

IV Congreso



SEICAV

Sociedad Española de Infecciones Cardiovasculares

Infecciones en pacientes con dispositivos de asistencia ventricular: *opciones de profilaxis y tratamiento antibiótico*



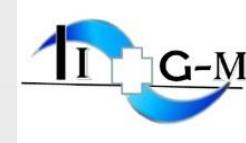
Santander, Viernes, 30 de Octubre 2015. 16:20-16:40

Patricia Muñoz

Hospital General Universitario Gregorio Marañón
Universidad Complutense de Madrid



**Hospital General Universitario
GREGORIO MARAÑÓN**



Dispositivos asistencia ventricular

- 1. De que hablamos cuando hablamos de “asistencias ventriculares”?**
- 2. Infecciones?**
- 3. Tratamiento?**
- 4. Profilaxis?**



CARDIAC
FAILURE

ACUTE INTERMACS 1

ECMO
O
LEVITRONIX

RECOVERY

BRIDGE TO
DECISION

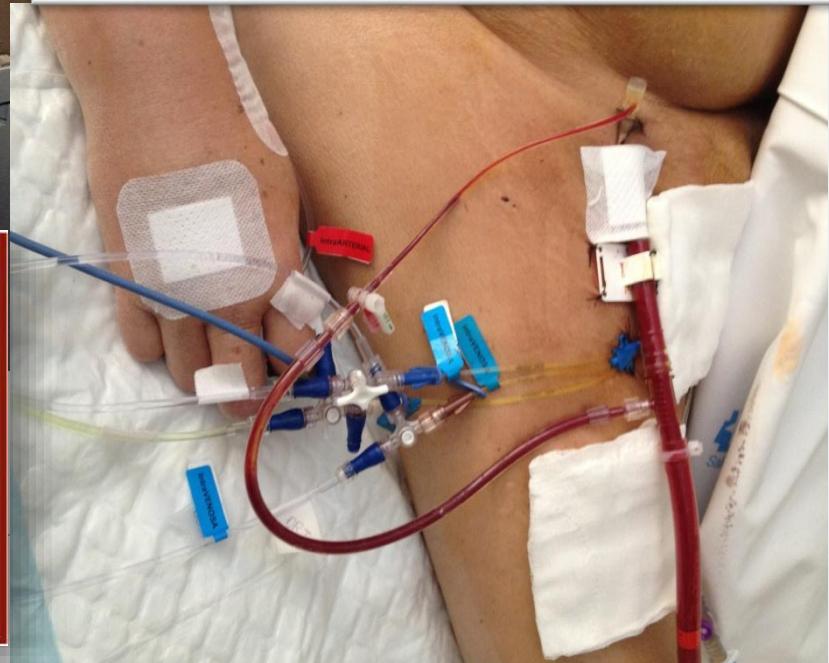
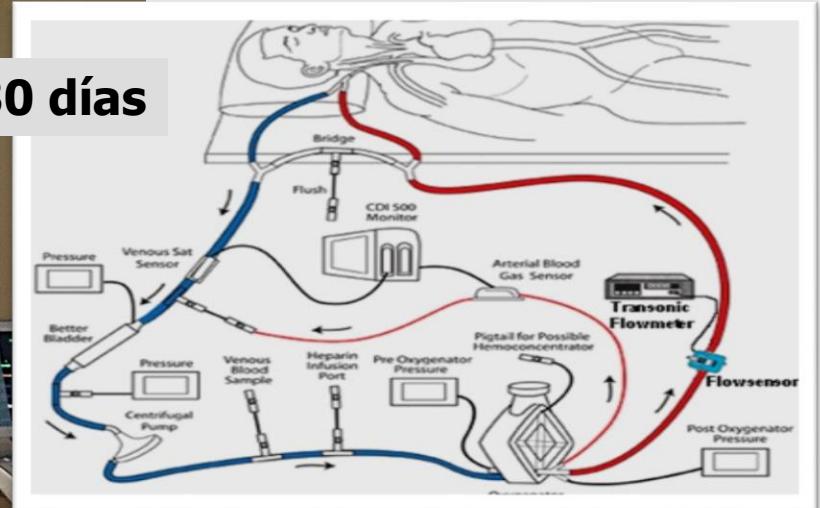
Bridge to bridge

Bridge to Tx

ECMO (extracorporeal membrane oxygenation (2000 € por set)



< 30 días



LEVITRONIX

(~7-10.000 €)

- < 60 d
- Cánulas esternotomía AD-AP y/o VI-Aorta, tubuladuras, bomba centrífuga
- Extubado y movilizable



Asistencias de larga duración aprobadas FDA

Type	Device
Durable devices	
Continuous flow	Thoratec HeartMate II HeartWare HVAD MicroMed DeBakey Child VA
Pulsatile extracorporeal	Thoratec PVAD Berlin Heart EXCOR
Pulsatile intracorporeal	HeartMate IP HeartMate VE HeartMate XVE Thoratec IVAD Novacor PC Novacor PCq SynCardia CardioWest AbioCor TAH
Total artificial heart	



HeartMate II



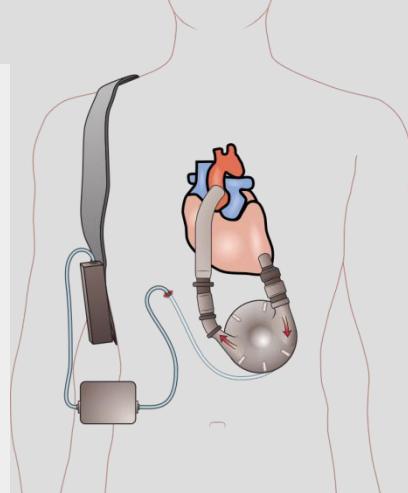
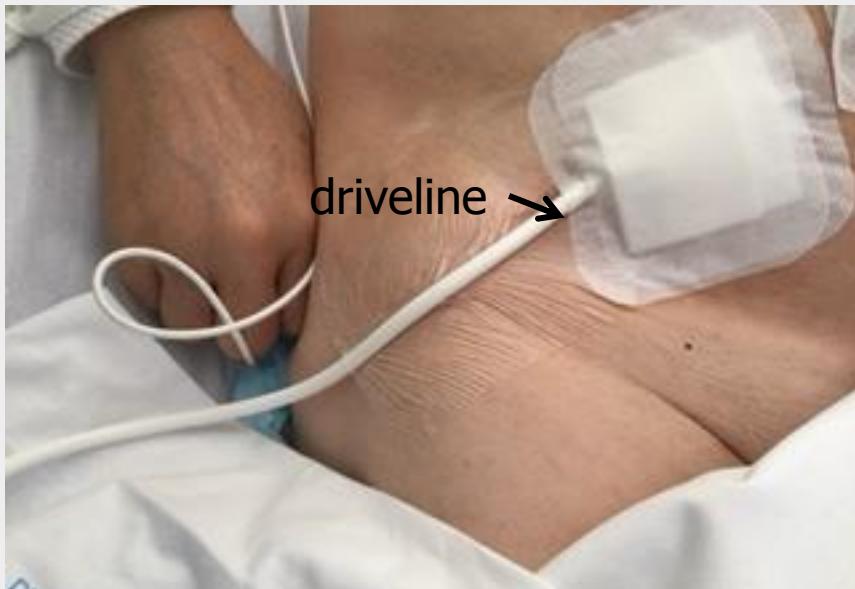
Berlin Heart EXCOR

Berlin Heart (~20.000 € cada ventrículo)



Heartmate II (~100.000 €)

Años

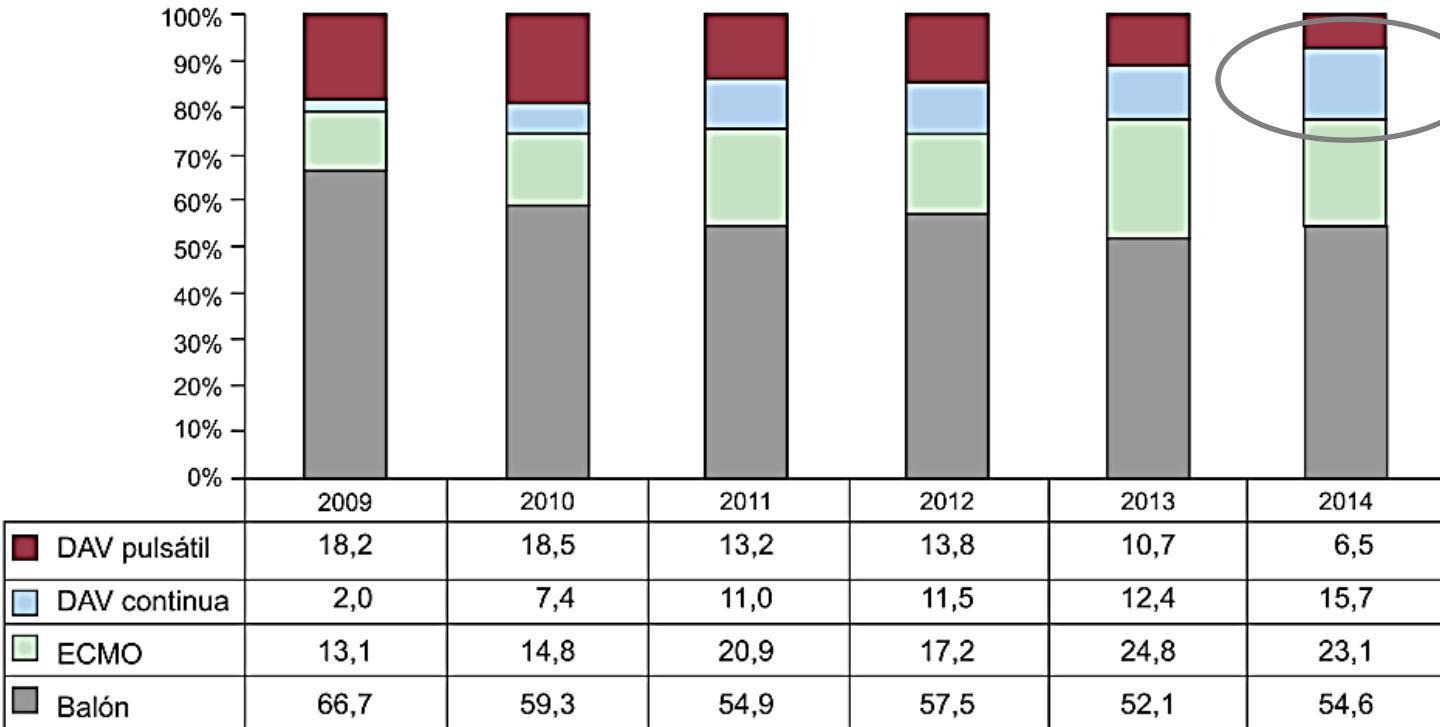


Ojo, La mayoría de artículos se refieren a este tipo de asistencias, pero en España aún son muy raras



Spanish Heart Transplantation Registry

26th Official Report (1984-2014)



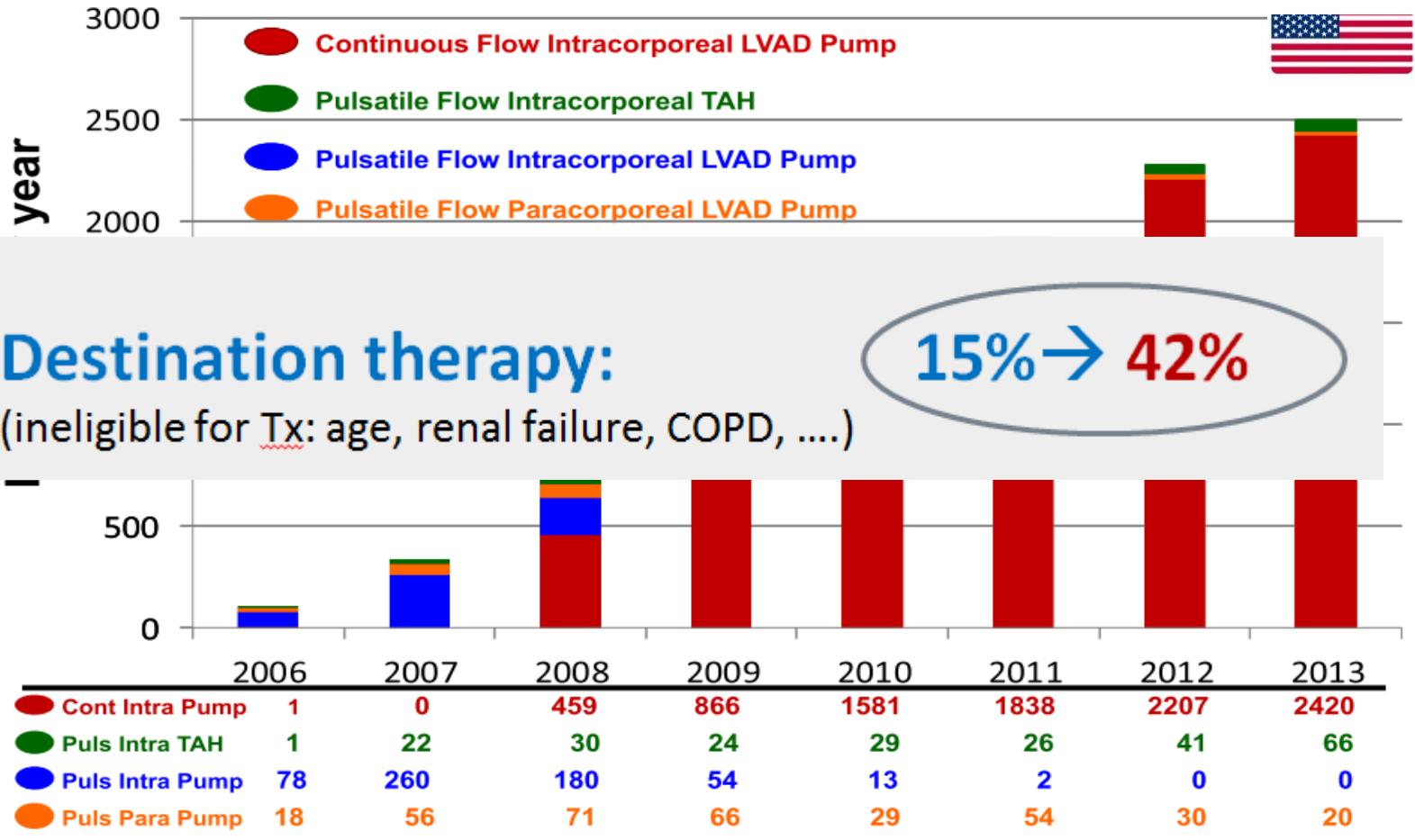
- En 2014, se usó una asistencia temporal en el **18.8% de los TXC (50/266)**
- Las asistencias de flujo continuo: 2,0% en 2009 y **15,7% en 2014 (~8)**
- El peor pronóstico: TXC urgente en **ECMO** (usarlo sólo como puente a decisión)

Uso de asistencias USA

Survival

- 1yr: 80%

- 2 yrs: 70%



Dispositivos asistencia ventricular

1. De que hablamos cuando hablamos de
“asistencias ventriculares”?
2. *Infecciones?*
3. Tratamiento?
4. Profilaxis?





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J Am Coll Cardiol. 2014 July 29; 64(4): 372–381. doi:10.1016/j.jacc.2014.04.052.

MANAGEMENT PRACTICES AND MAJOR INFECTIONS AFTER CARDIAC SURGERY

Annette C. Glijns, PhD*, Alan J. Moskowitz, MD*, Michael A. Acker, MD†, Michael

5,158 cardiac surgery patients

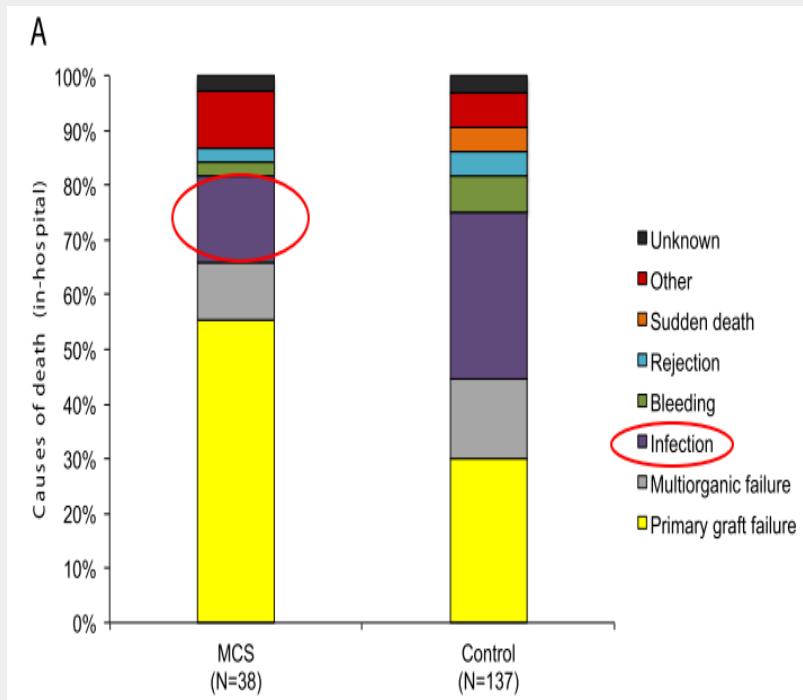
Baseline and Procedure Characteristics Associated With Infection

Baseline Variable	HR (95% CI)	P Value
COPD (yes/no)	1.66 (1.21, 2.26)	0.002
Heart failure (yes/no)	1.47 (1.11, 1.95)	0.007
Corticosteroids (yes/no)	1.91 (1.19, 3.05)	0.007
Creatinine, mg/dL	1.15 (1.08, 1.22)	<.001
Hemoglobin, g/dL	0.90 (0.84, 0.97)	0.008
LVAD/Tx (yes/no)	2.89 (1.86, 4.50)	<.001
Open sternum (yes/no)	6.35 (2.62, 15.38)	<.001
Duration of surgery (hours)	1.31 (1.21, 1.41)	<.001

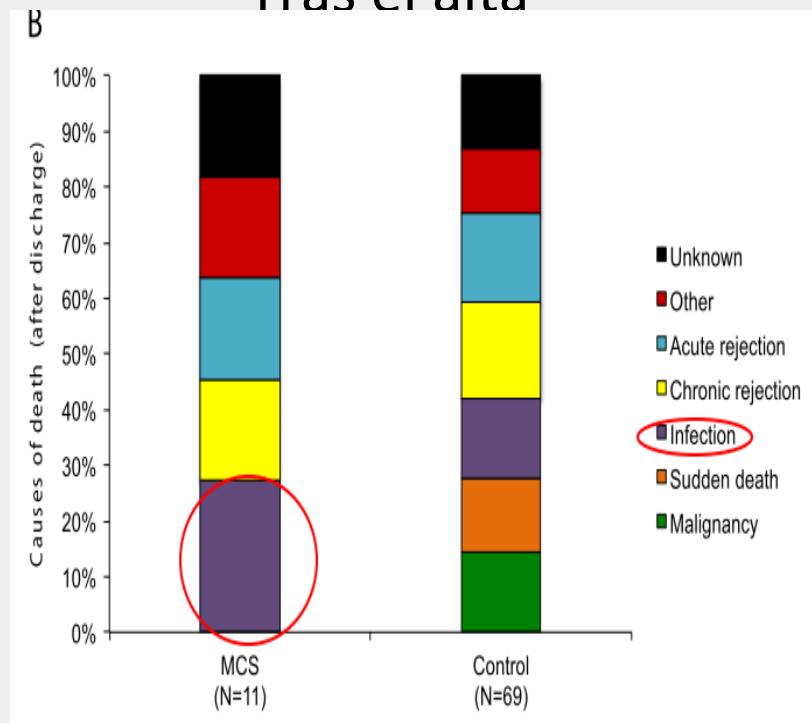
Mortalidad en TXC urgentes (> si precisó AV)

Mayor mortalidad global (OR 1.75, 95% CI 1.05–2.91) y mortalidad postrasplante (aHR 1.60, 95% CI 1.15–2.23).

Intrahospitalaria



Tras el alta

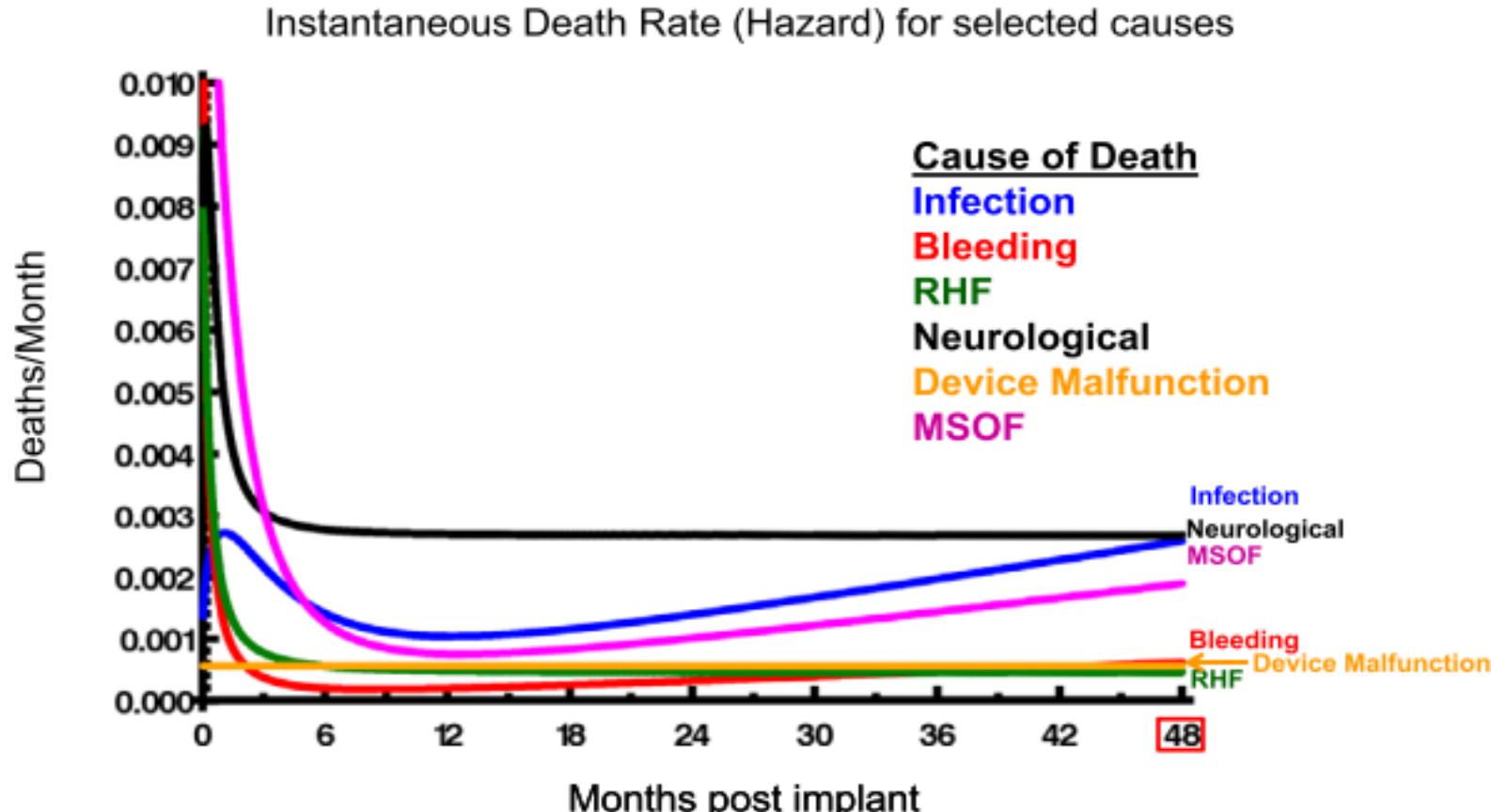


NO factor independiente de mortalidad

Sixth INTERMACS annual report: A 10,000-patient database

James K. Kirklin, MD,^a David C. Naftel, PhD,^a Francis D. Pagani, MD, PhD,^b Robert L. Kormos, MD,^c Lynne W. Stevenson, MD,^d Elizabeth D. Blume, MD,^e Marissa A. Miller, DVM, MPH,^f J. Timothy Baldwin, PhD,^f and James B. Young, MD^g

Intermacs Continuous Flow LVAD/BiVAD Implants: 2008 – 2013, n = 9372



Working formulation for the standardization of definitions of infections in patients using ventricular assist devices

Margaret M. Hannan, MD^l, Shahid Husain, MD,^b Frauke Mattner, MD,^c Lara Danziger-Isakov, MD,^d Richard J. Drew, MB,^a G. Ralph Corey, MD,^e Stephan Schueler, MD, PhD,^g William L. Holman, MD,^h Leo P. Lawler, MD,^a Steve M. Gordon, MD,^d Niall G. Mahon, MD,^a John M. Herre, MD,^f Kate Gould, MB,^g Jose G. Montoya, MD,ⁱ Robert F. Padera, MD, PhD,^j Robert L. Kormos, MD,^k John V. Conte, MD,^l and Martha L. Mooney, MD^e

VAD-specific infections

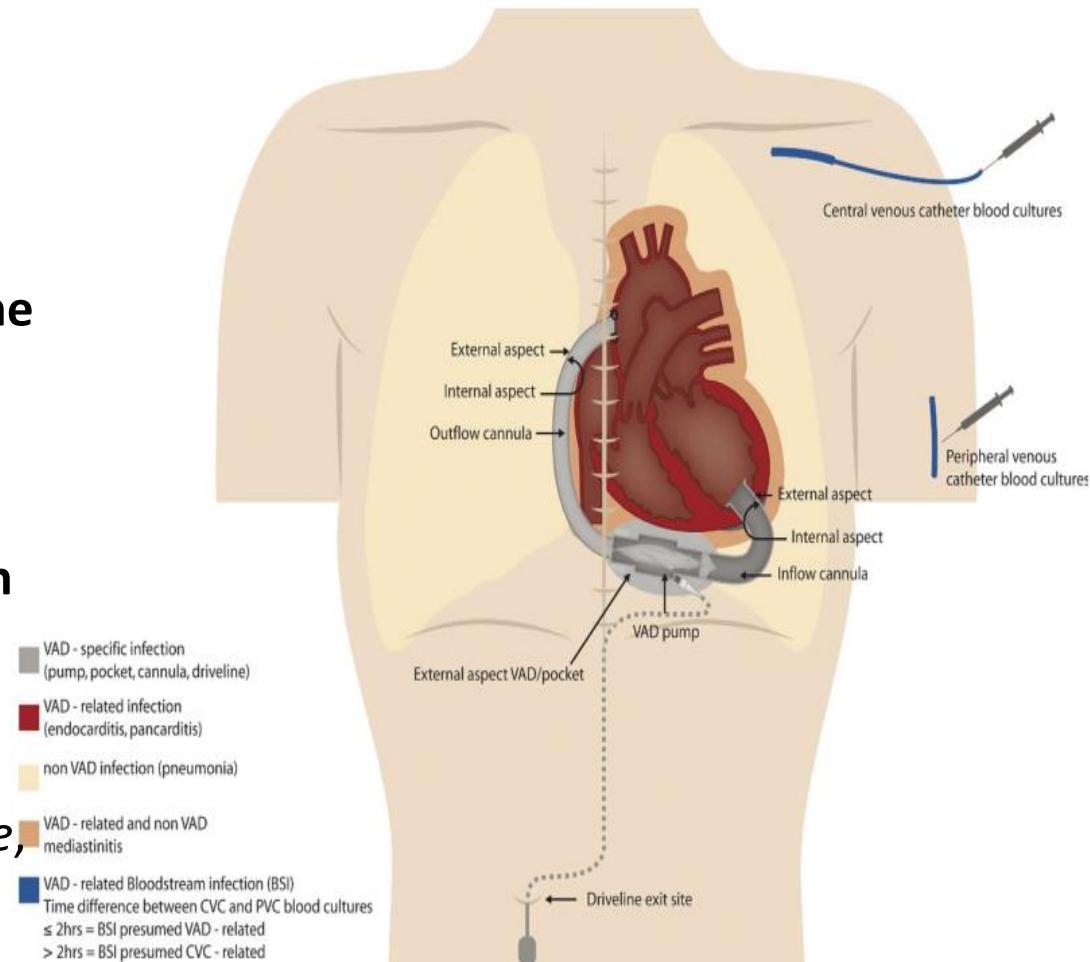
- Do not occur in other pts
- Related to hardware
 - Pump, cannula, pocket & percutaneous driveline

VAD-related infections

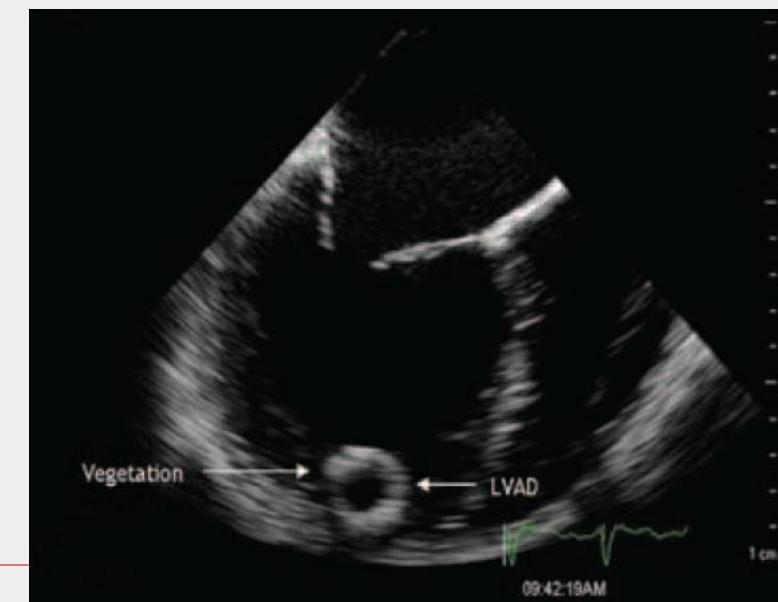
- Can occur without VAD
 - IE, BSI, mediastinitis, sternal wound infection
 - Specific considerations in pts with VADs

Non-VAD infections

- LRT, cholecystitis, *C. difficile*, UTI



- **Driveline:** inf tejidos blandos que rodean la salida (eritema, calor, exudado)
- **Bolsillo:** inf. cavidad que contiene la bomba de la asistencia
- **Endocarditis:** evidencia clínica de inf en la bomba y/o cánula + vegetación o fenómenos vasculares (Duke modificados)
- **Inf Bomba/cánula:** lo previo, pero si no se logra ver vegetación



Clinical presentation: UNSPECIFIC

- Fever 14/25 (56%)
- Leukocytosis 7/25 (28%)

Siempre hay que
sacar hemocultivos!!

INVESTIGACIONES PRINCIPALES

- Inlet obstruction, outflow rupture
- Bacteremia

Clinical Manifestations and Management of Left Ventricular Assist Device–Associated Infections

Objetivo del estudio: Manifestaciones clínicas y terapia de infecciones relacionadas con los dispositivos de asistencia ventricular con flujo continuo.

Campus de la Clínica Mayo entre 2005 y 2011

Incidencia: 110 infecciones en 78 pacientes (**32% de la cohorte**)

Tipo asistencia: Heartmate II (94%)

Indicación: 62% destino final



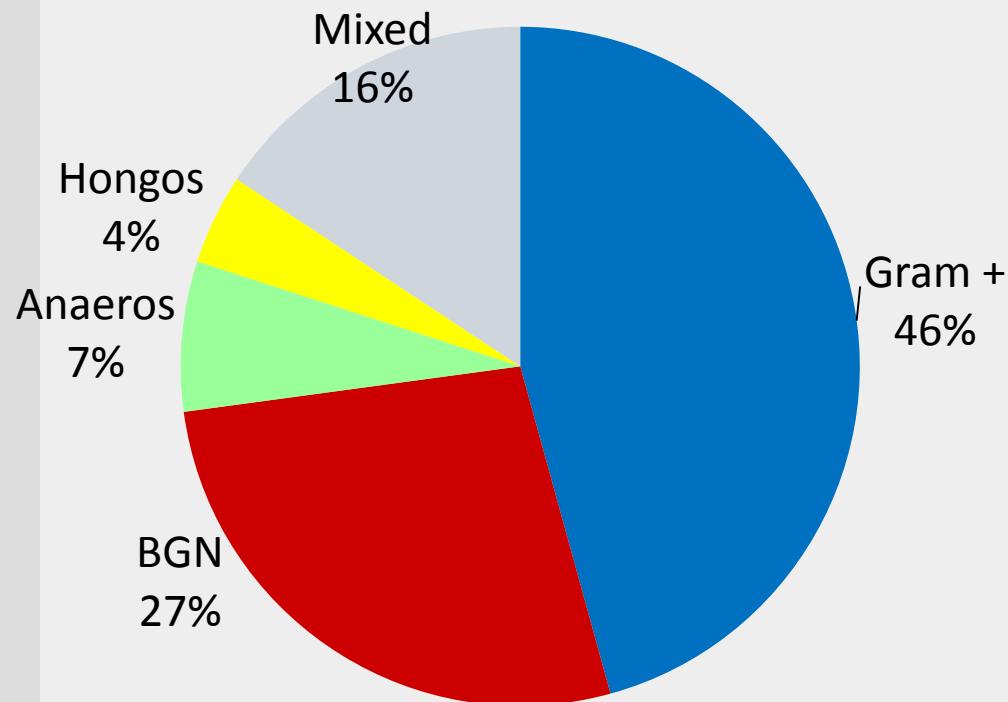
Clinical Manifestations and Management of Left Ventricular Assist Device–Associated Infections

LVADI clasificadas según los criterios ISHLT

TOTAL **32.8%**

	Infection Type	Cases per 100 Person-Years of LVAD Support (95 % CI)	
Infecciones Endovasculares (41)	Endocarditis	1.6 (.5–3.8)	
	Pump and/or cannula infection	4.9 (2.7–8.0)	
	Bloodstream infection		24%
	VAD related	7.5 (4.7–11.2)	
	Non-VAD related	6.8 (4.2–10.4)	
	CVC related	3.3 (1.6–6.0)	
Infecciones locales (37)	CVC associated	1.6 (.5–3.8)	
	Pocket infection	2.3 (.9–4.7)	
	Driveline infection	15.0 (10.9–20.0)	47%
	CIED infection	1.6 (.5–3.8)	
	Mediastinitis, VAD related	2.0 (.7–4.2)	

Etiología



- **Gram negativos**
 - + destination therapy
 - > Charlson
 - Abs al implante
 - BSIs **NO relacionadas LVAD**

- **Gram positivos**
 - BSI relacionadas asistencia
 - > necesidad tto supresor

La distribución de los microorganismos entre las infecciones endo-vasculares y locales ha sido similar

Device Related Features and Clinical Manifestations

- ✓ 21 % de los pac. con **infección activa** al momento del implante

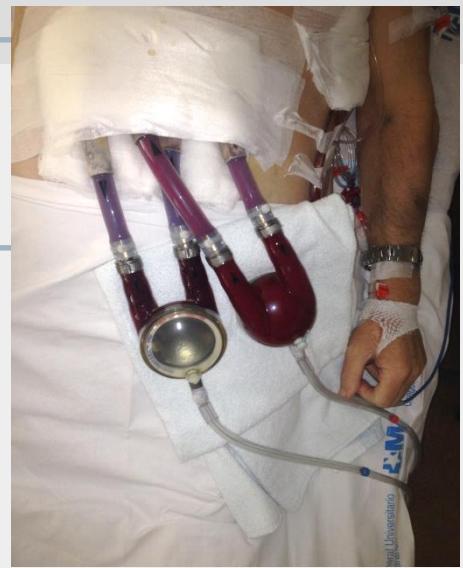
	Total (n=78)	Endovascular (n=41)	Local (n=37)
Time to infection onset, m	4.4 (1-13.5)	1.6 (0.3-7.3)	7.1 (3-19.8)*
Fever	37 (48)	30 (73)	7 (19)*
Met SIRS criteria	19 (25)	16 (39)	3 (8)*
Leucocytosis	39 (51)	29 (71)	10 (29)*
Creatinine level, mg/dl	1.2 (0.9-1.5)	1.4 (1.2-1.9)	1 (0.9-1.2)
Albumin level < 3.5 mg/dl	17 /57 (30)	14/31 (45)	3/26 (12)
Driveline trauma	12 (16)	4 (10)	8 (24)

- ✓ Los 12 pts que sufrieron trauma en la driveline, se infectaron

Infecciones en BERLIN HEART EXCOR

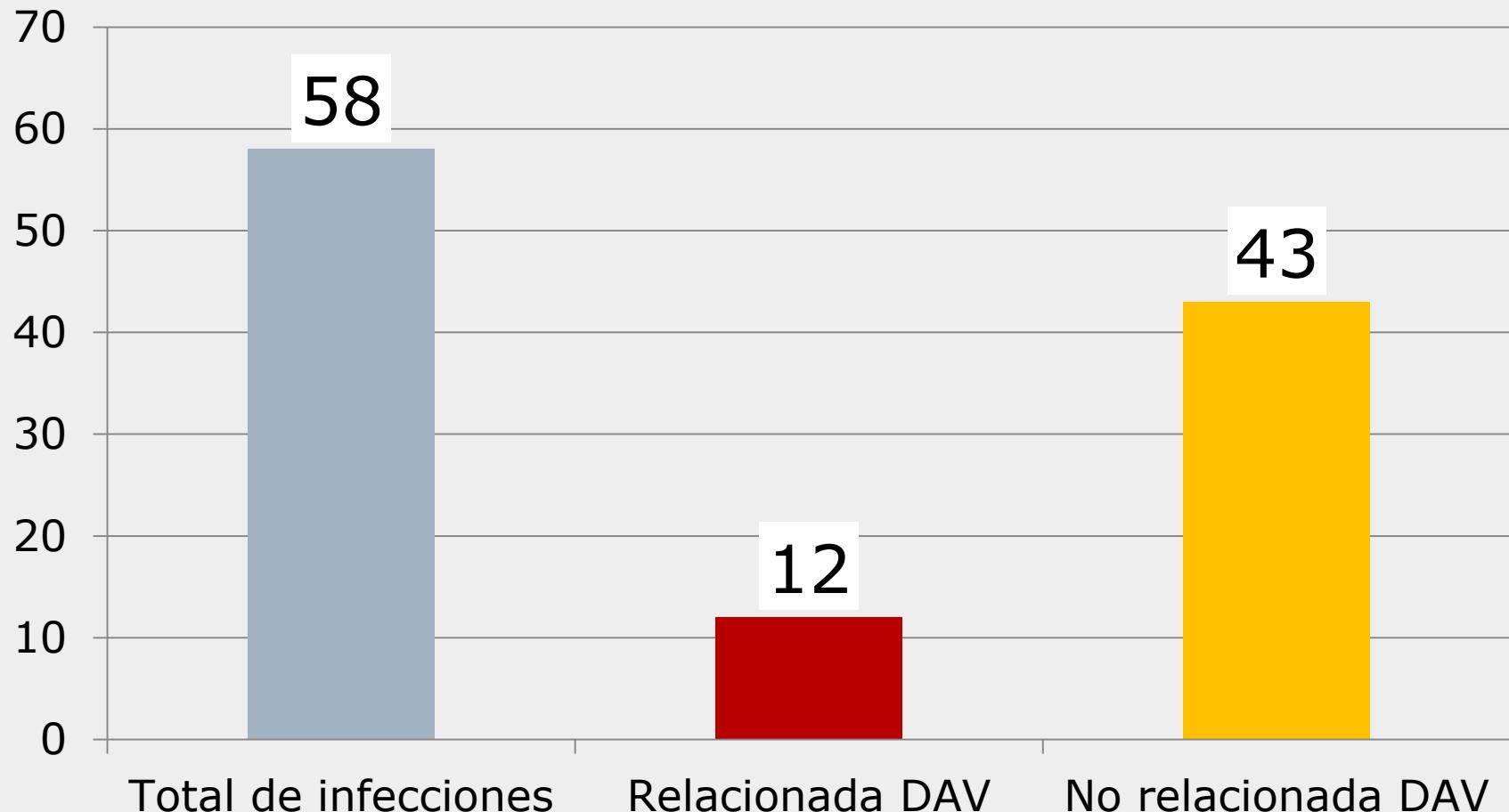
	Portador MO MR
PACIENTE 1	<i>Pseudomonas</i> Multi-R
PACIENTE 2	<i>E. faecium</i> Vanco R
PACIENTE 3	SAMR <i>E. coli</i> BLEE
PACIENTE 4	<i>Klebsiella</i> BLEE
PACIENTE 5	<i>Klebsiella</i> BLEE
PACIENTE 6	<i>Klebsiella</i> BLEE
PACIENTE 7	<i>Klebsiella</i> BLEE
PACIENTE 8	No colonizado :)
PACIENTE 9	SAMS
PACIENTE 10	SAMS

- 10 pacientes
- Profilaxis: 8 cefazolina, 2 Vanco+Meronem
- Colonizados patógenos resistentes

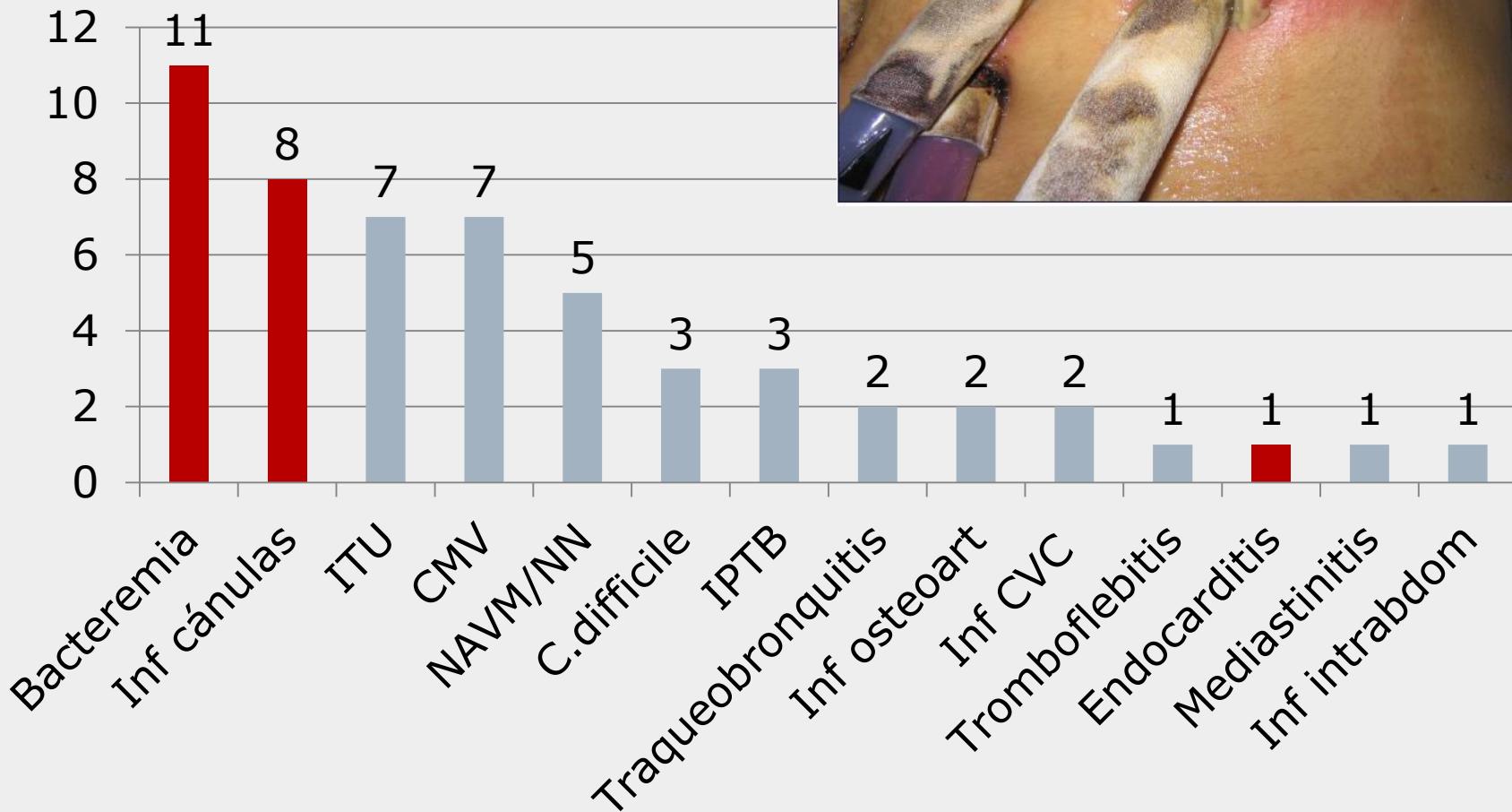


Infecciones Berlin Heart

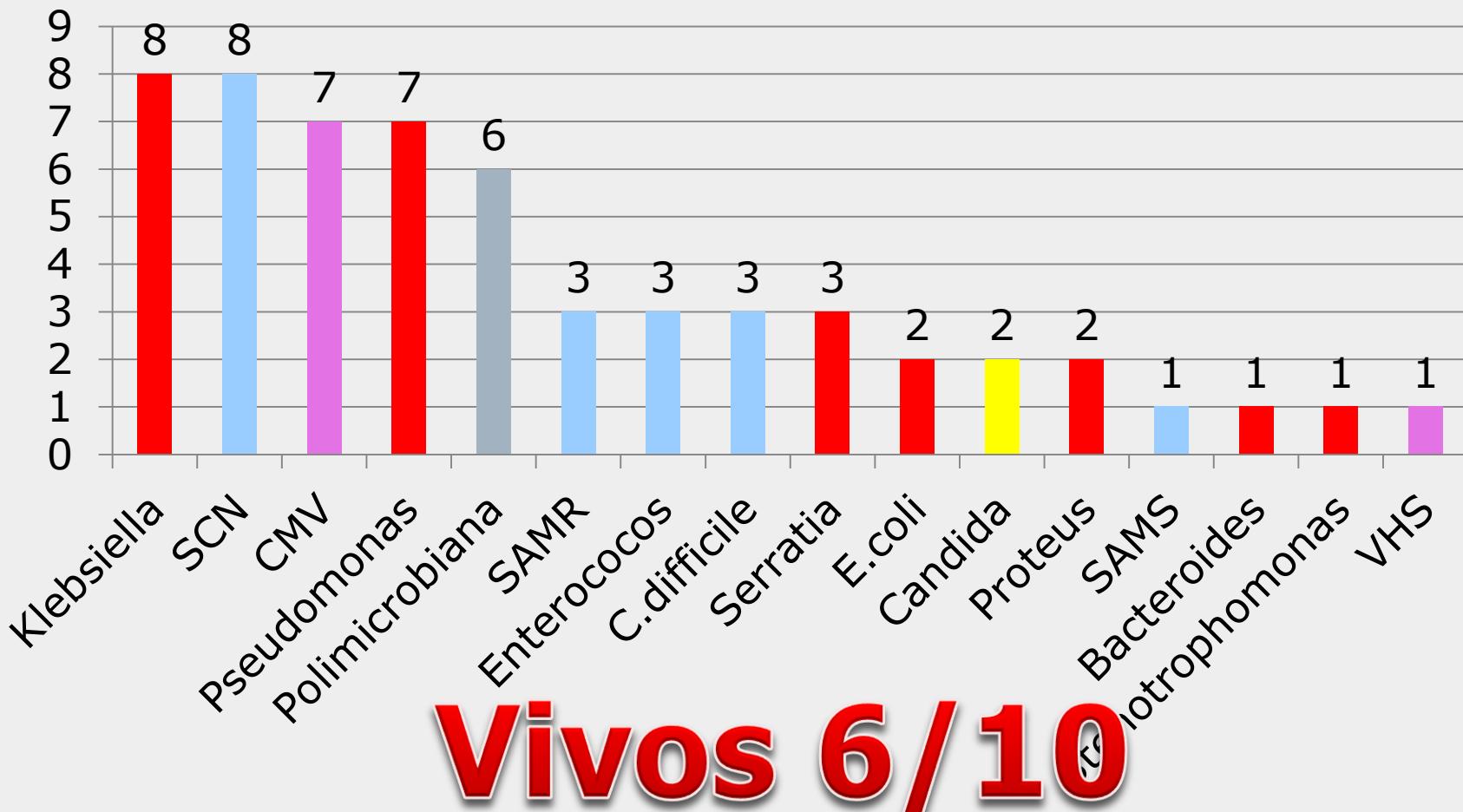
Infección: 10/10 pacientes (media 5,8/pte)



Tipo de infecciones



Microorganismos causales





Bacteraemia in Ventricular Assist Devices: A Common Complication that Need Not Affect Clinical Outcomes

Franklin L. Rosenfeldt, MD, FRACS^{a*}, Lachlan J. Kwa, MEd

- 170 devices in 148 pts
(Novacor 12; Thoratec 100, Ventrassist 36)
- 21 Bi-Ventricular and 127 LVAD
- **Bacteremia 45%!!**
(median time 45 days)

Table 1 Prophylaxis and Treatment of Infections.

Antibiotic prophylaxis

1990–2002

48 h perioperative

Cephazolin 2 g or vancomycin
1 g IV

2003–2009

Pre-operative

Intra-operative

Rifampacin 600 mg
Vancomycin 500 mg + gentamicin
320 mg + fluconazole 200 mg
Fluconazole 200 mg 5 days

Post-operative

Wound care

All devices

Daily dressing change with aseptic
povidone iodine/chlorhexidine
wash of drivelines

Ventrassist

Medihoney antibacterial gel
applied to drivelines weekly
Shower with driveline cover,
triclosan 3% wash after shower

Antibiotic therapy

Diagnosis of bacteraemia Initial empirical antibiotic therapy

Culture and antibiogram Directed antibiotic therapy

Other measures

IV cannulae

Optimal care and early removal

Collections

Prompt surgical drainage of
collections at device and
drivelines

Dispositivos de asistencia ventricular

- 1. Que son?**
- 2. Infecciones**
- 3. Tratamiento**
- 4. Prevención?**



Dificultades de tratamiento

Challenges

The greatest challenge that hinders our efforts is difficulty in determining the extent of infection in patients with driveline infection (driveline versus device). Although a computed tomographic scan was used in this process, unless an obvious fluid collection is present around the left ventricular assist device, the infection status of the device is difficult to determine. In many

- Ademas....

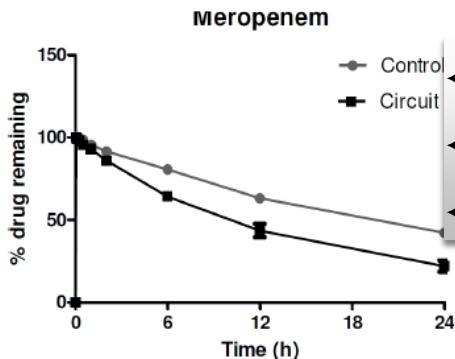
Dificultades de tratamiento

- Disfunción de la **respuesta inmune**
- Reducida **biodisponibilidad** de los fármacos en el lugar de la infección por poca vascularización
- **Interacciones medicamentosas**
- Imposibilidad de **retirar el material extraño** infectado (biofilm)
- Frecuentemente **cursos largos** de Abs con armamento limitado

Sequestration of drugs in the circuit may lead to therapeutic failure during extracorporeal membrane oxygenation

Shekar et al. Critical Care 2012, 16:R194

Kiran Shekar^{1*}, Jason A Roberts², Charles I McDonald¹, Stephanie Fisquet¹, Adrian G Barnett³, Daniel V Mullany¹, Sussan Ghassabian⁴, Steven C Wallis², Yoke L Fung¹, Maree T Smith⁴ and John F Fraser¹



- ◆ "Secuestro" del F en la membrana
- ◆ Aumento del Vd
- ◆ Disminución/Aumento del Cl



Intensive Care Med (2007) 33:1018–1024
DOI 10.1007/s00134-007-0606-2

PEDIATRIC ORIGINAL

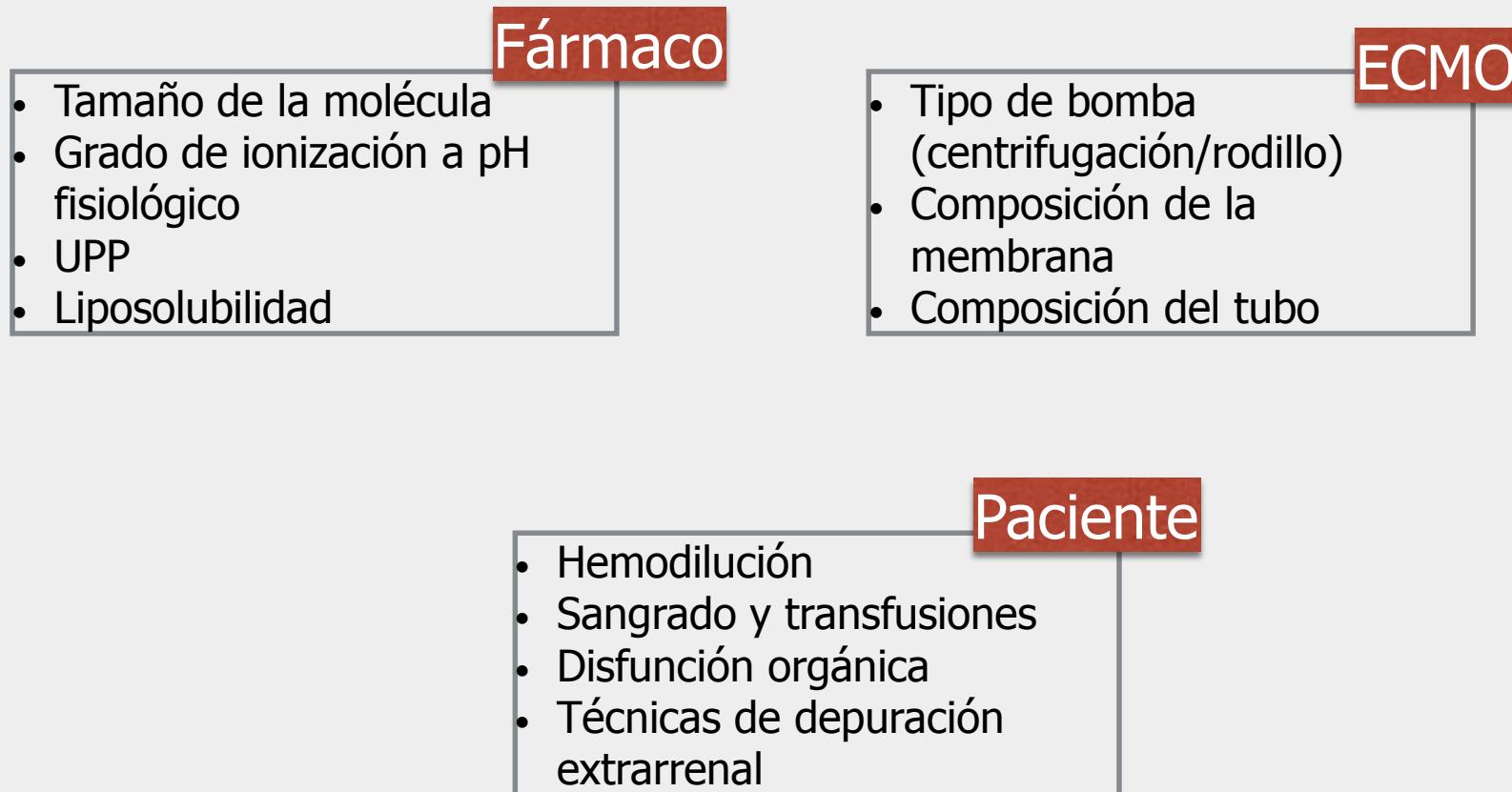
Nilesh M. Mehta
David R. Halwick
Brenda L. Dodson
John E. Thompson
John H. Arnold

Potential drug sequestration during extracorporeal membrane oxygenation: results from an ex vivo experiment

- Dramatic sequestration of **voriconazole** (up to $\geq 70\%$) in the ECMO circuit
- Loss of 15.4% of ampicillin, 21% of cefazolin
- 31.4% of fosphenytoin
- 53.3% of heparin and 100% of fentanyl
- **Meropenem 42%**

De Rosa FG. Int J Antimicrob Agents 2013

¿Que características influirán en estos cambios?



Tratamiento antimicrobiano pacientes en ECMO:

- Muchas publicaciones sobre variabilidad parámetros PK en pacientes con ECMO (la mayoría *case reports*).
- Distintos efectos en diferentes fármacos
- Posibilidad fallo terapéutico
- Siempre que sea posible monitorizar los niveles del fármaco y tratar de individualizar las dosis
- Valorar infusiones extendidas en beta lactámicos
- Necesitamos más datos

ISHLT guidelines

■ Medical therapy

- No recommendations on
 - Drugs of choice
 - Duration

■ Surgical

- Need to establish the site of infection
- Debridement or device replacement?

■ Recurrence 38%

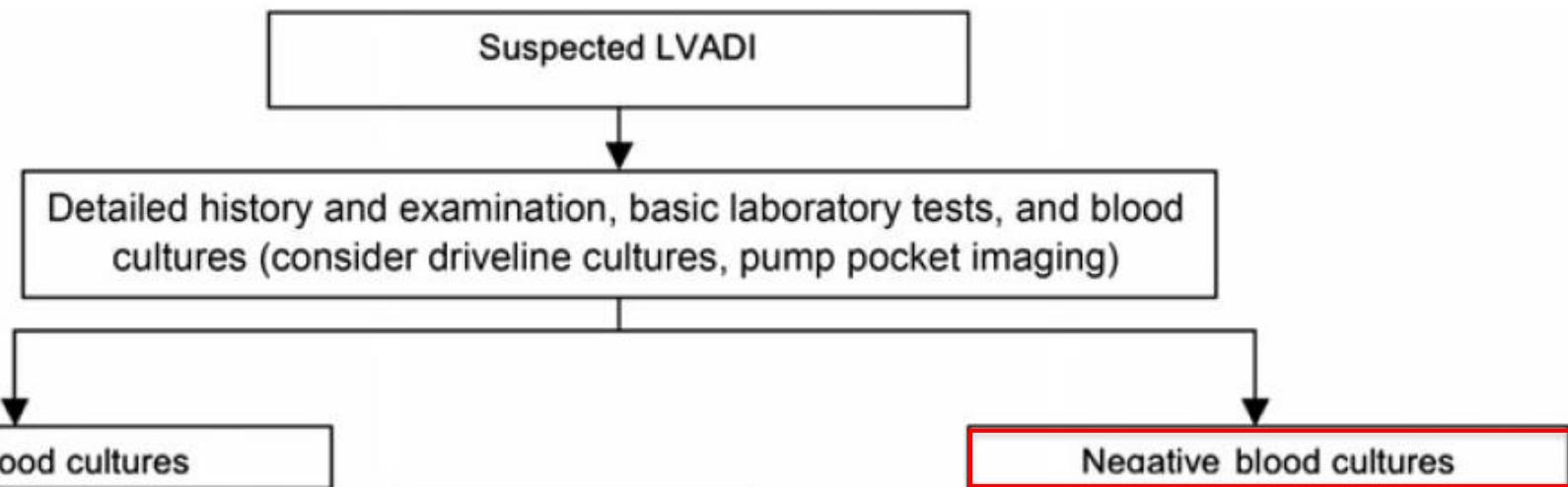
Tratamiento infecciones asistencias ventriculares

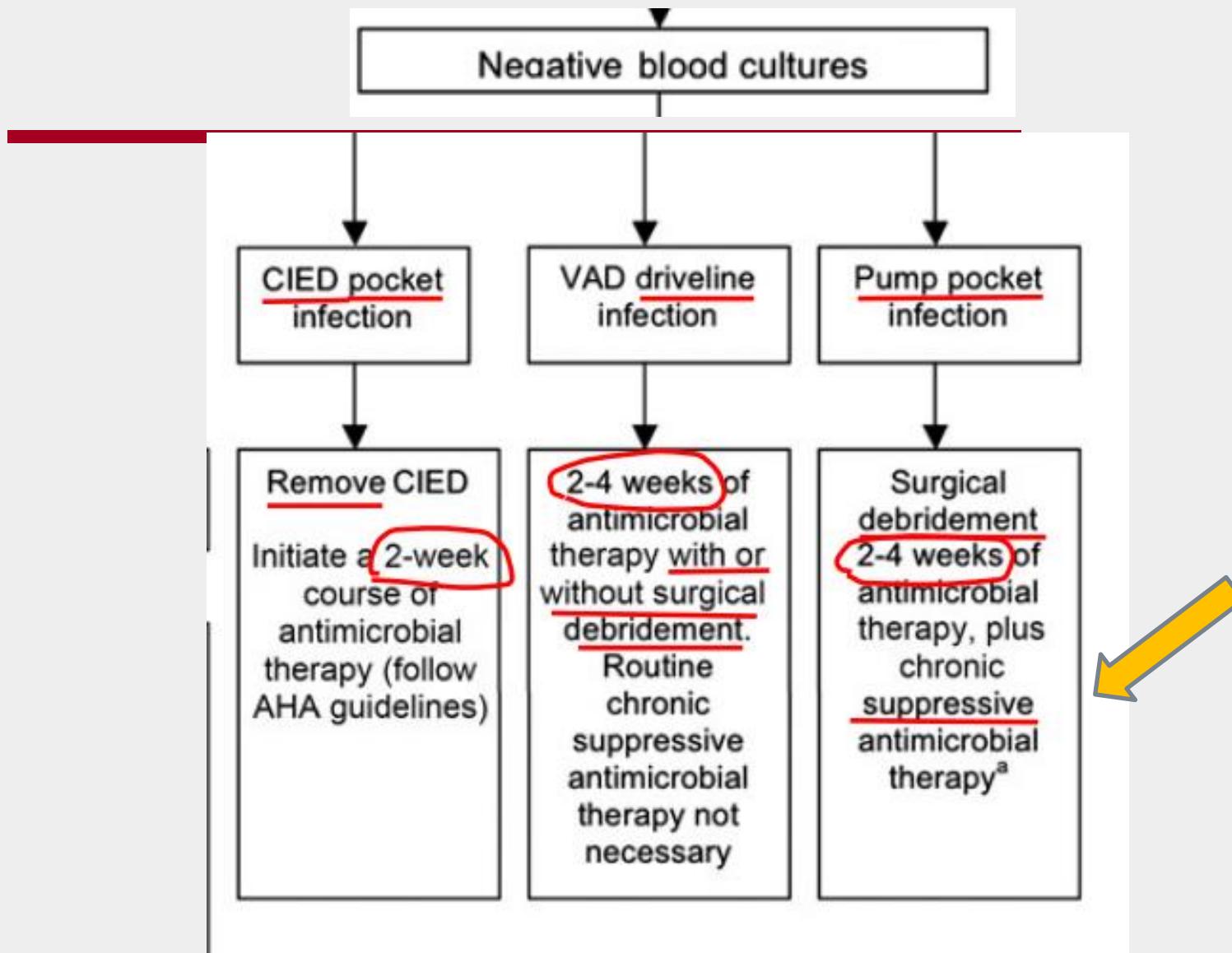
- Duración media del tto. **28 días**
- **42%** tratamiento supresor (hasta muerte, retirada de la asistencia o limitación de esfuerzos) si sospecha de afectación de la asistencia
- 76% de los pacientes **NO cirugía**
 - **14% desbridamiento quirúrgico** con mantenimiento del dispositivo
 - **3 pacientes retirada del dispositivo**
- **29% experimentaron recidiva** (29% (8/28) con tto. crónico Vs 11% (5/45) sin tto. crónico)
- **Mortalidad a 2 años: 43%. Tx en 43% de los 30 candidatos**

Clinical Manifestations and Management of Left Ventricular Assist Device–Associated Infections

Variable		Total (n = 78)	Endovascular (n = 41)	Local (n = 37)
Antibiotic therapy duration, d ^a				
Overall	n = 76	28.0 (14.5–42.5)	33.0 (15.5–42.5)	23.5 (13.0–44.0)
Parenteral antibiotics (primarily) ^a	n = 53	36.0 (17.0–49.0)	34.5 (16.0–43.0)	39.0 (26.0–132.0)
Oral antibiotics (primarily) ^a	n = 23	14.0 (10.0–24.0)	15.5 (14.0–17.0)	14.0 (10.0–24.0)
Receipt of suppressive oral antimicrobials		29 (37)	16 (39)	13 (35)
Receipt of suppressive parenteral antimicrobials ^b		4 (5)	2 (5)	2 (5)
Surgical management	n = 76			
None		58 (76)	33 (80)	25 (71)
Bedside debridement		3 (4)	1 (2)	2 (6)
Intraoperative debridement with device retention		10 (13)	4 (10)	6 (17)
LVAD removal		3 (4)	1 (2)	2 (6)
Other ^c		2 (3)	2 (5)	0 (0)
Duration of LVAD support follow-up, y		1.6 ± 1.1	1.3 ± 0.8	2.0 ± 1.2
Death at 2-y follow-up ^d		25 (40)	19 (53)	6 (26)
Heart transplantation at 2-y follow-up (among bridge-to-transplant patients ^d)	n = 30	10 (47)	5 (40)	5 (55)

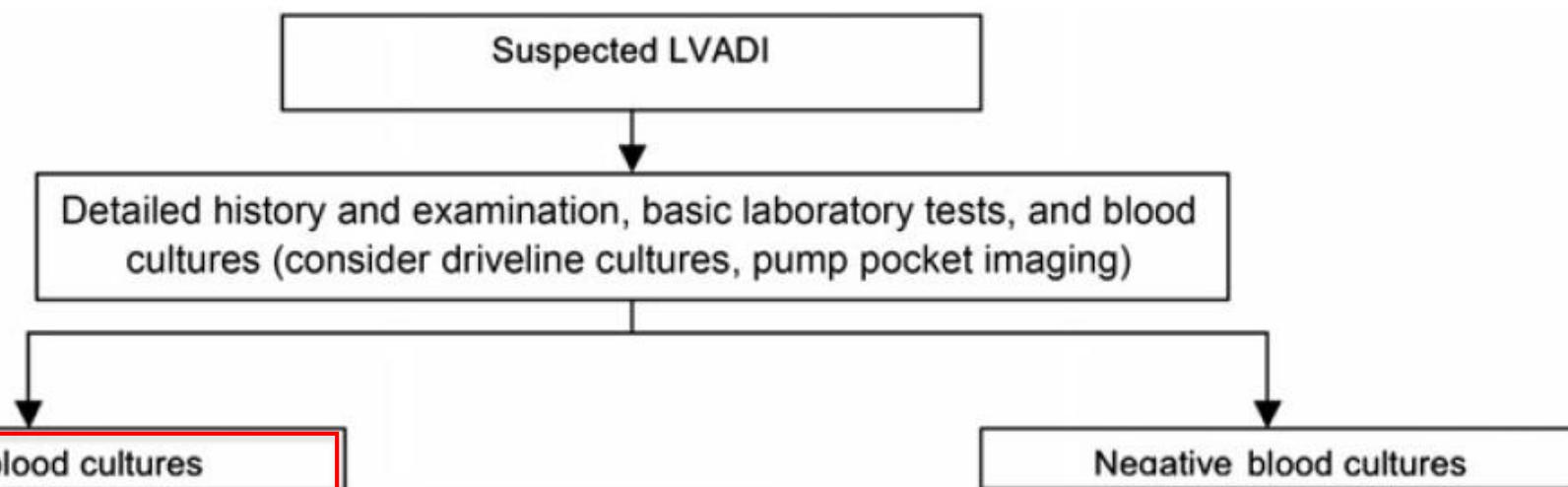
Propuesta de algoritmo

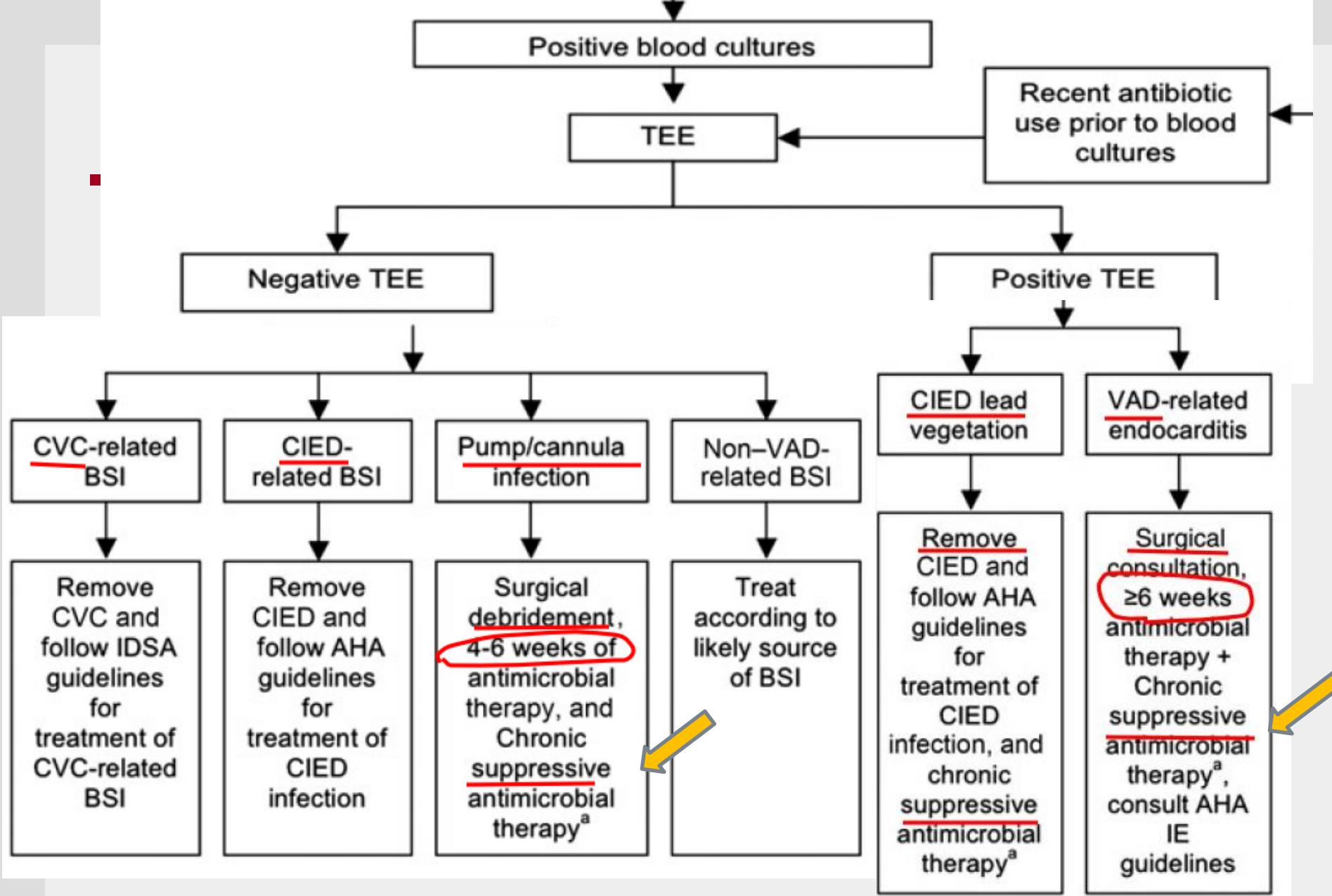




CIED, cardiovascular implantable electronic device

Recomendaciones





**Clinical Outcomes Associated With
Chronic Antimicrobial Suppression
Therapy in Patients With Continuous-Flow
Left Ventricular Assist Devices**

*†*Douglas L. Jennings, ‡Anuvrat Chopra,*

- **Chronic Abs** (after 6 wks of IV Therapy): 16/140 (**11.5%**) with DEVICE-RELATED infection
- SXT 37.5%, drivelines infections (69%)
- **Failure** (clinical deterioration needing switch to IV or to other IV Ab, elevation to status 1A of tx list due to infection or device/driveline exchange or death): 5/16- **31% after a mean of 175 days of therapy (10-598)**
- Sobreinfecciones, AEs y *C. difficile*

1. Que son?
2. Infecciones?
3. Manejo?
4. **Prevención?**

{ **Antimicrobianos**
Otras actuaciones

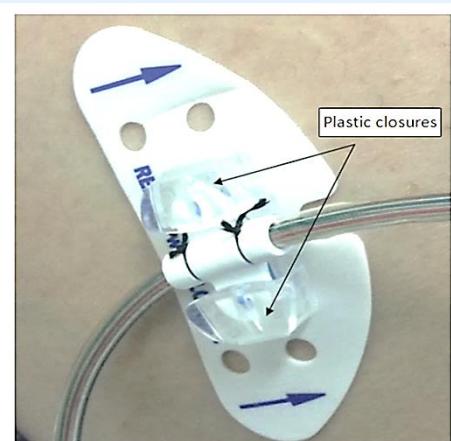


Fig 1. Generalized clinical example of a patient with a CVC device. The skin discolouration

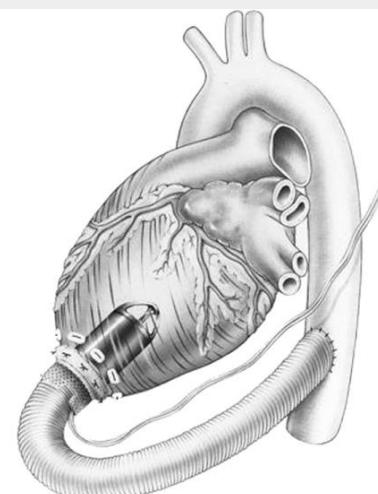
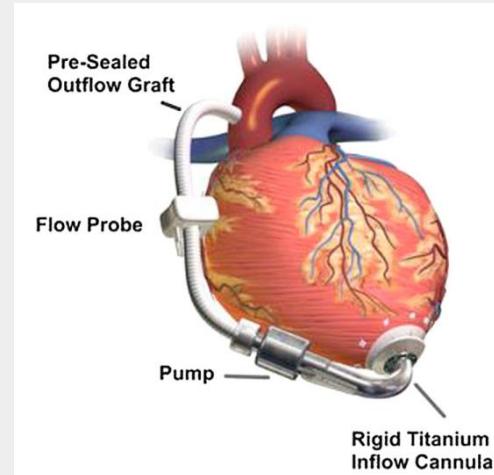
Prevention. No clinical trials

- Colonization screening before surgery
- Maximum surgical prevention strategies

- Operating room traffic, HEPA filters
- Wrapping the pump and drivelines in Ab pads?? Wrapping the pump omentum?
- Tunneling driveline contralateral to pump pocket
- Occlusive dressing of driveline exit
- Chlorhexidine bathing

- Postoperative infection prevention

- Extubation, pulmonary toilet
- Removal of catheters
- Nutrition.....



Frequency of driveline exit-site dressing change

Left ventricular assist device driveline infection and the frequency of dressing change in hospitalized patients

Lisa Wus, DNP, CRNP, PCCN-CMC^{a,*}, MaryLou Manning, PhD, CRNP, CIC, FAAN^b, John W.C. Entwistle III, MD, PhD^c

^a Thomas Jefferson University Hospital, 111 South 11th Street, Suite 5480N, Philadelphia, PA 19107, USA

^b Thomas Jefferson University, Jefferson School of Nursing, 901 Walnut Street, Suite 814, Philadelphia, PA 19107, USA

^c Division of Cardiothoracic Surgery, Department of Surgery, Thomas Jefferson University, 1025 Walnut Street, Suite 607 College Building, Philadelphia, PA 19107, USA

- Retrospectivo. 2008-2013: 68 pacientes con Heartmate II
NO infecciones del driveline
- **No diferencias entre cambios diarios, cada tres días o cada semana.**

The Evidence Base for Prophylactic Antibiotics in Patients Receiving ECMO



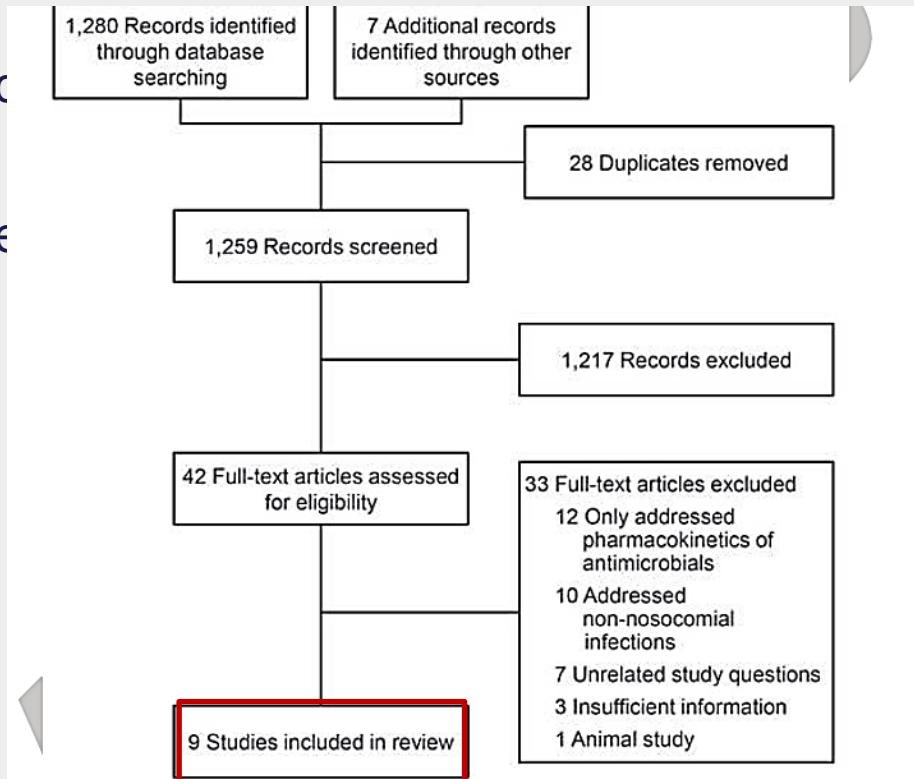
AIM OF THE SYSTEMATIC REVIEW:

- Evaluate the evidence for the use of antibiotic prophylaxis in patients receiving extracorporeal membrane oxygenation (ECMO) therapy

PROPHYLACTIC DRUG USED varied substantially!

No relationship was observed regarding incidence between studies using prophylaxis or not

Consider if open chest



Prevention of Percutaneous Driveline Infection After Left Ventricular Assist Device Implantation: Prophylactic Antibiotics Are Not Necessary

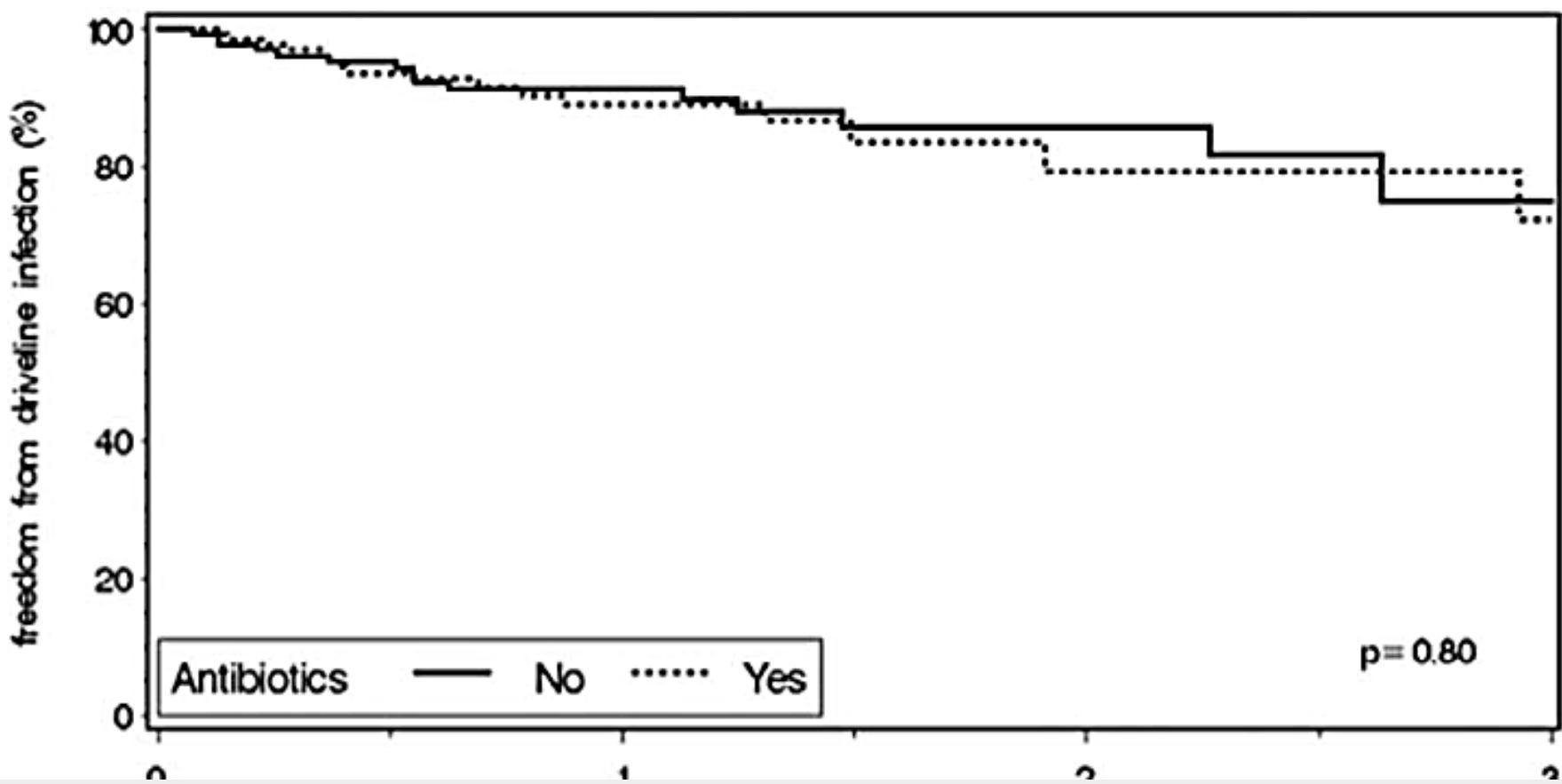
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- Comparacion de la incidencia de infecciones en dos grupos:
 - 141 pacientes en la clínica Mayo con Heartmate: Limpieza estéril, recambios estériles de los apóritos y **NO antibióticos** salvo perioperatorio
 - 144 pacientes en la Michigan University: Lo mismo PERO **CON ANTIBIÓTICOS**

Driveline infections

B

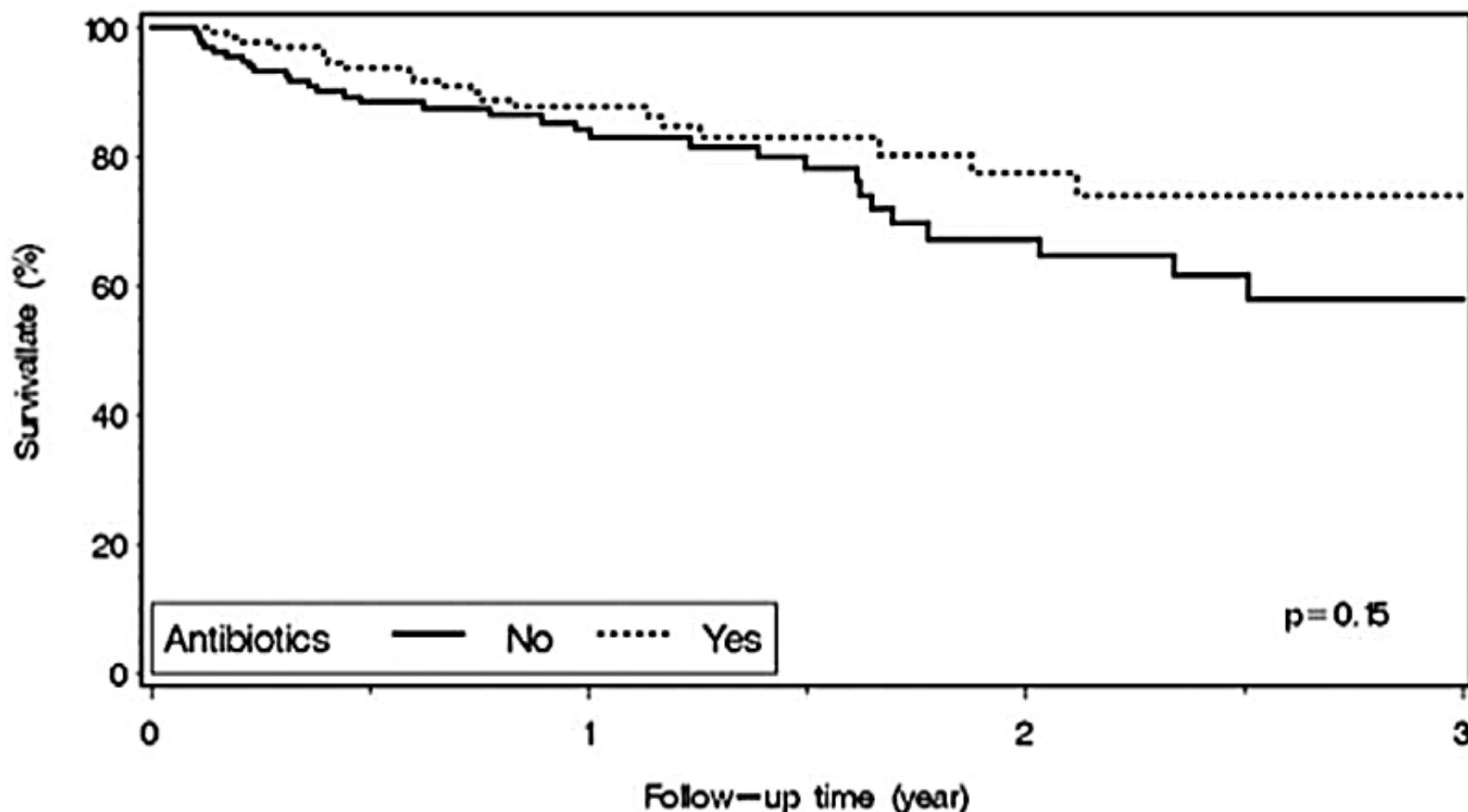
Freedom from driveline infection by antibiotics group



Survival

B

late survival by antibiotics group

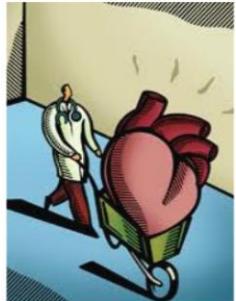


En resumen



- A pesar de los avances, las infecciones continúan causando importante morbi-mortalidad, tanto a corto, como a largo plazo
- El diagnóstico de la profundidad de la infección sigue siendo complicado en la vida real
- Necesitamos más datos para establecer los esquemas terapéuticos médicos y quirúrgicos así como la duración óptima del tratamiento
- No hay evidencia de que sea necesario administrar pautas profilácticas de gran espectro
- La protección frente a los microtraumas en el driveline es esencial, y se están desarrollando mecanismos para evitarlos
- Pacientes con gran carga emocional para todos y que necesitan ser manejados en equipo y probablemente con protocolos nacionales.

Grupo de Apoyo al Manejo de las Asistencias Ventriculares (GAMAV)



- **Cardiología:** Yago Sousa, Eduardo Zataraín, Francisco Fernández-Avilés
- **Cirugía Cardiaca:** Manuel Ruiz, Gregorio Cuerpo, Hugo Abella, Juan Fco del Cañizo, Ángel Pinto.
- **Anestesia:** Javier Hortal, José María Barrio, Alejandro Garrido
- **Inmunología:** Elisabeth Sarmiento
- **Microbiología:** Patricia Muñoz, Maricela Valerio, Alia Eworo, Emilio Bouza



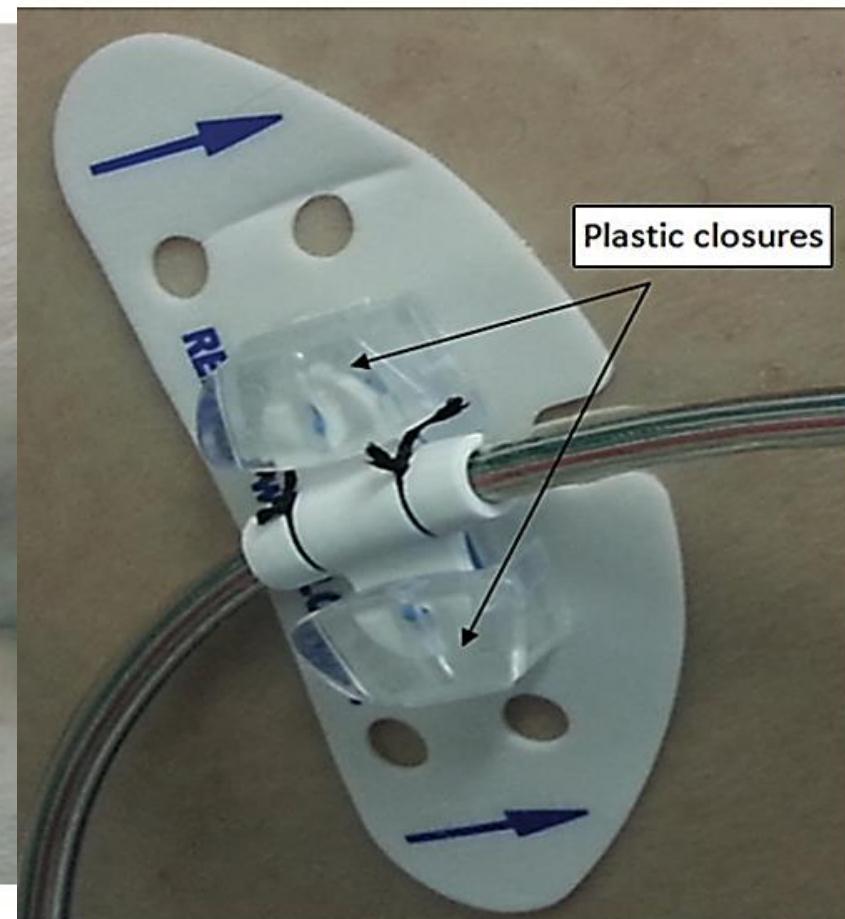
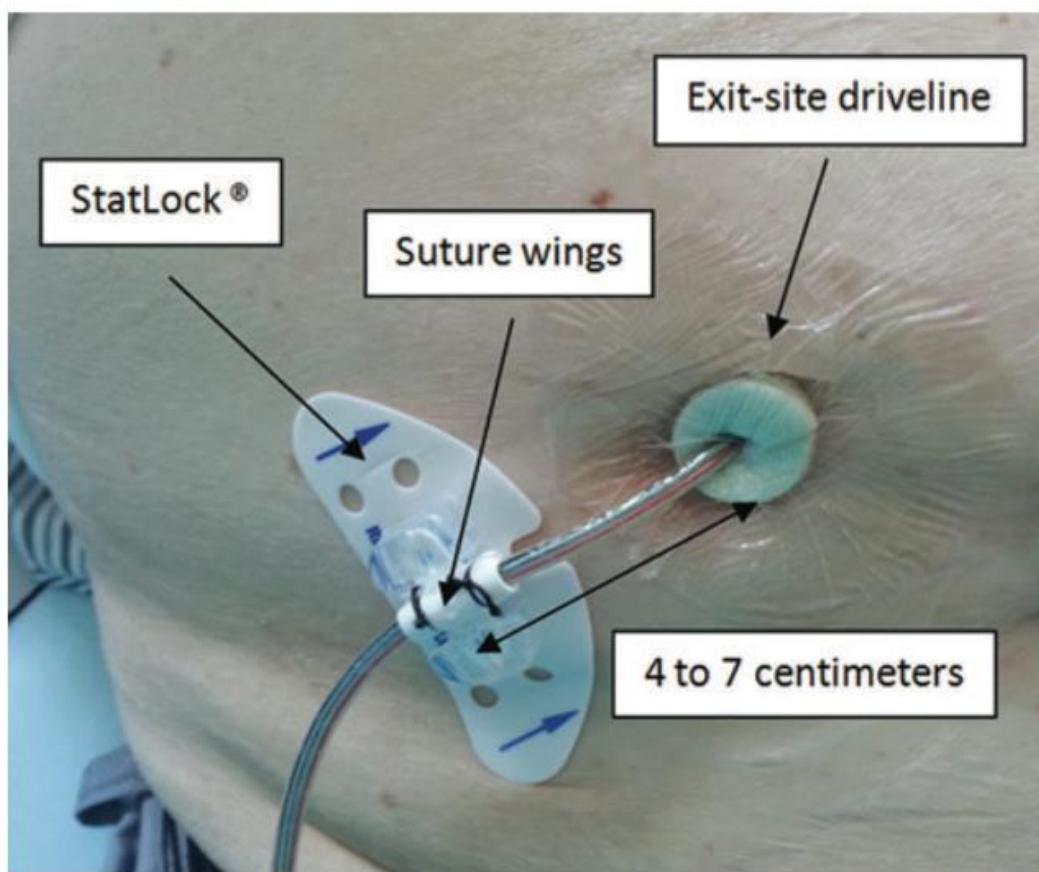
Muchas gracias!!



A simple device to secure ventricular assist device driveline and prevent exit-site infection

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Reduction in driveline infection rates: Results from the HeartMate II Multicenter Driveline Silicone Skin Interface (SSI) Registry

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Antony Tatooles, MD,^d Brett C. Sheridan, MD,^e Robert J. Brewer, MD
Christian Caldeira, MD,^g David J. Farrar, PhD,^b and Shahab A. Akhter
on Behalf of the SSI Registry Investigators



■ Comparación infección de driveline y VAD en HeartMate II

- 200 (2009 – 2012) driveline tunelizado
- 201 (2007 y 2009) técnica clásica

Comparing velour versus silicone interfaces at the driveline exit site of HeartMate II devices: infection rates, histopathology, and ultrastructural aspects



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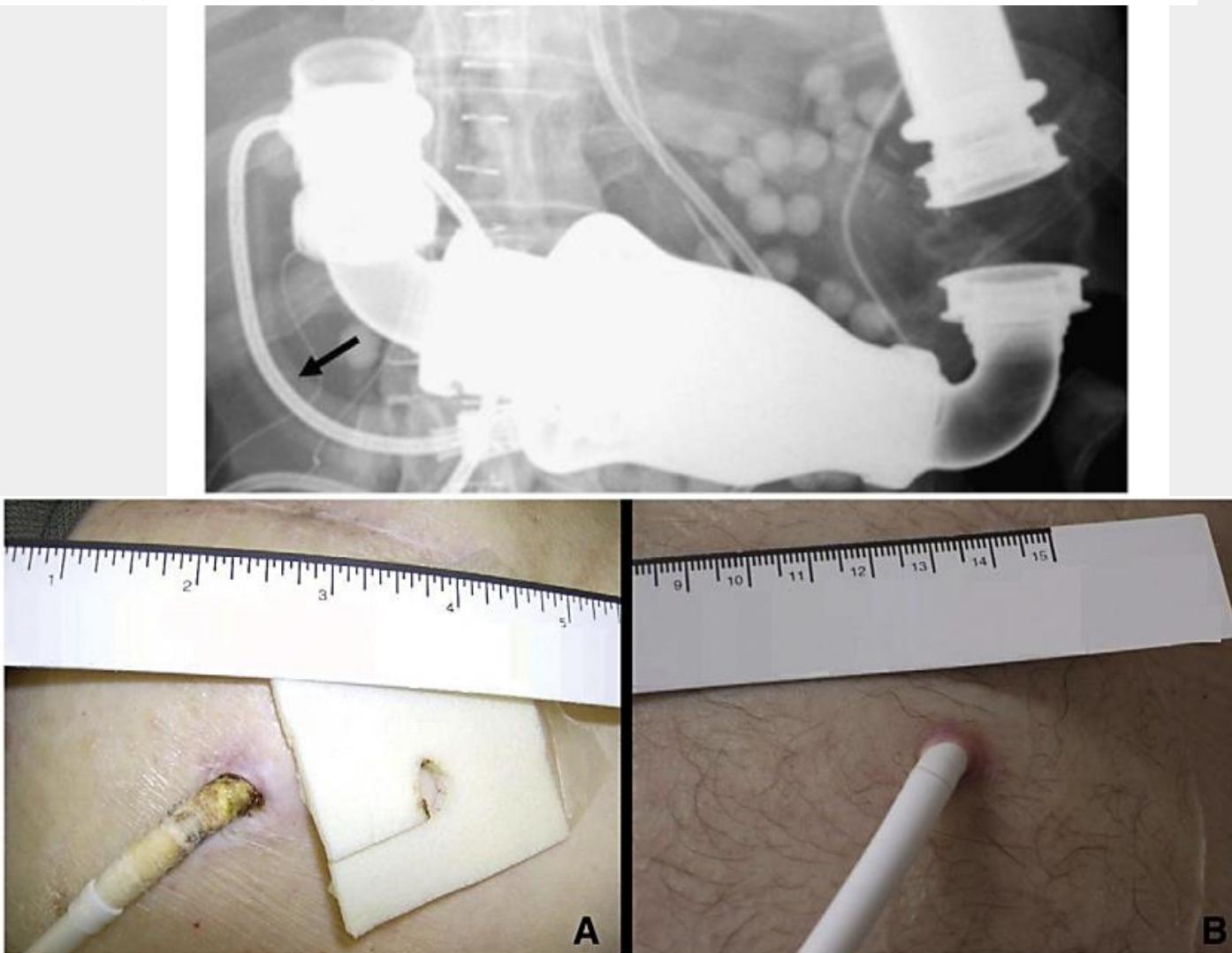


Fig. 2. Photographs showing typical fully incorporated velour and silicone DLES with velour (A) and smooth silicone (B) interfaces. Notice bloody material adhered to the velour sheath. The silicone DLES is free of debris, and skin is cleanly adhered to the driveline. Both photographs show the DLES at similar stages of wound healing.

Infección driveline

