X REUNIÓN CIENTÍFICA
GEIO 2025

Shorter is better… ¿También en IPA?

Dr. Mikel Mancheño Losa
Servicio de Medicina Interna
Hospital Universitario 12 Octubre

GEIO
GRUPO DE ESTUDIO DE LA INFECCIÓN OSTEOARTICULAR
seimc

seimc

Infección de prótesis articular

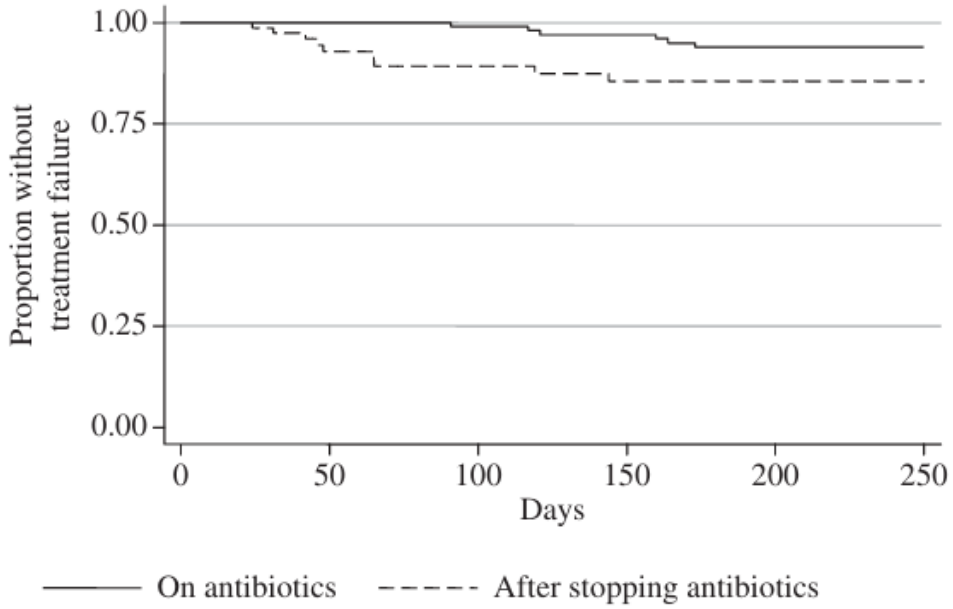
Manejo con retención del implante **(DAIR)**

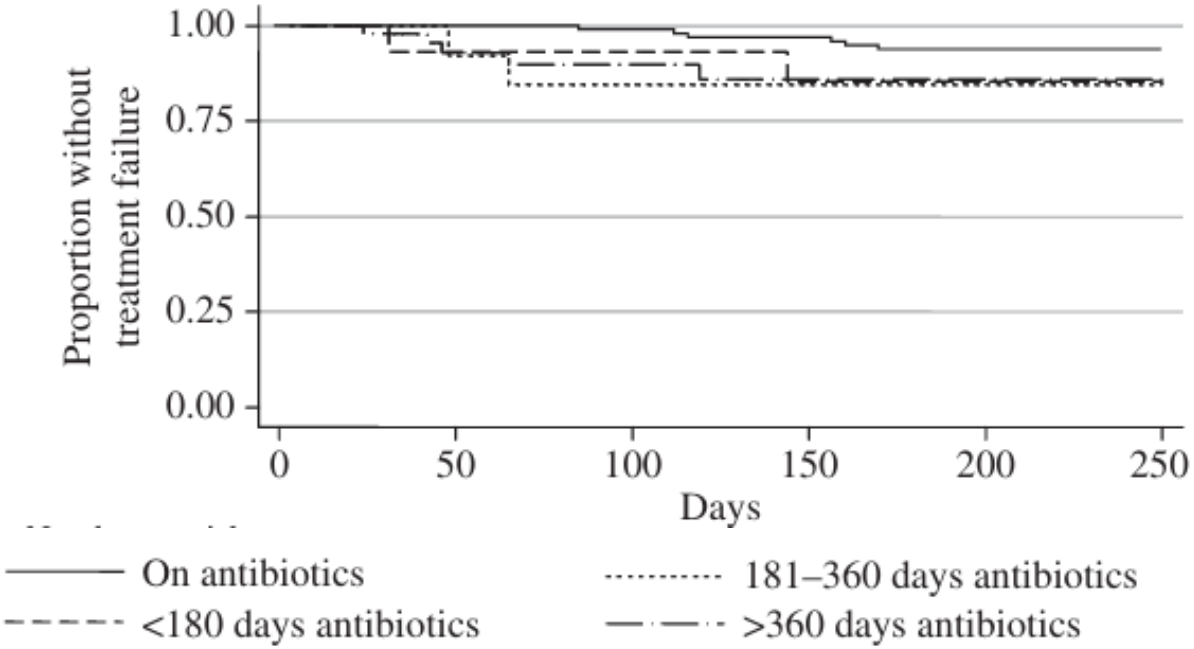
Too long is not better!

One hundred and twelve infected arthroplasties treated with 'DAIR' (debridement, antibiotics and implant retention): antibiotic duration and outcome

JAC 2009

I. Byren[1,2*†], P. Bejon[1,2†], B. L. Atkins[1–3], B. Angus[2], S. Masters[1], P. McLardy-Smith[1], R. Gundle[1] and A. Berendt[1]





to test this. One might conclude that most patients cured of PJI by DAIR are cured early on, and that prolonged antibiotic therapy does not prevent treatment failures in those who are not cured, but merely postpones them. However, there were

Infección de prótesis articular

Manejo con retención del implante **(DAIR)**

Second INTERNATIONAL CONSENSUS MEETING (ICM) on MUSCULOSKELETAL INFECTION

25-27 julio 2018, Philadelphia
Voted by 540 delegates

Hip and Knee Section, Treatment, Debridement and Retention of Implant: Proceedings of International Consensus on Orthopedic Infections

Jean Noël Argenson [1], Marius Arndt [12], George Babis [1], Andrew Battenberg [2],

J Arthroplasty 2019

Question 12: What is the optimal length of antibiotic treatment after debridement, antibiotics, and implant retention (DAIR) for acute periprosthetic joint infections (PJIs)?

Recommendation:

heterogeneity regarding the length, dose, and administration of treatment. A minimum of 6 weeks of antibiotic therapy seems to be sufficient in most cases of PJIs managed by DAIR-provided surgical treatment.

Level of Evidence: Moderate

Delegate Vote: Agree: 91%, Disagree: 8%, Abstain: 1% (Super Majority, Strong Consensus)

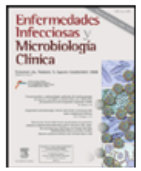
Infección de prótesis articular

Manejo con retención del implante **(DAIR)**

ELSEVIER

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc



Consensus statement

Executive summary of management of prosthetic joint infections. Clinical practice guidelines by the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC)

2017

Javier Ariza (Coordinator)[a], Javier Cobo (Coordinator)[b,*], Josu Baraia-Etxaburu[c], Natividad Benito[d],

What is the optimal duration of the antimicrobial treatment?

- For acute staphylococcal PJI managed with rifampin and levofloxacin, an 8-week schedule of treatment after debridement appears sufficient for most patients **(B-I)**.
- For PJI caused by other microorganisms treated with antibiotics with good activity against biofilm-embedded bacteria (i.e. ciprofloxacin for PJI caused by GNB), 8 weeks is also a reasonable duration **(B-III)**.
- In other clinical scenarios, the most appropriate duration of treatment remains uncertain. A variable period between 8 and 12 weeks may be adequate **(B-III)**.

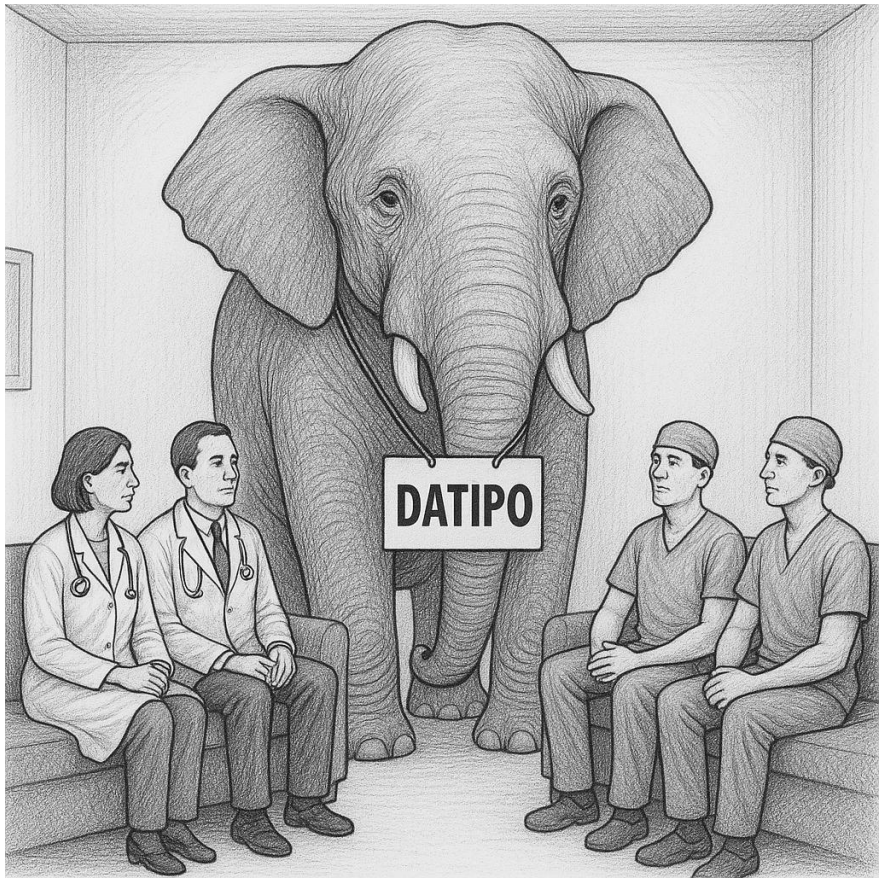
Infección de prótesis articular

Manejo con retención del implante **(DAIR)**

ORIGINAL ARTICLE

Antibiotic Therapy for 6 or 12 Weeks for Prosthetic Joint Infection

L. Bernard, C. Arvieux, B. Brunschweiler, S. Touchais, S. Ansart, J.-P. Bru, E. Oziol, C. Boeri, G. Gras, J. Druon, P. Rosset, E. Senneville, H. Bentayeb, D. Bouhour, G. Le Moal, J. Michon, H. Aumaître, E. Forestier, J.-M. Laffosse, T. Begué, C. Chirouze, F.-A. Dauchy, E. Devaud, B. Martha, D. Burgot, D. Boutoille, E. Stindel, A. Dinh, P. Bemer, B. Giraudeau, B. Issartel, and A. Caille



Recomendaciones clásicas DAIR*: 3 meses en PTC – 6 meses en PTR

*a principios de siglo

Cortesía de la Dra. Ojeda

Debridement:

→ Correctamente indicado **(Algoritmo Zimmerli)**

→ Correctamente realizado **(Recambio de PLE)**

Antibiotics:

→ Uso de antimicrobianos con alta actividad anti*biofilm*

…It's not just the length, but also the choice!

8 semanas

6 semanas

Evidencia III -
Estudios observacionales
no comparativos

Recomendaciones clásicas DAIR*: 3 meses en PTC – 6 meses en PTR

*a principios de siglo

Ref.	N	Etiología	Duración ATB	Tasa curación
Berdal, CMI 2005	29	Varias	**3 meses**	**83%**
Soriano, CMI 2006	47	Varias	**2.7 meses**	**77%**
Martínez-Pastor, AAC 2009	47	BGN	**84 días**	**75%**
Hsieh, CID 2009	27	BGN	**87 días**	**27%**
Cobo, CMI 2010	117	Varias	**81 días**	**57%**

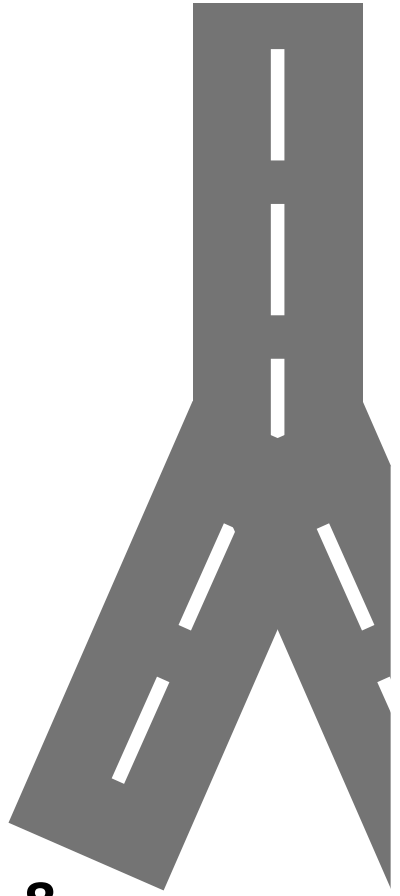
Evidencia III - Estudios observacionales **comparativos**

ORIGINAL ARTICLE — INFECTIOUS DISEASES

Short-course antibiotics for prosthetic joint infections treated with prosthesis retention

Puhto et al. CMI 2011

PRE PTC – 3 meses PTR – 6 meses	Abril 2006	**POST** PTC – 2 meses PTR – 3 meses	
60	N	72	
171.5 (RIQ 88–189)	Duración ATB (días)	88 (RIQ 63–92)	p < 0.001
34/60 **(57%)**	**Tasa curación ITT**	48/72 **(58%)**	p = 0.85
34/38 **(90%)**	**PP**	42/48 **(88%)**	p = 0.78

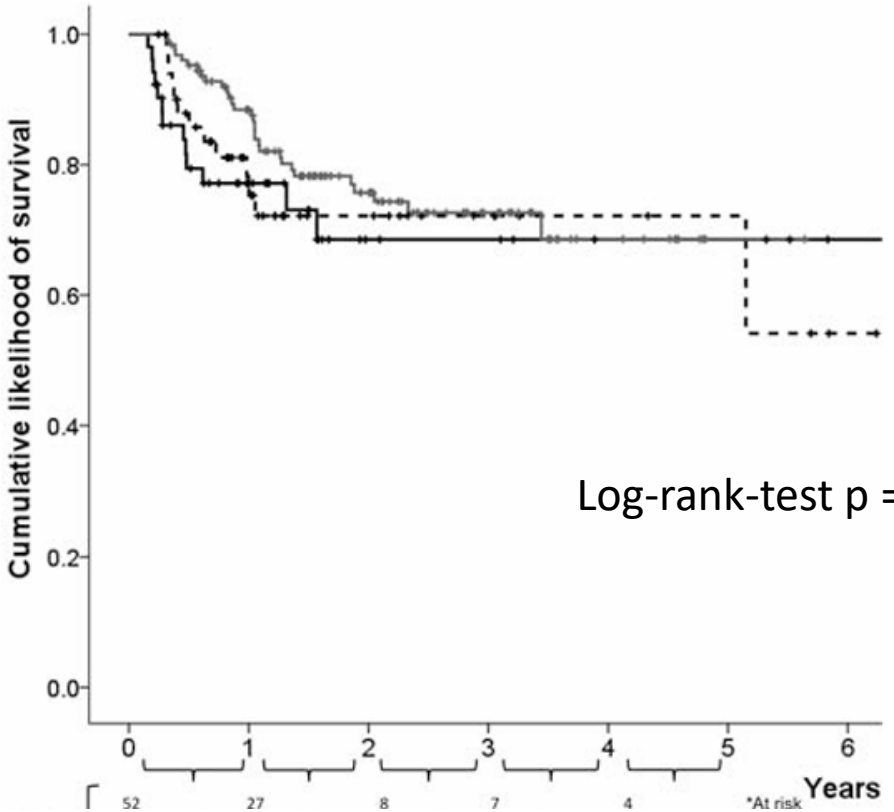


8 semanas

Evidencia III - Estudios observacionales **comparativos**

A Large Multicenter Study of Methicillin–Susceptible and Methicillin–Resistant *Staphylococcus aureus* Prosthetic Joint Infections Managed With Implant Retention

Lora-Tamayo et al. CID 2012



N = 345

terminaron Tto ATB sin fracasar = 239

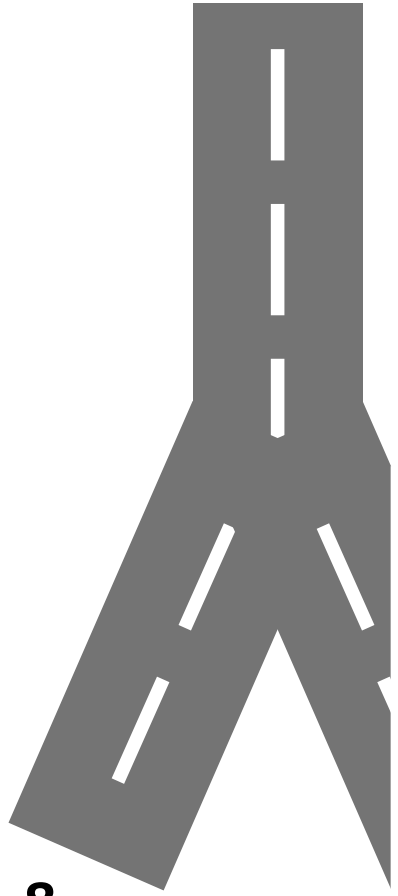
Fracaso tras ATB: 57/239 (**24%**)

Log-rank-test p = 0.434

——— ≤60 días: 13/52 **(25%)**

- - - - - 61 - ≤ 90: 12/52 **(23%)**

——— >90 días: 29/127 **(23%)**



8 semanas

Evidencia I –
Ensayos clínicos

Short- versus long-duration levofloxacin plus rifampicin for acute staphylococcal prosthetic joint infection managed with implant retention: a randomised clinical trial ☆

IJAA 2016

Jaime Lora-Tamayo [1,*], Gorane Euba [2], Javier Cobo [3], Juan Pablo Horcajada [4], Alex Soriano [5], Enrique Sandoval [6], Carles Pigrau [7], Natividad Benito [8], Luis Falgueras [9], Julián Palomino [10], María Dolores del Toro [11], Alfredo Jover-Sáenz [12], José Antonio Iribarren [13], Mar Sánchez-Somolinos [14], Antonio Ramos [15], Marta Fernández-Sampedro [16], Melchor Riera [17], Josu Mirena Baraia-Etxaburu [18], Javier Ariza [2], Prosthetic Joint Infection Group of the Spanish Network for Research in Infectious Diseases—REIPI

Ensayo clínico aleatorizado, abierto, comparativo
17 Hospitales españoles, de 2009 a 2013

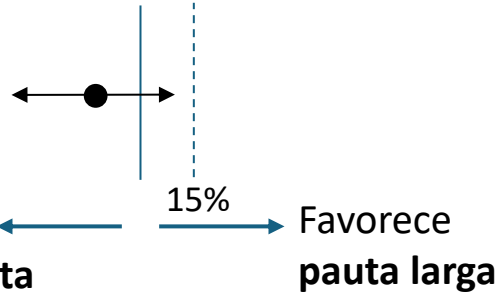
Criterios de inclusión:
- Infección estafilocócica aguda
- Retención del implante (DAIR)

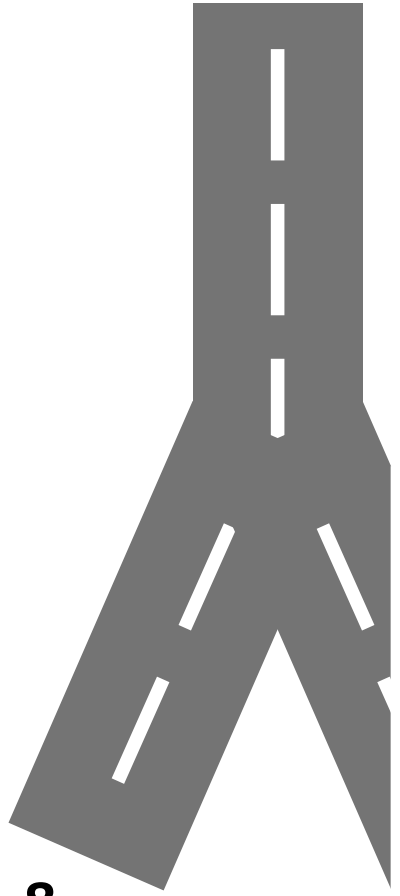
Pauta corta = 8 semanas
Prótesis cadera & rodilla

Rifampicina 600 mg/d
Levofloxacino 750 mg/d

Pauta larga (SOC)
- Prótesis cadera = 3 meses
- Prótesis rodilla = 6 meses

Objetivo: Tasa de curación
Hipótesis de no-inferioridad
Δ = 15%, α=0.025, 1-β=0.80



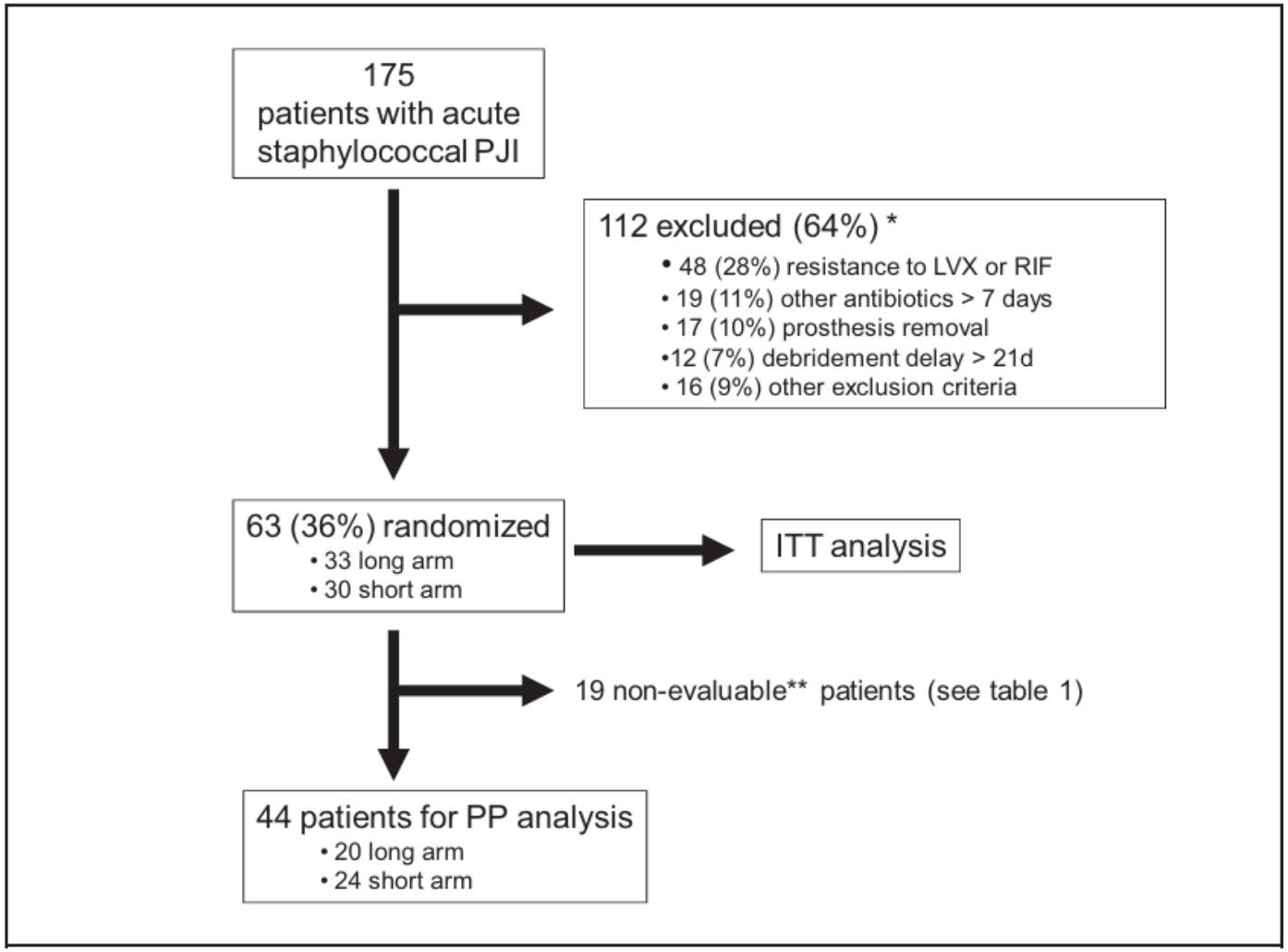


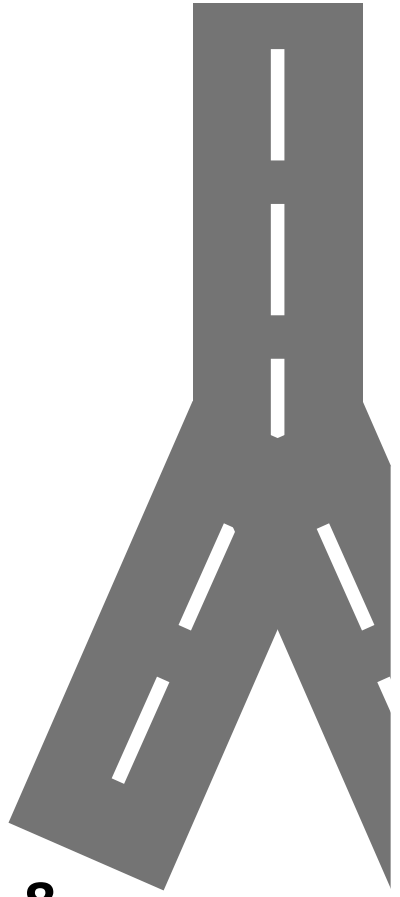
8 semanas

Evidencia I –
Ensayos clínicos

Short- versus long-duration levofloxacin plus rifampicin for acute staphylococcal prosthetic joint infection managed with implant retention: a randomised clinical trial ☆

Lora-Tamayo et al. IJAA 2016





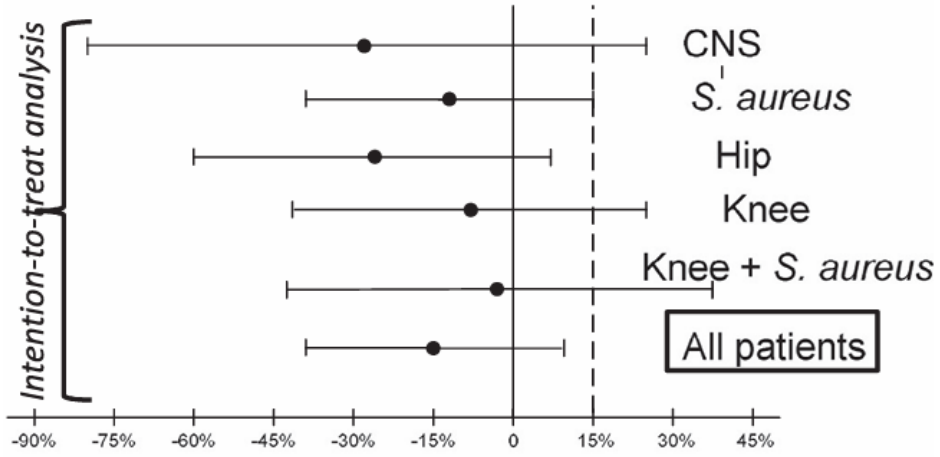
8 semanas

Evidencia I –
Ensayos clínicos

Short- versus long-duration levofloxacin plus rifampicin for acute staphylococcal prosthetic joint infection managed with implant retention: a randomised clinical trial ☆

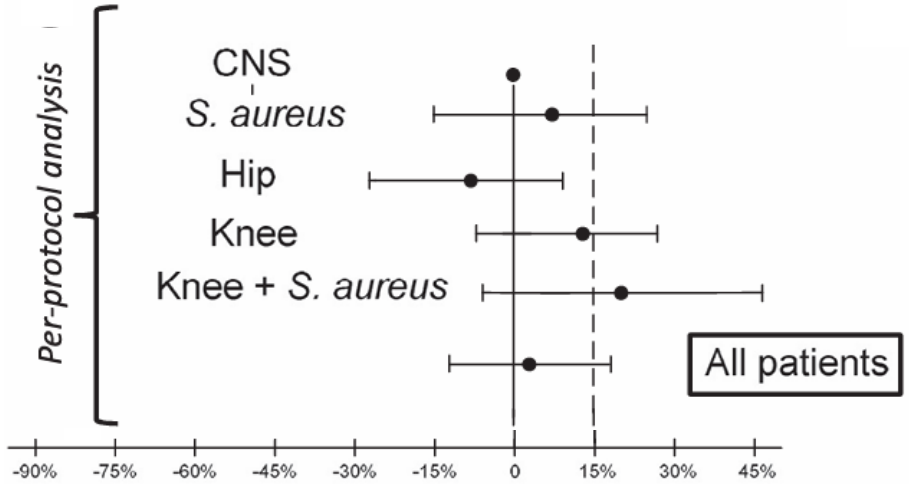
Lora-Tamayo et al. IJAA 2016

Análisis por intención de tratar



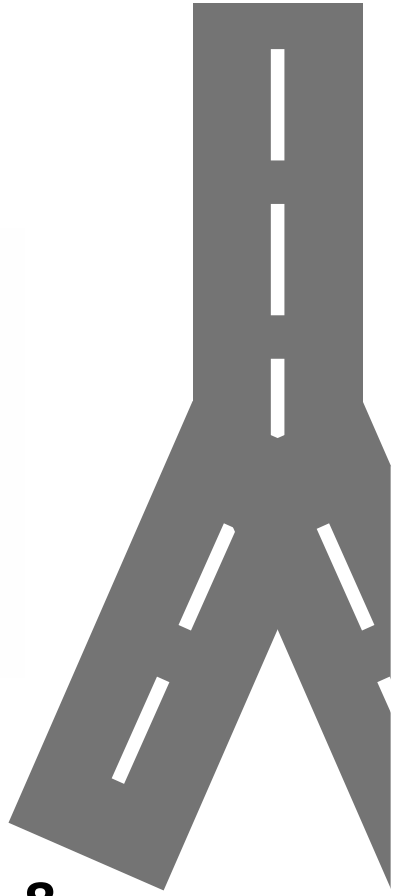
Favorece **pauta corta** ← → Favorece **pauta larga**

Análisis por protocolo



Favorece **pauta corta** ← → Favorece **pauta larga**

Tasa curación:	22/30 **(73%)**	19/33 **(58%)**	19/20 **(92%)**	22/24 **(95%)**



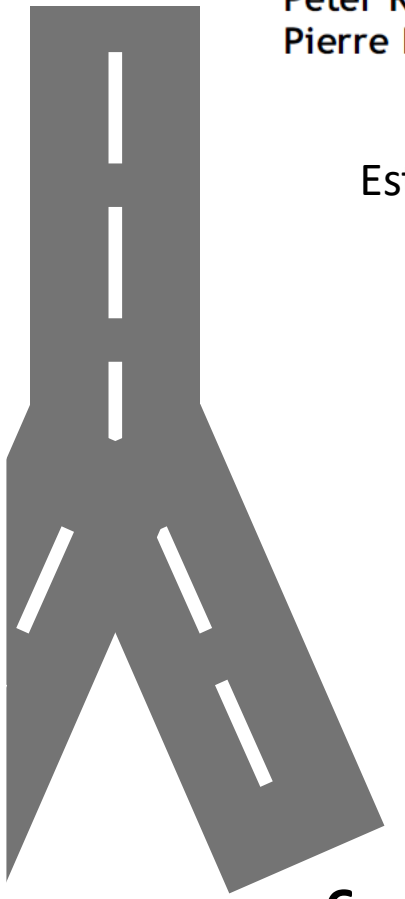
8 semanas

Evidencia III - Estudios observacionales **comparativos**

Six weeks of antibiotic treatment is sufficient following surgery for septic arthroplasty☆

Louis Bernard [a,d], Laurence Legout [a], Line Zürcher-Pfund [a], Richard Stern [a], Peter Rohner [b], Robin Peter [a], Mathieu Assal [a], Daniel Lew [c], Pierre Hoffmeyer [a], Ilker Uçkay [a,c,*]

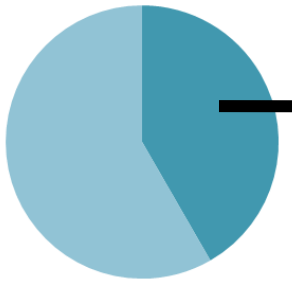
J Infection, 2010



6 semanas

Estudio prospectivo (1996-2007), observacional, unicéntrico, **n=144**

- 12 semanas (traumatólogo): n = 70; DAIR 54%; ATB-IV 15 días; **curación 82%**
- 6 semanas (infectólogo): n = 74; DAIR 29%; ATB-IV 10 días; **curación 85%**



DAIR n = 60

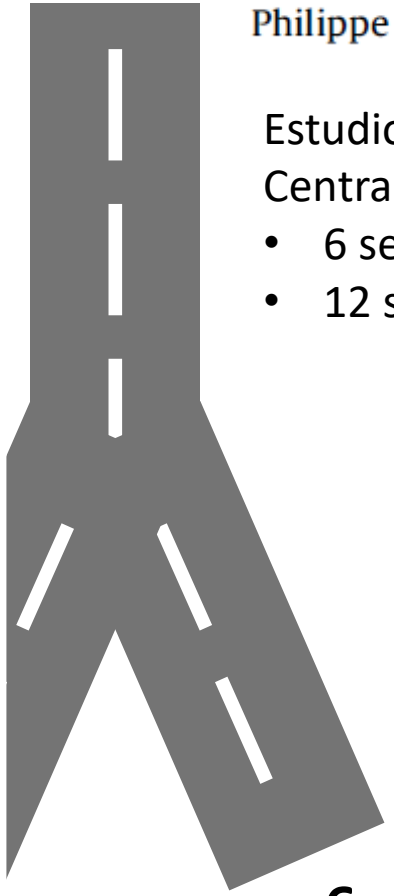
- **20 casos tratados 6 sem → Curación 90%**
- 40 casos 12 sem

Evidencia III - Estudios observacionales **comparativos**

Antibiotic therapy duration for prosthetic joint infections treated by Debridement and Implant Retention (DAIR): Similar long-term remission for 6 weeks as compared to 12 weeks

Int J ID 2017

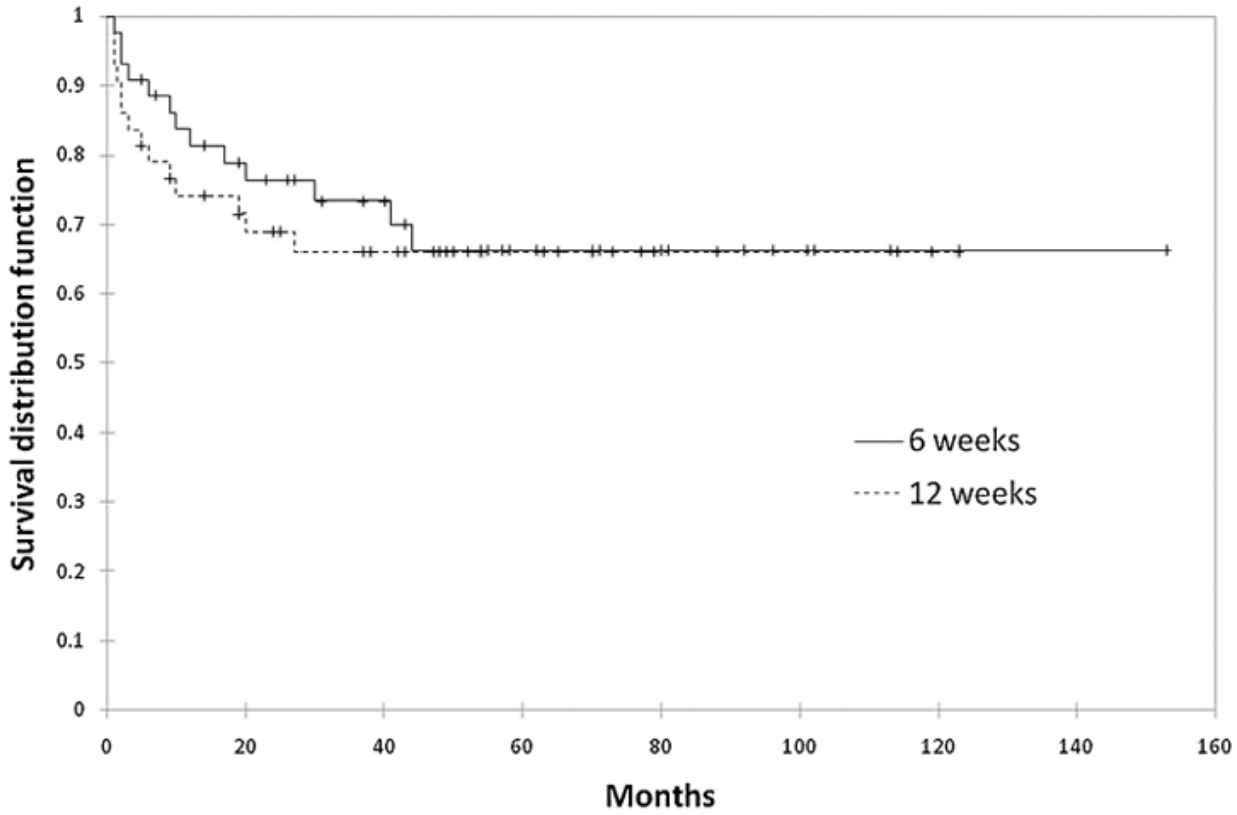
Hélène Chaussade[a], Ilker Uçkay[b,*], Albert Vuagnat[c], Jérôme Druon[a], Guillaume Gras[a], Philippe Rosset[a], Benjamin A. Lipsky[b,d], Louis Bernard[a,b]



6 semanas

Estudio retrospectivo multicéntrico (1989-2011)
Centrado en **DAIR (n = 87)**

- 6 sem exactas: n = 44 ; **curación 71%**
- 12 sem exactas: n = 43; **curación 67%**



Evidencia I –
Ensayos clínicos

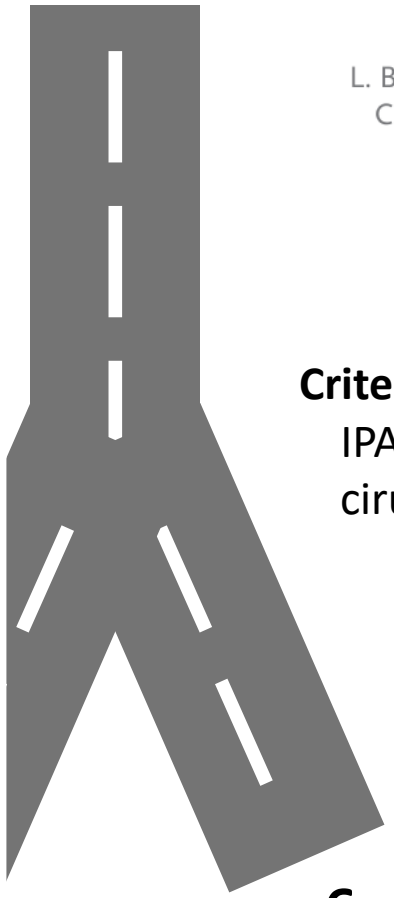
ORIGINAL ARTICLE

Antibiotic Therapy for 6 or 12 Weeks for Prosthetic Joint Infection

NEJM 2021

L. Bernard, C. Arvieux, B. Brunschweiler, S. Touchais, S. Ansart, J.-P. Bru, E. Oziol, C. Boeri, G. Gras, J. Druon, P. Rosset, E. Senneville, H. Bentayeb, D. Bouhour, G. Le Moal, J. Michon, H. Aumaître, E. Forestier, J.-M. Laffosse, T. Begué, C. Chirouze, F.-A. Dauchy, E. Devaud, B. Martha, D. Burgot, D. Boutoille, E. Stindel, A. Dinh, P. Bemer, B. Giraudeau, B. Issartel, and A. Caille

Ensayo clínico aleatorizado, abierto, controlado, comparativo
24 Hospitales franceses, 2011 a 2015



6 semanas

Criterios de inclusión:
IPA manejada con cirugía según SOC

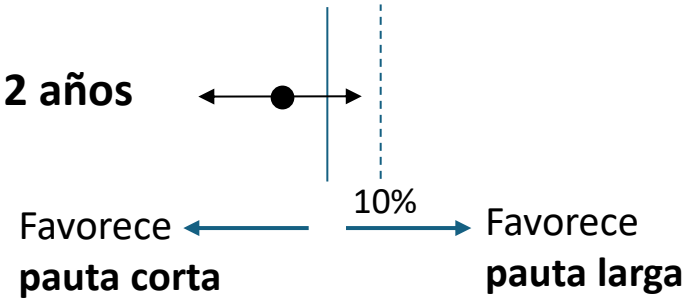
<21d

Aleatorización 1:1, estratificada:
- Tipo de cirugía
- Núm. Episodio inf.
- Rodillas vs Caderas

Pauta corta = 6 semanas
n = 203;
DAIR 40%; *S. aureus* 38%; CoNS 30%

Pauta larga = 12 semanas
n = 201;
DAIR 42%; *S. aureus* 30%; CoNS 35%

Objetivo: Persistencia de infección a 2 años
Hipótesis de no-inferioridad
Δ = 10%, α=0.025, 1-β=0.80



Evidencia I –
Ensayos clínicos

ORIGINAL ARTICLE

Antibiotic Therapy for 6 or 12 Weeks for Prosthetic Joint Infection

Bernard et al. NEJM 2021

Subgroup	6-Wk Therapy	12-Wk Therapy	Risk Difference (95% CI)
	no. of patients with event/total no. (%)		*percentage points*
All patients	**32/190 (16.8%)**	**15/188 (8%)**	**8.9 (2.2-15.6)**
Surgical procedure			
Débridement	23/75 (30.7)	11/76 (14.5)	16.2 (2.9 to 29.5)
Two-stage revision	6/40 (15.0)	2/41 (4.9)	10.1 (–3.1 to 23.3)
One-stage revision	3/75 (4.0)	2/71 (2.8)	1.2 (–4.8 to 7.1)
Affected joint			
Hip	19/122 (15.6)	9/117 (7.7)	7.9 (–0.2 to 16.0)
Knee	13/68 (19.1)	6/71 (8.5)	10.7 (–0.9 to 22.2)
Episode of prosthetic joint infection			
First	27/162 (16.7)	13/160 (8.1)	8.5 (1.4 to 15.7)
At least the second	5/28 (17.9)	2/28 (7.1)	10.7 (–7.0 to 28.4)

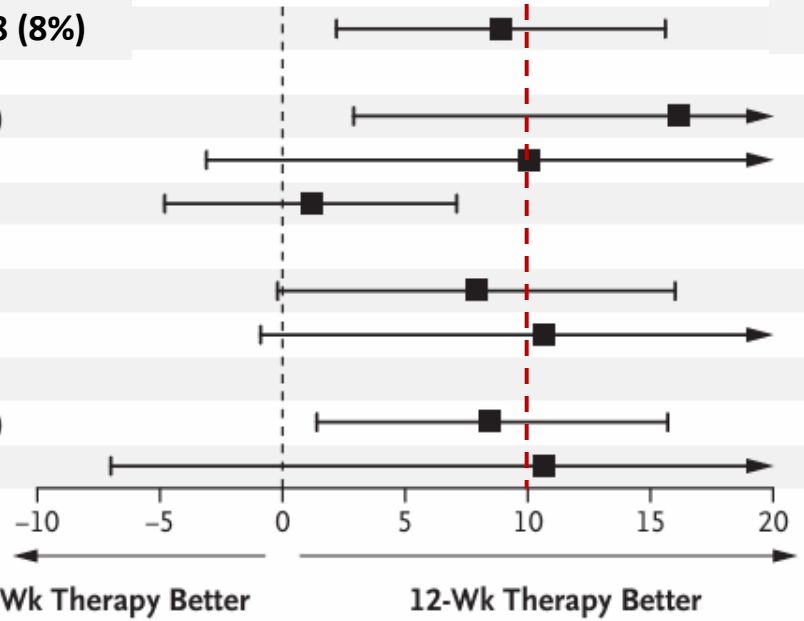
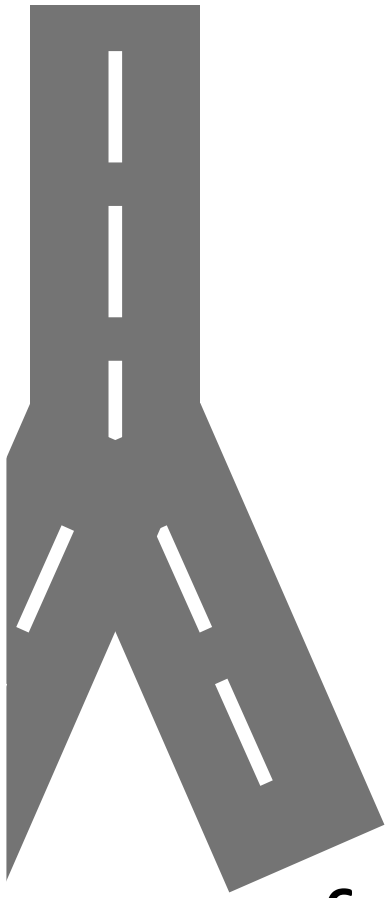


Figure 2. Exploratory Subgroup Analyses of Persistent Infection within 2 Years after the Completion of Antibiotic Therapy (Primary Outcome).

6 semanas

Evidencia I –
Ensayos clínicos



6 semanas

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antibiotic Therapy for 6 or 12 Weeks for Prosthetic Joint Infection

L. Bernard, C. Arvieux, B. Brunschweiler, S. Touchais, S. An[illegible] J.-P. Bru, E. Oziol, C. Boeri, G. Gras, J. Druon, P. Rosset, E. Senneville, H. B[illegible]yeb, D. Bouhour, G. Le Moal, J. Michon, H. Aumaître, E. Forestier, J.-M. Laffosse, T. Bégué, C. Chirouze, F.-A. Dauchy, E. Devaud, B. Martha, D. Burgot, D. Boutoille, E. Stindel, A. Dinh, P. Bemer, B. Giraudeau, B. Issartel, and A. Caille

ABSTRACT

BACKGROUND

The management of prosthetic joint infection usually consists of a combination of surgery and antimicrobial therapy. The appropriate duration of antimicrobial therapy for this indication remains unclear.

METHODS

We performed an open-label, randomized, controlled, noninferiority trial to compare 6 weeks with 12 weeks of antibiotic therapy in patients with microbiologically confirmed prosthetic joint infection that had been managed with an appropriate surgical procedure. The primary outcome was persistent infection (defined as the persistence or recurrence of infection with the initial causative bacteria, with an antibiotic susceptibility pattern that was phenotypically indistinguishable from that at enrollment) within 2 years after the completion of antibiotic therapy. Noninferiority of 6 weeks of therapy to 12 weeks of therapy would be shown if the upper boundary of the 95% confidence interval for the absolute between-group difference (the value in the 6-week group minus the value in the 12-week group) in the percentage of patients with persistent infection within 2 years was not greater than 10 percentage points.

RESULTS

A total of 410 patients from 28 French centers were randomly assigned to receive antibiotic therapy for 6 weeks (205 patients) or for 12 weeks (205 patients). Six patients who withdrew consent were not included in the analysis. In the main analysis, 20 patients who died during follow-up were excluded, and missing outcomes for 6 patients who were lost to follow-up were considered to be persistent infection. Persistent infection occurred in 35 of 193 patients (18.1%) in the 6-week group and in 18 of 191 patients (9.4%) in the 12-week group (risk difference, 8.7 percentage points; 95% confidence interval, 1.8 to 15.6); thus, noninferiority was not shown. Noninferiority was also not shown in the per-protocol and sensitivity analyses. We found no evidence of between-group differences in the percentage of patients with treatment failure due to a new infection, probable treatment failure, or serious adverse events.

CONCLUSIONS

Among patients with microbiologically confirmed prosthetic joint infections that were managed with standard surgical procedures, antibiotic therapy for 6 weeks was not shown to be noninferior to antibiotic therapy for 12 weeks and resulted in a higher percentage of patients with unfavorable outcomes. (Funded by Programme Hospitalier de Recherche Clinique, French Ministry of Health; DATIPO ClinicalTrials.gov number, NCT01816009.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Bernard at the Division of Infectious Diseases, University Hospital Bretonneau, 2 Boulevard Tonnellé, 37044 Tours CEDEX 9, France, or at l.bernard@chu-tours.fr.

N Engl J Med 2021;384:1991-2001.
DOI: 10.1056/NEJMoa2020198

HETEROGENEIDAD

Diferentes tipos de IPA

Varios manejos quirúrgicos

sis. Future studies should be directed at a single surgical procedure such as débridement with implant retention or prosthetic joint replacement but not both in the same trial. Second, this trial was open-label, but detection bias was mini-

Varias etiologías (>% *S.aureus* en 6s)

Múltiples regímenes antimicrobianos

the choice of antibiotics was left to the treating physician, antibiotic treatment was not standardized, which led to the use of a wide variety of molecules, with different routes of administration. Prosthetic joint infection is typically man-

Infección de prótesis articular

Manejo con retención del implante **(DAIR)**

- La duración del Tto ATB en IPA manejada con DAIR no debe ser inferior a 6 semanas
- En escenarios favorables probablemente 8 semanas de Tto ATB sea suficiente
- En escenarios desfavorables y ante una evolución subóptima es adecuado mantener el tratamiento hasta cumplir 12 semanas

Debridement:

✓ Correctamente indicado **(Algoritmo Zimmerli)**

✓ Correctamente realizado **(Recambio de PLE)**

Antibiotics:

✓ Uso de antimicrobianos con alta actividad anti*biofilm*

…It's not just the length, but also the choice!

Infección de prótesis articular

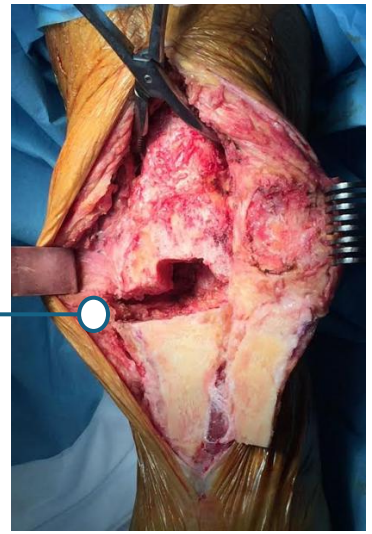
Manejo con explante protésico

Cortesía de la Dra. Ojeda

ORIGINAL ARTICLE

Antibiotic Therapy for 6 or 12 Weeks for Prosthetic Joint Infection

L. Bernard, C. Arvieux, B. Brunschweiler, S. Touchais, S. Ansart, J.-P. Bru, E. Oziol, C. Boeri, G. Gras, J. Druon, P. Rosset, E. Senneville, H. Bentayeb, D. Bouhour, G. Le Moal, J. Michon, H. Aumaître, E. Forestier, J.-M. Laffosse, T. Begué, C. Chirouze, F.-A. Dauchy, E. Devaud, B. Martha, D. Burgot, D. Boutoille, E. Stindel, A. Dinh, P. Bemer, B. Giraudeau, B. Issartel, and A. Caille



Cortesía del Dr. Cano

SOC: 4 - 6 semanas

Osmon et al. CID 2012

¿Se puede reducir todavía más?

- Retirada del dispositivo
- Erradicación mecánica del biofilm
- Posibilidad de utilización de ATB local

Evidencia III - Estudios observacionales **no comparativos**

- Estudios unicéntricos, observacionales, la mayoría prospectivos
- Principalmente infecciones crónicas, SCN en un 33-63% de los casos
- **Antibioterapia local**: vancomicina + aminoglucósido

Ref	n/Loc	Sys ATB	Follow-up	*outcome* Need 2nd debrid	PIOC at 2nd step	Relapse/ Persist
Hoad-Reddick 2005	39/Knee	5 days	56 m	15%	18%	11%
Hart & Jones 2006	48/Knee	14 days iv	49 m	13%	23%	-
Stockley 2008	114/Hip	1 day	74 m	4%	16%	12%
Whittaker 2009	44/Hip	14 days (vanco)	49 m	7%	2%	7%
McKenna 2009	31/Hip	5 days	35 m	0%	0%	0%

Evidencia III - Estudios observacionales **comparativos**

Two-stage revision of infected hip arthroplasty using an antibiotic-loaded spacer: retrospective comparison between short-term and prolonged antibiotic therapy

Hsieh et al. JAC 2009

Estudio pre-post retrospectivo, unicéntrico
ATB local variable: vanco 79%; genta 53%; aztreonam 32%

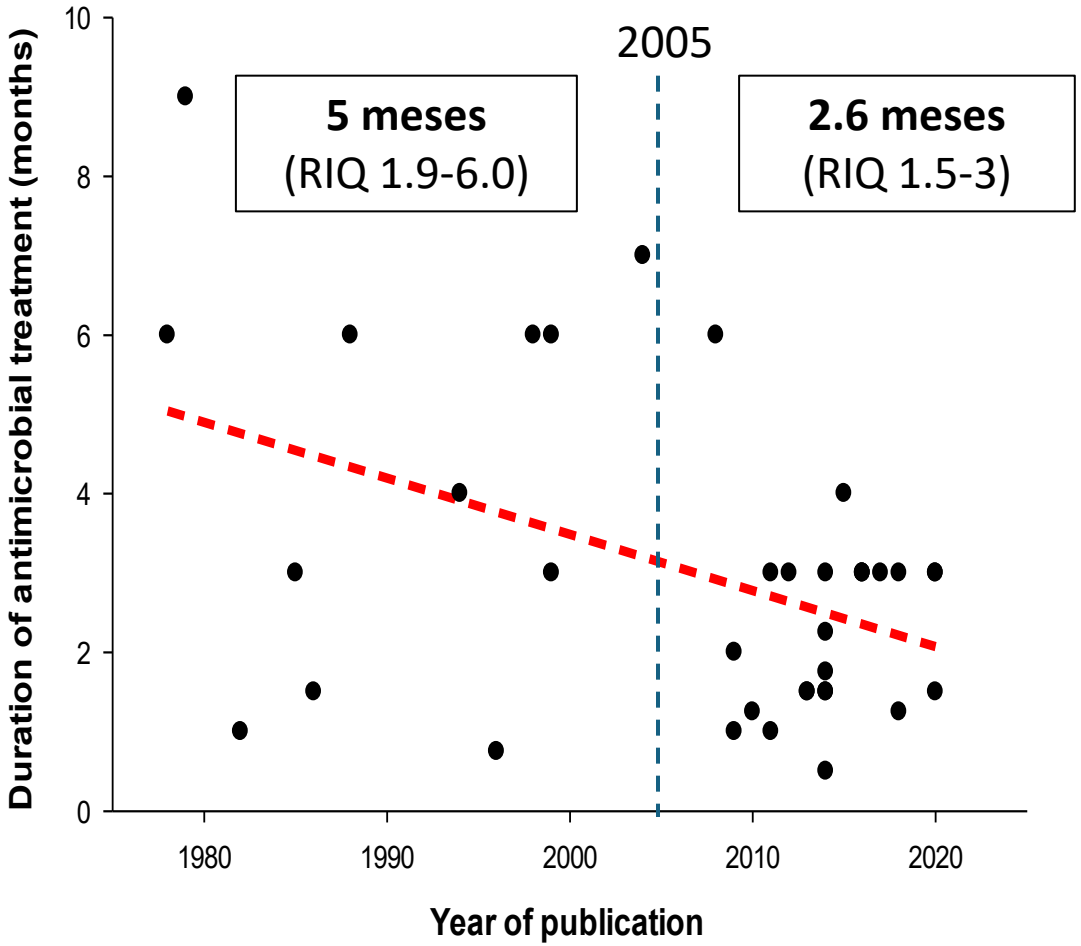
	2002-03 **ATB 4 sem (iv) ± 2 sem (oral)** **N=46**	**2004-05** **ATB 1 semana (iv)** **N=53**
Necesidad de nuevo desbridamiento	9%	6%
Recidiva tras el segundo tiempo	4%	6%

Evidencia I –
Ensayos clínicos

The SOLARIO Trial

¡¡¡ Por favor no publicar imágenes en web o redes sociales !!!

Recambio en 1 tiempo



Lora-Tamayo et al. Antibiotics 2024

Evidencia III - Estudios observacionales **no comparativos**

Six-week antibiotic therapy after one-stage replacement arthroplasty for hip and knee periprosthetic joint infection

Chieffo et al. Med Mal Infect 2020

Estudio observacional retrospectivo
IPA manejada con R1T
n = 50; 70% aislamientos: SCN + C. *acnes*

84% prótesis cementada (gentamicina)

ATB 6 semanas (RIQ 6-7)

Tasa de curación: 44/49 **(90%)**

Infección de prótesis articular

Manejo con explante protésico

R1T:

- Estudios observacionales y un subanálisis de un ECA invitan a pensar que 6 semanas de antibioterapia podrían ser suficientes, particularmente si se utilizan prótesis cementadas con ATB

R2T:

- El uso de antibioterapia local activa podría permitir una reducción drástica de la duración de antibioterapia sistémica, probablemente a no más de 7 días

Cortesía del Dr. Cano

Muchas gracias por su atención