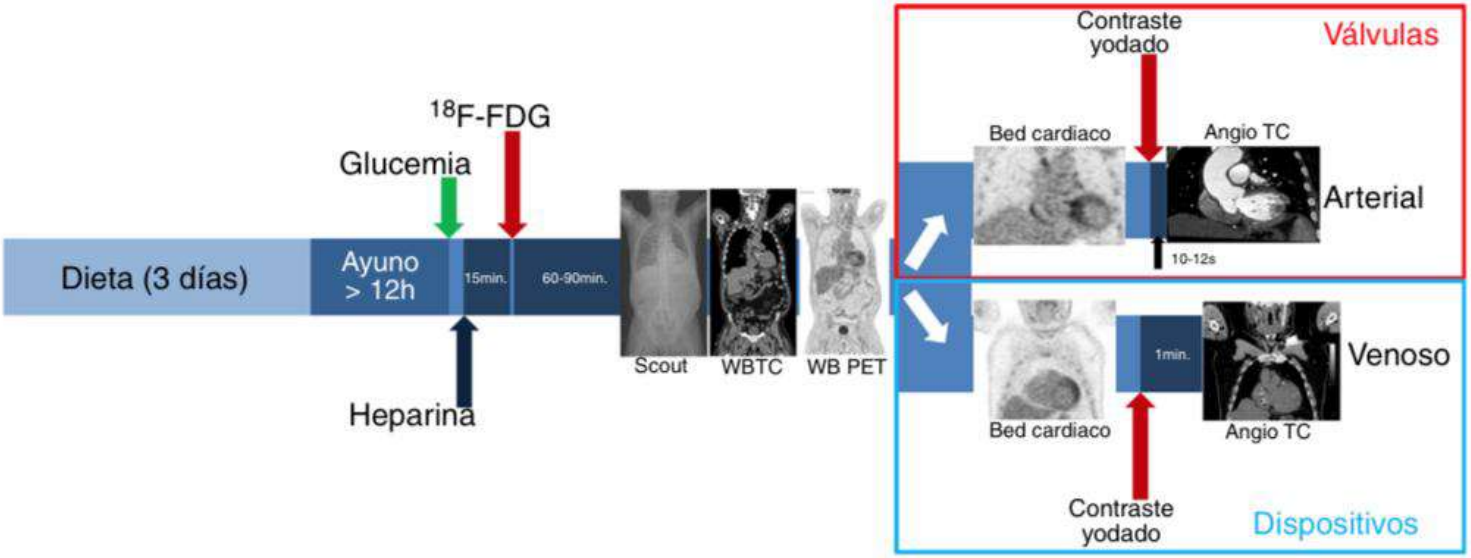

Figura 1. Línea del tiempo global de una PET/TC de frenación miocárdica y angio-TC cardíaca, para estudio tanto de endocarditis valvular (arterial) como de dispositivos implantables (venoso).
FDG: Flúor desoxiglucosa, WB TC: TC de cuerpo entero, WB PET: PET de cuerpo entero.

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¿Qué harías tú con el paciente?

- Al 10 día el paciente se encontraba prácticmente asintomático, andando por la planta, y se le hizo una ECO-ETE sin empeoramiento valvular y sin vegetación, PET/TC no sugerente de infección.

¿Qué harías tu con el paciente?

- 1-Lo dejaría ingresado hasta que complete el tto antibiótico iv durante 6 semanas.
- 2- Le daría el alta y le pondría el tratamiento antibiótico iv ambulatorio en domicilio o en hospital de día (dependiendo de las opciones de cada centro).
- 3-Le pondría tto antibiótico oral (a la vista de los buenos resultados publicados recientemente sobre el tto de EI por vía oral).
- 4-Le pondría Dalbavancina 1000mg/iv en una sola dosis antes de irse a su domicilio, 500mg semanales (3 dosis) y lo citaría en 4 semanas con una ECOcardio y revisión en consulta.

Clin Microbiol Infect. 2016 Jul;22(7):607-12. doi: 10.1016/j.cmi.2016.04.003. Epub 2016 Apr 16.

Switch to oral antibiotics in the treatment of infective endocarditis is not associated with increased risk of mortality in non-severely ill patients.

Mzabi A[1], Kernéis S[2], Richaud C[2], Podglajen I[2], Fernandez-Gerlinger MP[2], Mainardi JL[3].

- N= 426 EI (2000-2012), 369 EI definida
- Edad 64,5 años (7-98)
- 106 (25%) EI nosocomial/nosohusial
- Microorganismo de las EI: 99 (33%) Streptococos, 81 (19%) Estafilococos.
- 92 (22%) fallecieron.
- Después del tto con ab iv durante una media de 21 días (0-70) iv pasaron a v.o., 214 (50%) pacientes, que tenían en comparación menos, comorbilidades y casos de *S. aureus*.
- Ab oral: 109 casos amoxicilina sola, el resto combinación de clindamicina, fluorquinolos, rifampicina y/o amoxicilina
- Seguimiento: rama oral 2 recidivas y 4 reinfecciones; rama iv 9 recidivas y 8 reinfecciones.

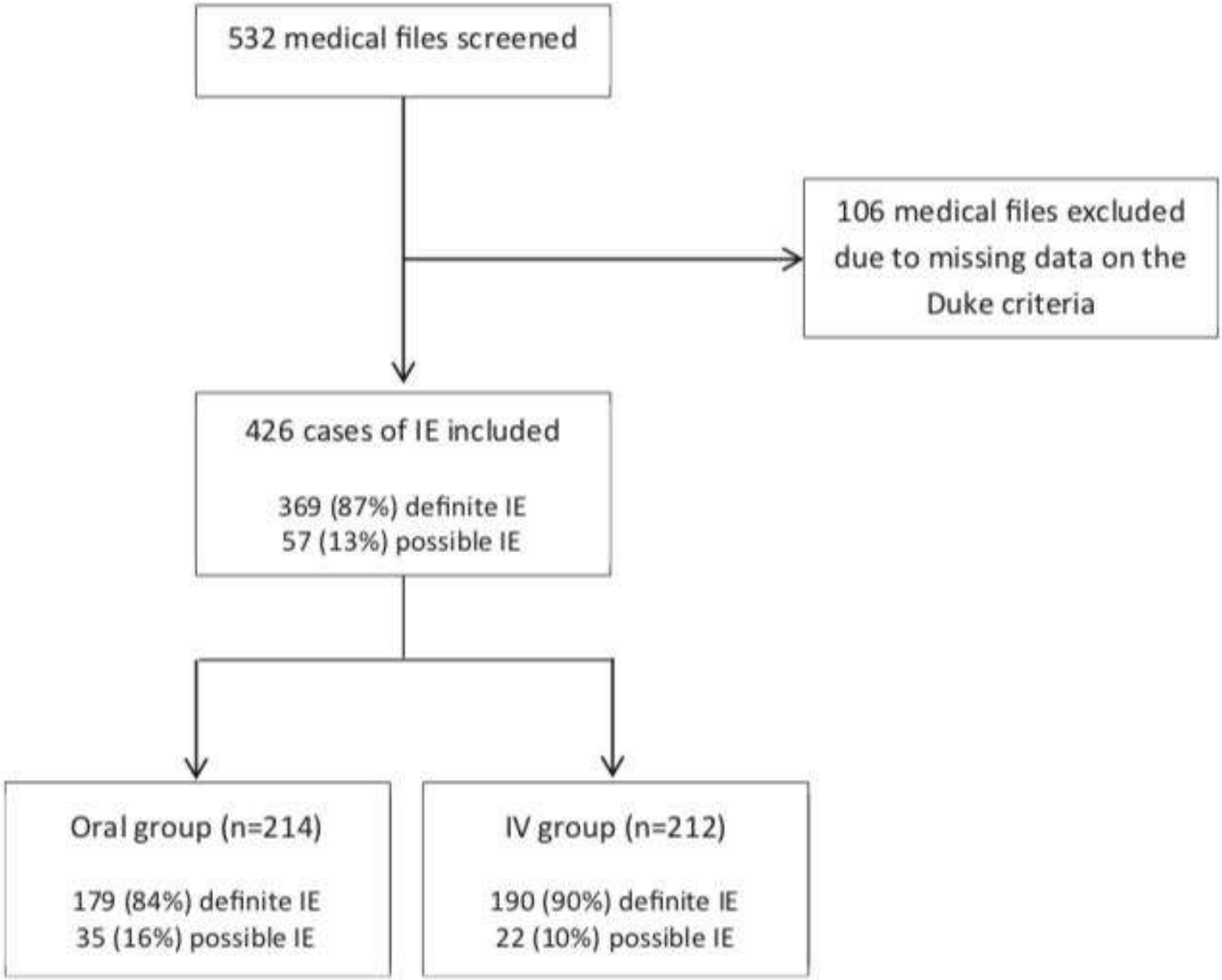

Fig. 1. Flow diagram of process for patient selection.

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Table 1
Main characteristics of 426 patients with IE

Characteristic	Value
Age, years	64.5 (7–98)
Men	291 (68)
Comorbidities	
Risk factors for IE	
Prosthetic heart valve	100 (23)
Permanent pacemaker	52 (12)
Congenital heart disease	35 (8)
History of previous IE	37 (9)
Cancer	78 (18)
Colon cancer	18 (4)
Breast cancer	15 (4)
Obesity	14 (4)
Type 1 diabetes	15 (4)
Type 2 diabetes	30 (7)
Chronic renal failure	46 (11)
Cirrhosis	16 (4)
Clinical presentation	
Temperature >38°C	367 (86)
New heart murmur	110 (26)
Peripheral embolism	154 (36)
Cerebral	69 (16)
Splenic	39 (9)
Pulmonary	38 (9)
Osteoarticular	29 (7)
Acute heart failure	154 (36)
Shock	45 (11)
Healthcare-associated IE	106 (25)
Nosocomial IE	68 (16)

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Imaging data	
Vegetation	310 (73)
Valvular regurgitation	279 (66)
Valvular abscess	53 (12)
Disinsertion of a prosthetic valve	12 (3)
Location of IE	
Left heart	335 (79)
Right heart	27 (6)
Permanent pacemaker	52 (12)
Intracardiac device[a]	12 (3)
Native valve	262 (62)
Prosthetic valve	100 (23)
Bioprosthesis	53 (12)
Mechanical prosthesis	47 (11)
Microorganisms	
Streptococci	171 (40)
Oral streptococci	99 (23)
Streptococcus bovis/gallolyticus	42 (10)
Pyogenic streptococci	24 (6)
Other Streptococcaceae	6 (1)
Staphylococci	129 (30)
Staphylococcus aureus	81 (19)
Methicillin-susceptible *S. aureus*	67 (16)
Methicillin-resistant *S. aureus*	14 (3)
Coagulase-negative staphylococci	48 (11)
Enterococci	50 (12)
Enterococcus faecalis	49 (12)
Enterococcus faecium	1
HACCEK group	21 (5)
Bartonella spp.	14 (3)
Coxiella burnetii	8 (2)
Other microorganisms	28 (7)
No microorganism identified	5 (1)

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Table 2
Main characteristics of patients who switched to oral route compared to those who received exclusively intravenous therapy

Characteristic	Oral antibiotic switch ($n = 214$)	Exclusively intravenous route ($n = 212$)	p[a]
Definite endocarditis	179 (84)	190 (90)	0.09
Men	149 (70)	142 (67)	0.60
Age, years	65 (7–98)	64 (12–93)	0.62
Previous episode of IE	20 (9)	17 (8)	0.73
Congenital heart disease	20 (9)	15 (7)	0.48
Left heart endocarditis	161 (75)	174 (82)	0.10
Right heart endocarditis	15 (7)	12 (6)	0.69
Pacemaker endocarditis	33 (15)	19 (9)	0.05
Intracardiac device	5 (2)	7 (3)	0.57
Native valve endocarditis	125 (58)	137 (65)	0.20
Prosthetic valve endocarditis	51 (24)	49 (23)	0.91
Diabetes	15 (7)	30 (14)	0.02
Chronic renal failure	17 (8)	29 (14)	0.06
Cirrhosis	4 (2)	12 (6)	0.04
Immunosuppression	25 (12)	34 (16)	0.20
Temperature >38°C	183 (86)	183 (86)	0.89
Acute heart failure	60 (28)	94 (44)	$<10^{-4}$
Shock	9 (4)	36 (17)	$<10^{-4}$
Cerebral emboli	27 (13)	42 (20)	0.05
CRP, mg/L	81 (10–512)	88 (10–525)	0.06
Serum creatinine >100 μmol/L	76 (36)	110 (52)	$<10^{-4}$
Surgery	120 (56)	126 (59)	0.49
Streptococci	91 (43)	80 (38)	0.32
Coagulase-negative staphylococci	26 (12)	22 (10)	0.64
Enterococci	23 (11)	26 (12)	0.65
Staphylococcus aureus	28 (13)	53 (25)	0.002
Susceptibility			0.12
Methicillin-susceptible *S. aureus*	26 (12)	41 (19)	
Methicillin-resistant *S. aureus*	2 (1)	12 (6)	
No. of deaths/No. of patients followed up after diagnosis			
Day 10	0/214	18/212	
Day 30	1/188	25/200	
Day 90	4/144	20/170	

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Table 3
Oral antibiotic regimen according to microorganism identified

Microorganism	Antibiotic regimen
Streptococci ($n = 91$)	• Amoxicillin ($n = 84$; 92%) • Amoxicillin—clindamycin ($n = 4$; 4%) • Amoxicillin—rifampin ($n = 3$; 3%)
Staphylococci ($n = 54$)	• Clindamycin—(rifampin or fluoroquinolone) ($n = 15$; 28%) • Fluoroquinolone—rifampin ($n = 13$; 24%) • Amoxicillin—(rifampin or fluoroquinolone or clindamycin) ($n = 9$; 17%) • Fluoroquinolone ($n = 4$; 7%) • Amoxicillin ($n = 4$; 7%) • Clindamycin ($n = 4$; 7%) • Rifampin—(Bactrim or doxycycline) ($n = 2$; 4%) • Linezolid ($n = 2$; 4%) • Rifampin ($n = 1$; 2%)
Enterococci ($n = 23$)	• Amoxicillin ($n = 21$; 91%) • Amoxicillin—rifampin ($n = 2$; 9%)

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Table 4
Multivariate analysis of predictors of mortality

Characteristic	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	Adjusted HR (95% CI)	p
Comorbidities				
Age >65 years	1.6 (1.1–2.5)	0.02[a]	1.8 (1.2–2.8)	0.005
Men	0.8 (0.5–1.2)	0.37		
Preexisting heart disease	0.8 (0.5–1.3)	0.42		
History of endocarditis	1.0 (0.5–2.0)	0.98		
Type 1 diabetes	2.9 (1.4–6.0)	0.01[a]	3.2 (1.5–6.7)	0.002
Type 2 diabetes	1.1 (0.5–2.5)	0.74		
Chronic renal failure	2.6 (1.6–4.2)	0.001[a]		
Immunosuppression	1.7 (1.1–2.7)	0.05[a]	1.8 (1.1–2.9)	0.03
Active smoking	0.8 (0.5–1.3)	0.41		
Obesity	0.4 (0.1–1.8)	0.19[a]		
Severity				
Shock	3.7 (2.3–6.0)	$<10^{-5}$[a]	2.8 (1.7–4.8)	0.0001
Cerebral emboli	1.6 (0.9–2.7)	0.08[a]		
Disinsertion of prosthetic valve	2.1 (0.8–5.1)	0.15[a]	3.0 (1.2–7.5)	0.02
Valvular abscess	1.6 (0.9–2.7)	0.09[a]		
Microorganism				
Staphylococcus aureus	2.8 (1.5–5.4)	0.002[a]	2.0 (1.3–3.3)	0.003
Streptococci	0.9 (0.5–1.9)	0.9		
Coagulase-negative staphylococci	1.7 (0.8–3.7)	0.19[a]		
Enterococci	1.5 (0.7–3.3)	0.35		

CI, confidence interval; HR, hazard ratio.
[a] Variables included in backward stepwise variable selection procedure.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

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Emil L. Fosbøll, M.D., Ph.D., Flemming Rosenvinge, M.D.,
Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc.,
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Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D.,
and Henning Bundgaard, M.D., D.M.Sc.

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1.2 DISEÑO DEL ESTUDIO

1954 pacientes

Sospecha de EI izquierda

Se confirma con Cx de Duke modificados

Inicia tto. IV (mediana 10 días, y al menos 7 días tras qca. si precisa)

Cumple Cx de selec-ción de paciente **

** Cxs serán vistos más adelante

Randomización de pacientes 1:1

400 (20%) pacientes

Completar oral

Completar IV

199 pacientes

201 pacientes

Seguimiento

1 Semana

1 Mes

3 Mes

6 Mes

ETE de control

TRIAL DESIGN AND OVERSIGHT

The Partial Oral Treatment of Endocarditis (POET) trial was a nationwide investigator-initiated, multi-center, randomized, unblinded, noninferiority tri-al performed at cardiac centers in Denmark. The

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1.3 OBJETIVOS

- Objetivar desde el momento de la randomización hasta los 6 meses tras completar antibio-terapia los siguientes efectos adversos:
    - Muerte por todas las causas.
    - Necesidad de cirugía urgente (no programada).
    - Evento embólico.
    - Recurrencia de la bacteriemia por el patógeno primario.

1.4 SELECCIÓN DE PACIENTES

- **HEMOCULTIVOS**:
  - Streptococcus
  - Enterococcus faecalis
  - Staphylococcus aureus meticilín sensible (** NINGÚN MARSA)
  - Staphylococcus coagulata negativo
- **CLÍNICAMENTE ESTABLES** tras tto. IV al menos 10 días (y al menos 7 tras cirugía)
  - Buena respuesta clínica (Afebril > 2 días)
  - PCR menor de < 25 mg/L y leucos < 15.000
  - ETE (< 48 horas) sin absceso o presencia de otra indicación de cirugía
- Edad > 18 años
- Cumple criterios de Duke modificados
- No alteraciones gastrointestinales.
- No necesidad de antibioterapia IV por otra causa.
- No diferencian si precisa cirugía.
- No diferencian si tienen dispositivo cardíaco.

1.4 SELECCIÓN DE PACIENTES (II)

IE due to Streptococci spp., *Staphylococcus aureus, Enterococcus faecalis* or Coagulase-negative Staphylococci?

→ Aislamiento por germen compatible

↓ Yes

IE treated intravenously with appropriate antibiotics for ≥10 days and ≥7 days in case of heart surgery during present IE?

→ Tratamiento IV previo correcto

↓ Yes

Satisfactory response to treatment; Afebrile >2 days, CRP <25% of peak level or <20 mg/l and Leucocytes <15 x 10^9/L?

→ Buena respuesta clínica

↓ Yes

Echocardiography (TOE) performed <2 days without abscess formation or presence of other indications for surgery?

→ ETE < 48 horas sin indicación qca.

↓ Yes

Other indications for prolonged intravenous antibiotics, suspected reduced gastro-intestinal uptake or BMI >40?

→ No obesidad, antibioterapia IV otra causa o alt. gastrointestinales

↓ No

Have bacterial susceptible examinations identified two different classes of orally administered antibiotics?

→ Antibiograma permite dos clases de ATB oral

↓ Yes

Consider shifting to oral therapy (2 antibiotics) and consider discharge to outpatient treatment*

1.5 SELECCIÓN DE ANTIBIOTERAPIA

- Las **pautas IV** siguieron las recomendaciones de la Guía de la Sociedad Europea de Cardiología.
- Las **pautas orales** se desarrollaron como parte del estudio.
    - Siempre dos ATBs
    - Diferentes familias
    - Diferentes mecanismos antimicrobianos
    - Diferentes vías metabólicas
    - Alta biodisponibilidad
    - Guiados por antibiograma
    - Ajustados por concentración

1.5 SELECCIÓN DE ANTIBIOTERAPIA: PAUTAS ORALES (III)

Susceptibility to penicillin, ampicillin or methicillin for the bacterial groups included

	Penicillin susceptibility streptococci (MIC < 1 mg/L)	Penicillin susceptibility staphylococci (large and tapered penicillin zone. Penicillinase induction test)	Ampicillin susceptibility (MIC ≤ 4 mg/L)	Methicillin resistance (Cefoxitin or oxacillin screening. Confirmed by mec gene analysis)
*Streptococcus spp**	194 susceptible 2 resistant			
Enterococcus faecalis			96 susceptible 1 resistant	
Staphylococcus aureus		27 susceptible 60 resistant		87 susceptible 0 resistant
Coagulase negative staphylococci		7 susceptible 16 resistant		15 susceptible 8 resistant

¡¡¡NINGÚN MARSA!!!

Antibiotic regimens in the POET trial.

	Oral regimens	Frequency n (%)
Staphylococcus aureus	Dicloxacillin and rifampicin	15 (33)
	Amoxicillin and rifampicin	13 (29)
	Moxifloxacin and rifampicin	3 (7)
	Amoxicillin and fusidic acid	2 (4)
	Dicloxacillin and fusidic acid	2 (4)
	Fusidic acid and linezolid	2 (4)
	Rifampicin and linezolid	2 (4)
	Penicillin and rifampicin	1 (2)
	Amoxicillin and clindamycin	1 (2)
	Ampicillin and rifampicin	1 (2)
	Moxifloxacin and fusidic acid	1 (2)
	Moxifloxacin and linezolid	1 (2)
	Linezolid and clindamycin	1 (2)
Enterococcus faecalis	Amoxicillin and moxifloxacin	24 (47)
	Amoxicillin and linezolid	13 (25)
	Amoxicillin and rifampicin	6 (12)
	Moxifloxacin and linezolid	5 (10)
	Amoxicillin and ciprofloxacin	2 (4)
	Amoxicillin	1 (2)
Streptococci	Amoxicillin and rifampicin	47 (52)
	Penicillin and moxifloxacin	12 (13)
	Rifampicin and linezolid	8 (9)
	Moxifloxacin and linezolid	8 (9)
	Amoxicillin and linezolid	7 (8)
	Penicillin	3 (3)
	Ampicillin and moxifloxacin	1 (1)
	Ampicillin and rifampicin	1 (1)
	Dicloxacillin and moxifloxacin	1 (1)
	Moxifloxacin and clindamycin	1 (1)
	Moxifloxacin and vancomycin	1 (1)
Coagulase negative staphylococci	Fusidic acid and linezolid	5 (38)
	Rifampicin and linezolid	4 (31)
	Amoxicillin and linezolid	1 (8)
	Dicloxacillin and rifampicin	1(8)
	Moxifloxacin and linezolid	1(8)
	Rifampicin and Fusidic acid	1(8)

1.6 RESULTADOS: OBJETIVO PRIMARIO

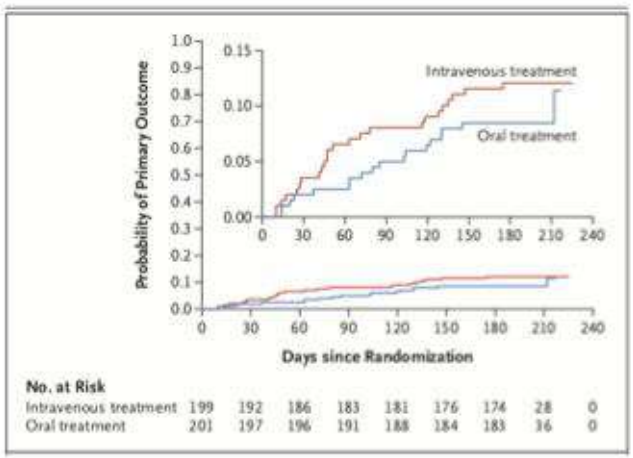
PRIMARY OUTCOME

All enrolled patients were followed for 6 months after the antibiotic treatment was completed or until death. No patients were lost to follow-up. The primary composite outcome occurred in a total of 42 patients (10.5%) — in 24 patients (12.1%) in the intravenously treated group and in 18 (9.0%) in the orally treated group (odds ratio, 0.72; 95% confidence interval [CI], 0.37 to 1.36). The between-group difference was 3.1 percentage points (95% CI, −3.4 to 9.6; P=0.40) in favor of oral treatment, and the criterion for noninferiority was therefore met. In the per-protocol

Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

Component	Intravenous Treatment (N=199)	Oral Treatment (N=201)	Difference	Hazard Ratio (95% CI)
	number (percent)		*percentage points (95% CI)*	
All-cause mortality	13 (6.5)	7 (3.5)	3.0 (−1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0)	6 (3.0)	0 (−3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic event	3 (1.5)	3 (1.5)	0 (−2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the positive blood culture†	5 (2.5)	5 (2.5)	0 (−3.1 to 3.1)	0.97 (0.28 to 3.33)

* Six patients, three in each group, had two outcomes.
† For details about relapse of the positive blood culture, see the Supplementary Appendix.



- Se alcanzó el criterio de no inferioridad.
- 24 pacientes presentaron objetivo primario en tratamiento IV.
- 18 pacientes presentaron objetivo primario en tratamiento oral.
- 6 paciente más fallecieron por cualquier causa en IV.
- Resto igual.
- La diferencia entre grupos fue favorable para el tratamiento oral (3,1%).
- No se perdieron pacientes durante el seguimiento.

DISCUSSION

In patients with endocarditis on the left side of the heart caused by streptococcus, *E. faecalis*, *S. aureus*, or coagulase-negative staphylococci, who were in clinically stable condition and who had had an adequate response to initial treatment, a shift from initial intravenous to oral antibiotic treatment was noninferior to continued intravenous antibiotic treatment. The patients in the orally treated group were shifted from intravenous to oral treatment on about day 17, the midpoint of the treatment period. Thus, during half the treatment period, the patients in the orally treated group were eligible for partial or complete outpatient treatment.

The results seemed consistent across prespecified subgroups, including the subgroups defined according to type of valve affected (native valve or prosthetic valve) and according to type of treatment (surgery during the disease course or conservative treatment). It should also be noted that the primary outcome seemed similar across the four different bacterial types. However, the trial was not powered to assess the primary outcome in any of the prespecified subgroups. The high rate of the primary outcome in patients with coagulase-negative staphylococci probably reflects diagnostic delays combined with the fact that it often occurred in older and more frail patients who had serious coexisting conditions.

2.1 CONCLUSIONES

- En pacientes con EI izquierdas por los gérmenes descritos y clínicamente estables tras la respuesta inicial positiva a antibioterapia IV el cambio a pautas orales se ha demostrado como no inferior.
- Este resultado se observa a su vez en todos los subgrupos estudiados (afectación valvular, necesidad de cirugía…) y en los distintos tipos de bacterias.
- Aunque el estudio no se realizó específicamente para demostrar el objetivo primario en estos subgrupos.

2.1 CONCLUSIONES (II)

- Este estudio sólo demuestra dicha no-inferioridad en menos de 1 de cada 4 pacientes con endocarditis izquierda. Criterios de inclusión estrictos.
- La duración de las pautas de antibioterapia oral e intravenosas utilizadas se basan en estudios observacionales.
- Las pautas orales se seleccionaron en función de su biodisponibilidad y mecanismos anti-bacterianos y de metabolización diferentes.
- No ha sido preciso cambiar ninguna pauta oral en base a los datos de farmacocinética (si modificar dosis en 7 pacientes).

The rationale for this trial was that in patients with normal gastrointestinal function, the uptake of orally administered antibiotics may allow sufficient plasma concentrations of antibiotics to achieve bacterial killing.[10] As part of the trial, oral regimens were developed, and specific combinations of oral antibiotics were chosen for each regimen (Table S2 in the Supplementary Appendix). The main concern related to the administration of oral antibiotics as compared with intravenous administration is whether the gastrointestinal uptake is sufficient. In this trial, only patients considered to have clinically normal gastrointestinal uptake were enrolled. The regimens that were developed for the trial included antibiotics generally known to have moderate to high bioavailability, and the antibiotics were carefully selected for each patient (Table S10 in the Supplementary Appendix). To address the risk of subtherapeutic antibiotic levels related to potentially reduced gastrointestinal uptake, as well as the risk of variations in pharmacokinetics of the orally administered antibiotics, all oral regimens included two antibiotics from different drug classes and with different antibacterial effects and different metabolization processes. In addition, pharmacokinetic measurements were performed. It was not necessary to change antibiotic therapy in any of the patients on the basis of pharmacokinetic findings. Therefore, we do not consider pharmacokinetics to be a factor when offering oral antibiotic therapy if the currently applied randomization criteria are met and two antibiotics with good bioavailability are prescribed (both carefully selected on the basis of bacterial identification and antimicrobial susceptibility testing) and the patient's gastrointestinal uptake is considered to be normal.

Recommendations for the duration of antibiotic therapy and for in-hospital intravenous administration in patients with endocarditis are based mainly on observational studies.[25,26] Lon-

Our trial has several limitations. Only patients with endocarditis on the left side of the heart were enrolled; however, it should be noted that patients with simultaneous infection of a cardiovascular implantable electronic device or endocarditis on the right side of the heart were not excluded. Only patients with endocarditis caused by certain bacterial species were eligible, and the results may not apply to the remaining 25 to 30% of patients who have endocarditis caused by other bacteria or to patients with culture-negative endocarditis. In addition, only five intravenous drug users were enrolled, only 22% of the enrolled patients had *S. aureus*, and, although it was not a criterion for exclusion, no patients with methicillin-resistant *S. aureus* or other antibiotic-resistant phenotypes were enrolled. Referral bias may have affected our findings, because some patients — most likely elderly patients who are fragile and have serious coexisting conditions — may not have been referred to one of the participating centers. The criteria for inclusion in the trial were strict, and clinicians should use these criteria in the decision to shift a patient from intravenous to oral therapy (see Fig. S4 in the Supplementary Appendix). In geographic areas with higher rates of antibiotic resistance, these criteria would also be applicable, since they are based on ence and the discretion of the treating physician. Therefore, the duration of outpatient treatment may have been underestimated. Only 20% of the screened population underwent randomization. Considering the reasons for exclusion (Fig. 1), it seems likely that a larger fraction of patients with endocarditis on the left side of the heart may be candidates for partial oral therapy.

2.2 LIMITACIONES

- Sólo algunos tipos de bacterias:
  - **EXCLUIDO EL SAMR** (entre otros).
  - No otros tipos de multirresistencias.
- La estimación del tratamiento domiciliario se ha infraestimado.
- De toda la población candidata sólo se ha podido incluir al 20% (1954 —-> se escogieron 400).
- Criterios de inclusión muy estrictos.
- Pacientes muy estables y con una evolución excelente.

Dalbavancina frente **biofilm**

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In vitro activity of dalbavancin against biofilms of staphylococci isolated from prosthetic joint infections

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ABSTRACT

The *in vitro* activity of dalbavancin was tested against biofilms of 171 staphylococci associated with prosthetic joint infection. Dalbavancin minimum biofilm bactericidal concentration (MBBC) values were: $MBBC_{50}$ for *Staphylococcus aureus* and *Staphylococcus epidermidis*, 1 μg/mL; $MBBC_{90}$ for *S. aureus*, 2 μg/mL; $MBBC_{90}$ for *S. epidermidis*, 4 μg/mL.

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Dalbavancin reduces biofilms of methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant Staphylococcus epidermidis (MRSE).

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Author information

Abstract

Activity of **dalbavancin** against methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant Staphylococcus epidermidis (MRSE) in **biofilm** was investigated and the microbicidal **biofilm** concentrations (MBC) were determined. **Biofilms** obtained from ten MRSA and ten MRSE bloodstream isolates, collected from patients in the General Hospital of Vienna between 2012 and 2015, were incubated with **dalbavancin** in trypticase soy broth (TSB) in serial dilution from 0.0625 mg/l to 256 mg/l using a microtiter plate **biofilm** model. The plates were incubated for 24 h at 37 ° C and 50% humidity. **Biofilms** were fixed with 2.5% glutaraldehyde and stained with crystal violet. Subsequently the optical density (OD_{620}) was used to measure the MBC, defined as the concentration of **dalbavancin** leading to a 50% reduction of **biofilm**. MBC for MRSA was 1 mg/l-4 mg/l (minimal inhibitory concentrations (MIC) 0.0312 mg/l-0.064 mg/l). MBC for MRSE was 2 mg/l-16 mg/l (MIC 0.023 mg/l-0.0625 mg/l). **Dalbavancin** successfully reduced MRSA and MRSE in **biofilms**, and therefore provides a promising option for the treatment of **biofilm**-associated infections.

Dalbavancina frente **biofilm**

JOURNAL OF MEDICAL MICROBIOLOGY

RESEARCH ARTICLE

Díaz-Ruíz *et al.*, *Journal of Medical Microbiology*

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MICROBIOLOGY SOCIETY

Can dalbavancin be used as a catheter lock solution?

Cristina Díaz-Ruíz,[1] Beatriz Alonso,[2,3] Emilia Cercenado,[2] Raquel Cruces,[2,3] Emilio Bouza,[4] Patricia Muñoz[2,3,4,5] and María Guembe[2,3,*]

Abstract

Purpose. The new lipoglycopeptide dalbavancin has only been approved for acute bacterial skin and skin structure infections. However, its alternative use as a catheter lock solution could facilitate the conservative management of catheter-related bloodstream infection. Our objective was to assess the stability and activity of dalbavancin alone and in combination with heparin against methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus epidermidis* (MRSE) biofilms. We also compared the results with those obtained with vancomycin alone and in combination with heparin.

Methodology. We used a 96-well plate *in vitro* model based on 24 h biofilms of MRSA and MRSE (ATCC 43300, ATCC 35984 and one clinical strain of each). The biofilms were exposed to dalbavancin (0.128 mg ml^{-1}) and vancomycin (5 mg ml^{-1}) alone and in combination with heparin (60 IU). The median percentage reductions in metabolic activity, biomass, bacterial load, and cell viability for each solution were compared.

Results. Dalbavancin combined with heparin significantly reduced the median [interquartile range (IQR)] percentage of metabolic activity in MRSA biofilms compared with vancomycin [90.0 % (70.4–92.9 %) versus 35.0 % (14.8–59.6 %), P=0.006]. For the remaining variables studied, the combination was not inferior to vancomycin for MRSA and MRSE.

Conclusions. Dalbavancin proved to be active against MRSA and MRSE biofilms. The combination of dalbavancin with heparin is a promising catheter lock solution that has the advantage of locking the catheter at home for 7 days.

Clinical Infectious Diseases

Dalbavancin as primary and sequential treatment for Gram-positive infective endocarditis: 2-Year Experience at the General Hospital of Vienna

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Abstract

In this retrospective study clinical outcomes and safety of dalbavancin as primary and sequential treatment of Gram-positive bacteremia with infective endocarditis were evaluated. Clinical success under dalbavancin was high (92.6%) but in the majority of patients (24/27) dalbavancin was only used after clearance of bacteria from bloodstream.

Se intervinieron:

- 68.8% (11/16) EI VN
- 1 /6 EI VP
- 4/5 EI MP

Se administró Dalbavancina de inicio: 1 EI VN, 1 EIVP, 1EI MP

Table 1

Duration of DALB Therapy	Pat No.	Types of IE	Pathogen	Duration of therapy prior DALB (weeks)	Reason to change of therapy to DALB	Failure of DALB treatment	Side effects	weekly regime (once/two)
1 week (n=1)	1	Prosthetic valve	*E. faecalis*	VAN (3)	Not documented	Death	No	Once
2 weeks (n=3)	2	Native valve	*S. aureus*	FLUOX + FOSF (2) CEFAZ + DAP (4)	Poor venous access	No	No	Once
	3	Native valve	*S. aureus*	FLUOX+DAP (5)	OPAT	No	No	Two
	4	Native valve	*S. aureus*	CEFU+DAP (4)	Poor venous access	No	No	Two
4 weeks (n=5)	5	Native valve	*E. faecalis*	CEFT+AMP (2)	OPAT	No	No	Once
	6	Prosthetic valve	*Streptococcus equi*	PEN G (1)	OPAT	No	Nausea	Two
	7	CDE	*S. epidermidis*	CEFAZ+FOSF (4)	OPAT	No	No	Two
	8	CDE	*S. epidermidis*	DAP (4)	OPAT	No	No	Two
	9	Native valve	*Streptococcus mitis*	CEFT+GEN (2)	OPAT	No	No	Two
6 weeks (n=10)	10	Prosthetic valve	*S. aureus*	FLUOX+RIF (2)	OPAT*	No	No	Once
	11	Native valve	*S. hominis*	FLUOX+DAP (2)	OPAT	No	No	Once
	12	CDE	*Streptococcus* spp. *S. epidermidis*	DAP** VAN (2)	OPAT	No	No	Once
	13	Prosthetic valve	*Streptococcus equinus*	PEN G (1)	OPAT	No	No	Two
	14	Suspected prosthetic valve	*Streptococcus sanguinis*	No	OPAT	No	RCI	Two
	15	Native valve	*E. faecalis*	CEFT+AMP (1)	OPAT	No	No	Two
	16	Native valve	*Aerococcus urinae*	PEN G (2)	OPAT	No	No	Two
	17	Native valve	*S. aureus*	FLUOX+DAP(1)	Poor venous access	No	No	Two
	18	Native valve	*S. aureus*	FLUOX+FOSF (1)	OPAT	No	No	Two
	19	Native valve	*Streptococcus sanguinis* *S. hominis*	FLUOX+AMP (1)	OPAT	No	No	Two
> 6 week (n=8)	20	Native valve	*E. faecalis*	No	OPAT	No	No	Once
	21	Native valve	*Streptococcus sanguinis*	VAN (1) DAP (1)	OPAT	No	No	Once
	22	CDE	*S. epidermidis*	No	OPAT	No	No	Once
	23	CDE	*S. aureus*	FLUOX (1)	OPAT	Resistance	No	Once
	24	Native valve	*S. aureus*	CEFT (1) DAP (1)	OPAT	No	No	Two
	25	Prosthetic valve	*S. aureus*	FLUOX+RIF (1)	OPAT	No	No	Two
	26	Prosthetic valve	*Streptococcus sanguinis*	PEN G (1)	OPAT	No	No	Two
	27	Native valve IE	*S. caprae*	CEFAZ (1)	OPAT	No	No	Two

DALBAVANCINA COMO TRATAMIENTO DE SECUENCIACIÓN EN PACIENTES CON ENDOCARDITIS Y/O BACTERIEMIA POR COCOS GRAM POSITIVO (Cohorte DALBACEN)

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VII CONGRESO SEICAV Sociedad Española de Infecciones Cardiovasculares SEVILLA 16 Y 17 DE NOVIEMBRE DE 2018

- **OBJETIVOS**
  - Analizar la efectividad en la práctica clínica de la DBV en pacientes con Bacteriemia o Endocarditis (EI) por CGP.
- **MÉTODOS**
  - Estudio multicéntrico, observacional, retrospectivo, de pacientes con EI y/o bacteriemia por CGP que han recibido al menos una dosis de DBV para su tratamiento (26/06/2016 hasta el 31/04/2018).
  - Se recogieron variables demográficas y relativas a la infección y evolución.
  - Se calculó el porcentaje de curación clínica y los días de estancia hospitalaria ahorrados.
  - Definimos:
    - EI según criterios de Duke modificados (2015)
    - Bacteriemia complicada como aquella con metástasis sépticas y/o sin retirada de catéter colonizado y/o sin respuesta rápida a las 48-72h.

RESULTADOS

Tabla 1. Características basales.

	N = 84
Edad, mediana (IQR)	69 (53-77)
Hombres, n (%)	62 (73.8)
Índice Charlson, n (%)	2 (1-4)
Tipo de infección, n (%)	
- EI definida	32 (38.1)
- EI probable	3 (3.6)
- Bacteriemia complicada	34 (40.5)
- Bacteriemia no complicada	15 (17.9)
Reducción días estancia, n (%)	71 (84.5)
Reducción días estancia, mediana (IQR)	14 (7-14)

Tabla 2. Microorganismos implicados.

Agente etiológico, n (%)	
- SAMS	22 (26.2)
- SAMR	12 (14.3)
- SCN	32 (38.1)
- Streptococo	6 (7.1)
- E. Faecalis	4 (4.8)
- E. Faecium	2 (2.4)
- Abiotrophia defectiva	1 (1.2)

Tabla 3. Antibióticos previos y motivo de administración de DBV.

	N=84
Días tratamiento previo, mediana (IQR)	15(5-29)
Tratamiento antibiótico previo, n (%)	80 (95,2)
- Dapto previo	46 (54.8)
- Ceftriaxona previo	20 (23,8)
- Linezolid previo	12 (14.3)
- Vancomicina previa	19 (22.6)
Motivo administración de la DBV, n (%)	
- Facilitar el alta	69 (82.1)
- Fracaso tratamiento previo	4 (4.8)
- Toxicidad	2 (2.4)

Tabla 4. Características de EI.

	N =35
Edad, mediana (IQR)	74 (65-81)
Hombres, n (%)	26 (74,3)
Índice Charlson, n (%)	2 (1-4)
Tipo de infección, n (%)	
- EI definida	32 (91,4)
- EI probable	3 (8,6)
Válvula, n (%)	
- Aórtica	18 (66,7)
- Mitral	8 (29,6)
- Tricúspide	1 (3,7)
Endocarditis, n (%)	
- Nativa	12 (33,3)
- Protésica precoz	5 (13,9)
- Protésica tardía	11 (30,9)
- Sobre marcapasos	8 (22,2)

Tabla 5. Microorganismos de EI

Agente etiológico, n (%)	EI (n= 35)
- SAMS	7 (20)
- SAMR	3 (8,6)
- SCN	15 (42,9)
- Streptococo	4 (11,4)
- *E. faecalis*	3 (8,6)

Tabla 6. Patología previa en bacteriemia vs EI

	Endocarditis n = 35
Enfermedad valvular previa	28 (80)
IRC	3 (8,6)
EPOC	7 (20)
DM	10 (28,6)
Enf neurológica	2 (5,7)
Hepatopatía crónica	3 (8,6)
Cirugía 3 meses previos	5 (14,3)
VIH	1 (2,9)
TOS	1 (2,9)
TPH	1 (2,9)
Neoplasia activa	1 (2,9)
QTP	1 (2,9)
Tto. Inmunosupresor	4 (11,4)
Corticoides	1 (2,9)

Tabla 7. Atb previos, motivos de DBV y resultados EI	N=35
Días tratamiento AB previo, mediana (IQR)	**29 (19-35)**
Tratamiento antibiótico previo, n (%)	
- Daptomicina	24 (68,6)
- Ceftriaxona	10 (28,6)
- Linezolid	3 (28,6)
- Vancomicina	8 (22,9)
Motivo administración de la DBV, n (%)	
- Facilitar el alta	31 (88,6)
- Fracaso tratamiento previo	3 (8,6)
Dosis de DBV, n(%) 1000mg (1d), 500mg (8d) 1000mg (1d) 1500mg (1d)	 11 (31,4) 6 (17,1) 18 (51,5)
Mediana de dosis de DBV administrada (P25-P75)	3 (2-3)
Pacientes que ha completado seguimiento 90 días, n(%)	35 (100)
Curación clínica, n(%)	35 (100)
Curación microbiológica, n(%)	34 (97,1)
Exitus relacionados con EI, n(%)	0
Mediana de reducción de la estancia hospitalaria	14 (7-17)

Seguimiento DALBACEN

- De los 35 pacientes con EI todos resolvieron clínicamente su infección, pero:
    - Un paciente ingresó para ser operado tras la EI por haberse quedado con disfunción valvular severa y en el cultivo de la válvula se aisló el SCN.
- Cuatro pacientes experimentaron efectos adversos (un paciente con astenia, otro eritrodermia sistémica, otro fiebre con tiritona autolimitadas y otro empeoramiento de la función renal).
- El tratamiento con DBV consiguió una reducción de la estancia hospitalaria de 14 (7-17), con una reducción total de 571 días con un ahorro de 283.187,45€ y para bacteriemias 636, 315.424,2€.

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Unsuccessful treatment of methicillin-resistant Staphylococcus aureus endocarditis with dalbavancin.

Steele JM[1,2], Seabury RW[1], Hale CM[3], Mogle BT[1].

Author information

Abstract

WHAT IS KNOWN AND OBJECTIVE: Limited evidence describes **dalbavancin** use in infective **endocarditis** (IE).

CASE DESCRIPTION: A 27-year-old pregnant female received 4 weeks of **dalbavancin** for methicillin-resistant Staphylococcus aureus (MRSA) bacteraemia and tricuspid valve IE after conventional therapy was no longer an option due to non-compliance. Despite having a smaller cardiac vegetation following **dalbavancin**, she was bacteraemic <2 weeks later with vancomycin-intermediate (VISA) and telavancin-non-susceptible S. aureus.

WHAT IS NEW AND CONCLUSION: This is the first report of unsuccessful IE treatment with **dalbavancin**. Blood cultures grew VISA and lipoglycopeptide-non-susceptible S. aureus <2 weeks following **dalbavancin**. Both outcomes raise concerns about using **dalbavancin** for IE.

Caso

- El paciente se fue de alta en tto con Dalbavancina recibió 1000mg y 3 dosis de 500mg 3 semanas.
- El paciente al mes acudió con nueva ECO ETE que no encontraba cambios con respecto a las previas.
- Analíticamente completamente normal.
- A los 90 días continuaba asintomático, analítica normal y ECO TT con FE 60%, válvula con I Aórtica leve.

Conclusiones

- En la actualidad existen diferentes opciones para el tratamiento de una EI y este debe realizarse de forma individualizada.
- El tratamiento de una EI debería plantearse siempre que sea posible en el seno de un equipo multidisciplinar un “Endocarditis –team”, que valore la mejor opción para el paciente.

Muchas gracias por vuestra atención