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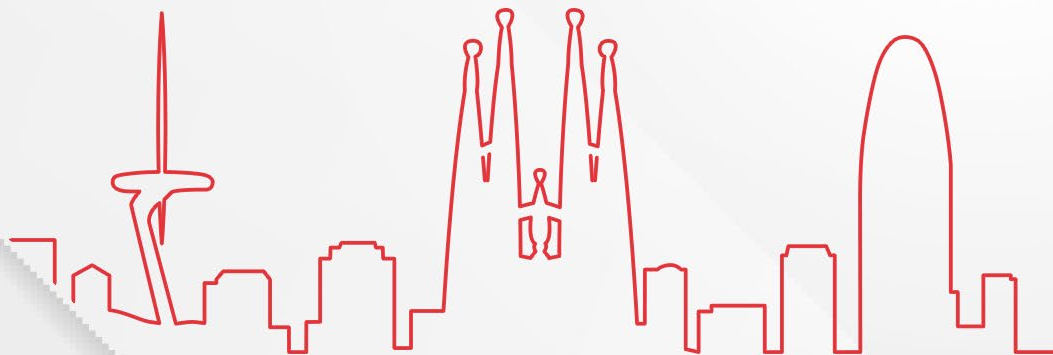
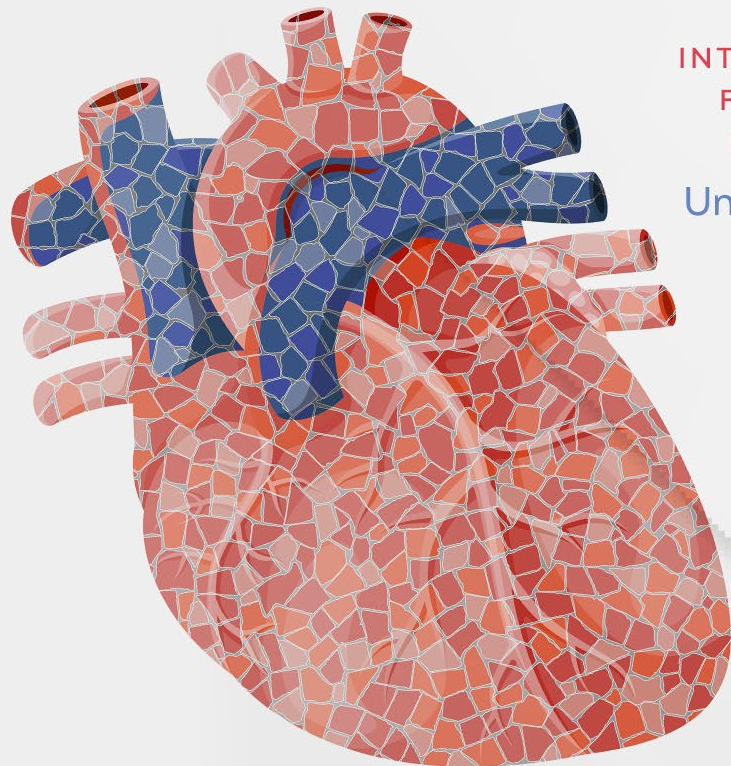
**JUNE 18TH - 20TH
2022**

**INTERNATIONAL SOCIETY
FOR CARDIOVASCULAR
INFECTIOUS DISEASES**

**University of Barcelona
Faculty of Medicine**

16TH SYMPOSIUM

ISCVID



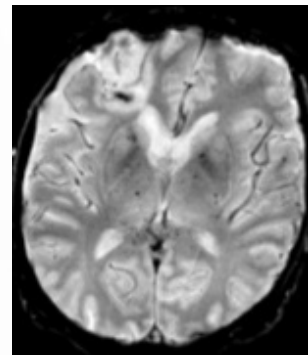
www.iscvid2022.com



Optimal timing for cardiac surgery after hemorrhagic stroke during IE



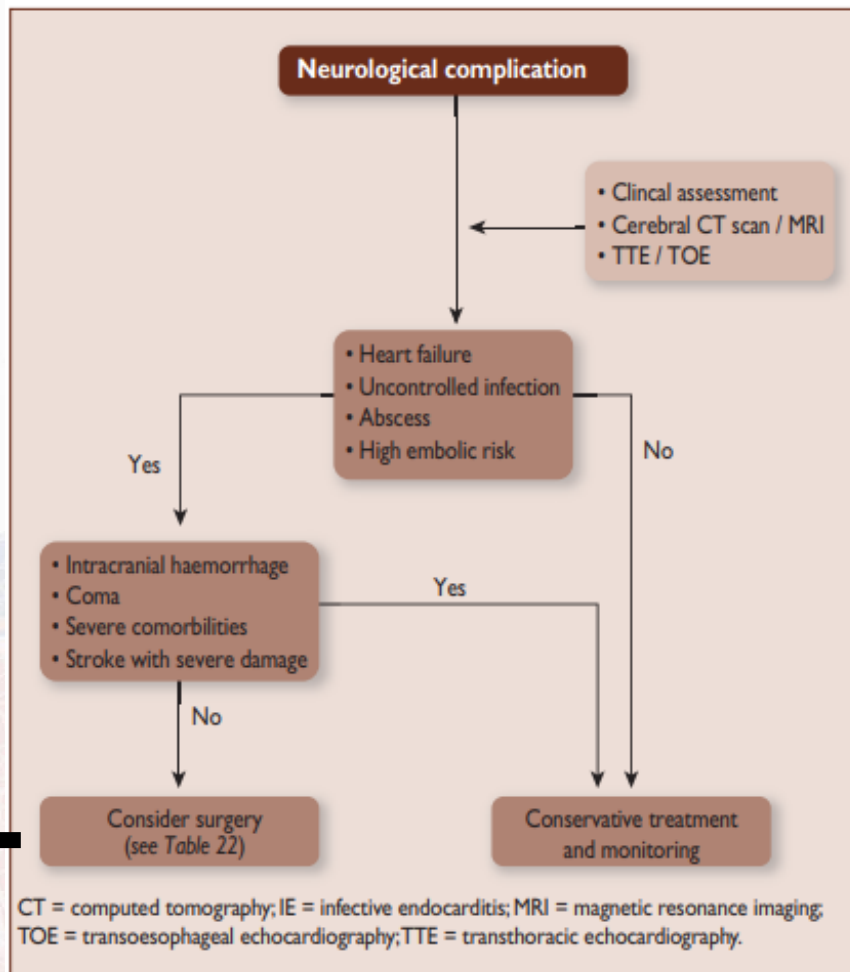
Prof. Dr. Torsten Doenst,
Department of Cardiothoracic Surgery
University of Jena, Germany





Background

- **Cardiac surgery is indicated in >50% of patients with infective endocarditis (IE)**
- **Many patients are denied surgery despite the presence of an indication for surgery (ca. 25%)**
- **Intracranial hemorrhage (ICH) represents the reason for denial of surgery in 15% of patients with IE**

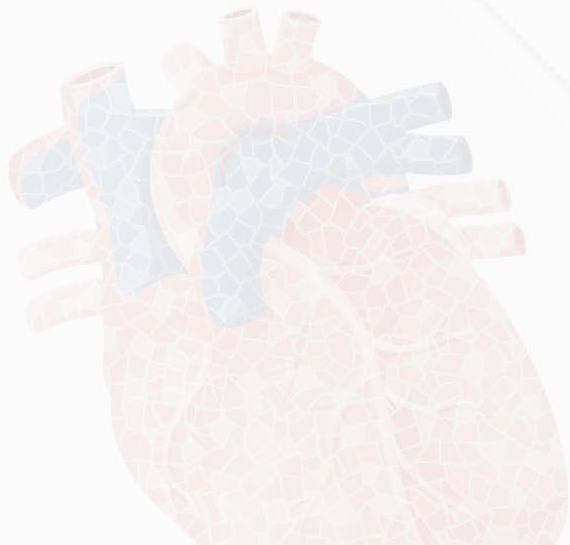


**Surgery after
30 days**



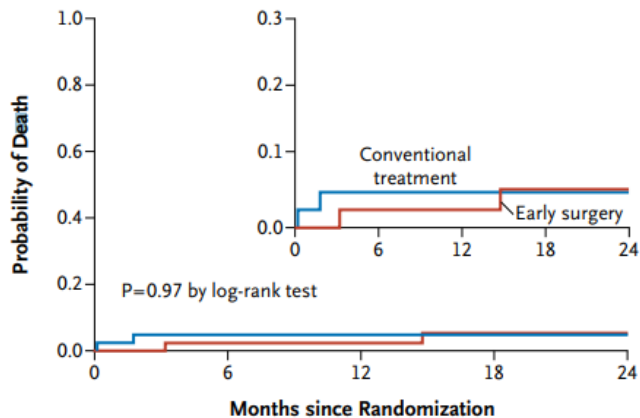


Why should we operate earlier on patients with IE ?



Early surgery prevents recurrent embolic events

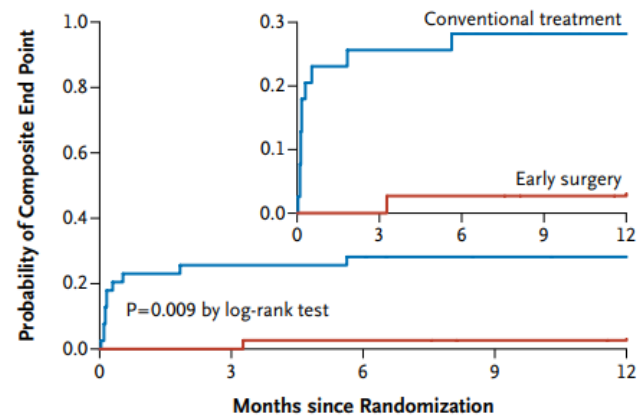
A



No. at Risk

Early surgery	37	36	33	28	21
Conventional treatment	39	37	31	27	23

B

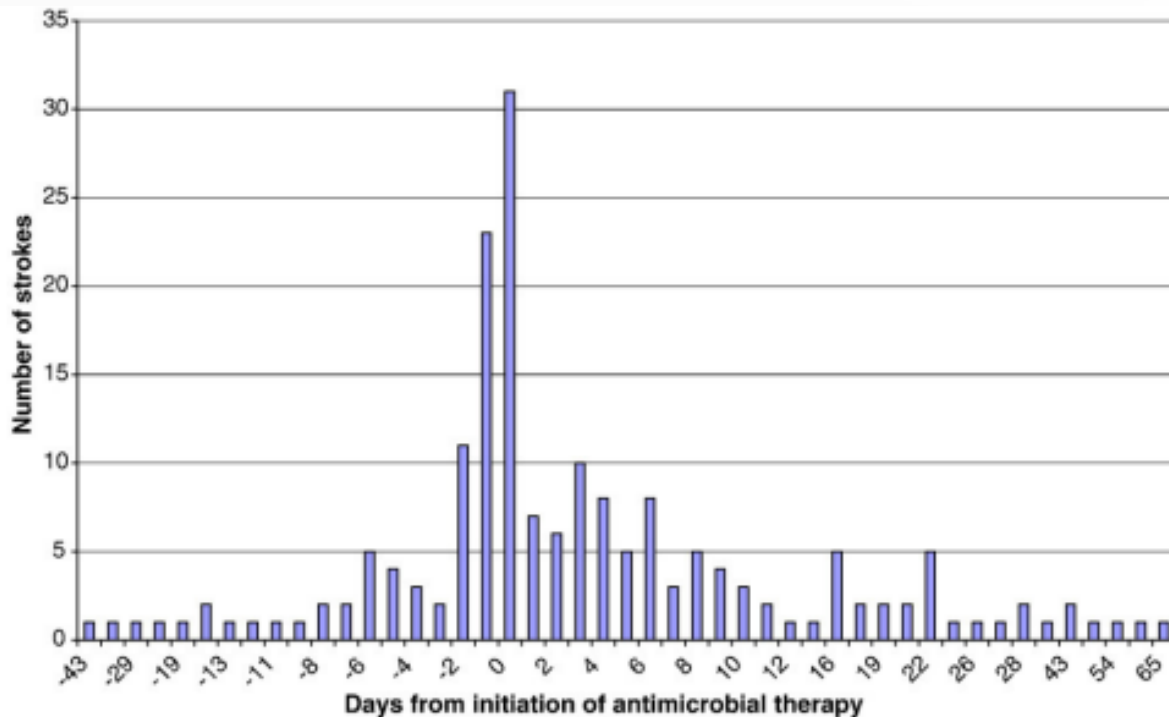


No. at Risk

Early surgery	37	37	36	34	33
Conventional treatment	39	29	28	25	24



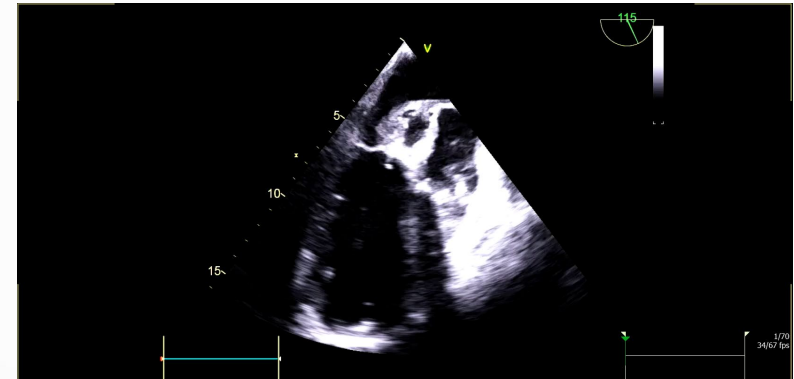
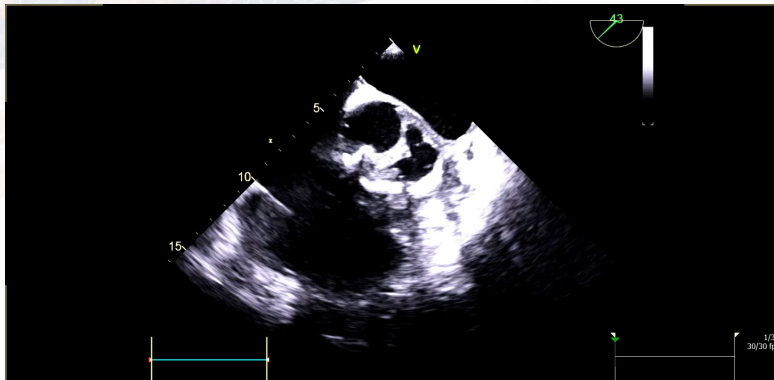
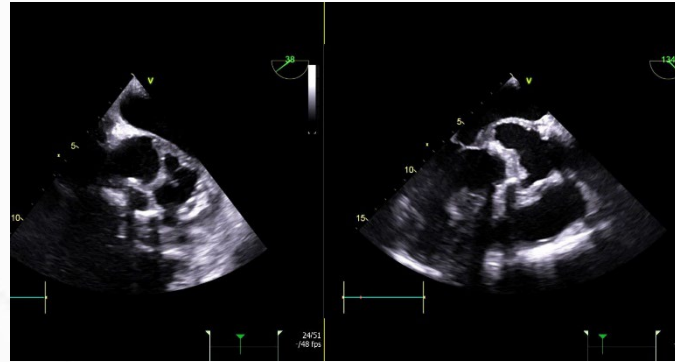
Data from Prospective Registry (ICE-PCS)



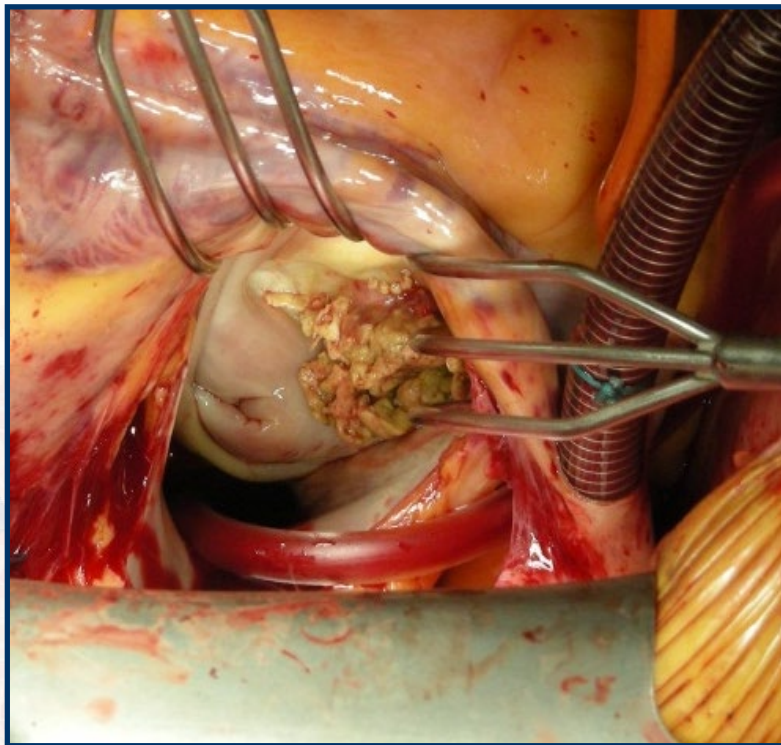
Daily incidence of stroke in ICE cohort.



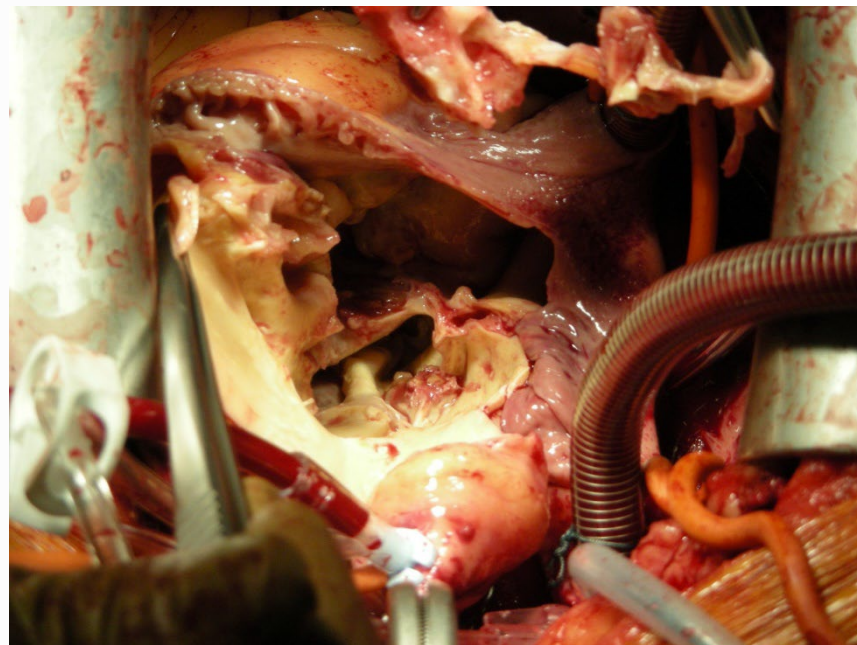
To avoid local extension of IE



Vegetation on the Mitral Valve



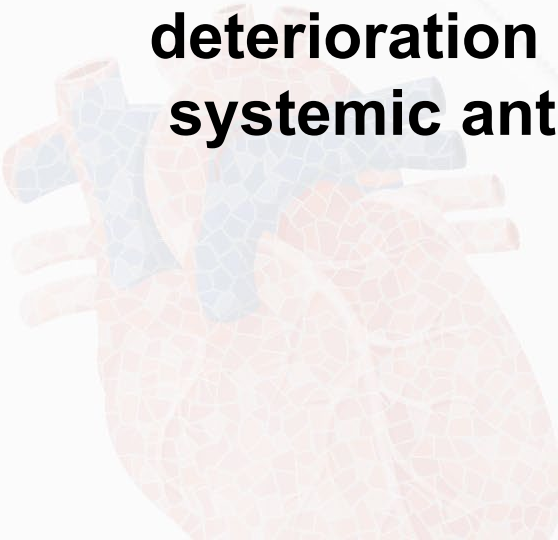
Destroyed Cardiac Base from Abscess





Why is it dangerous to operate on patients with ICH?

High risk of further bleeding and neurologic deterioration due to the inevitable use of high-dose systemic anticoagulation during cardiopulmonary bypass (CPB)





European Journal of Cardio-Thoracic Surgery 49 (2016) e119–e126
doi:10.1093/ejcts/ezw014 Advance Access publication 16 February 2016

ORIGINAL ARTICLE

Cite this article as: Diab M, Guenther A, Scheffel P, Sponholz C, Lehmann T, Hedderich J *et al.* Can radiological characteristics of preoperative cerebral lesions predict postoperative intracranial haemorrhage in endocarditis patients? *Eur J Cardiothorac Surg* 2016;49:e119–e126.

Can radiological characteristics of preoperative cerebral lesions predict postoperative intracranial haemorrhage in endocarditis patients?[†]

Mahmoud Diab^{a,b,†}, Albrecht Guenther^{c,†}, Philipp Scheffel^d, Christoph Sponholz^d, Thomas Lehmann^e, Johannes Hedderich^a, Gloria Faerber^a, Frank Brunkhorst^e, Mathias W. Pletz^f and Torsten Doenst^{a,*}

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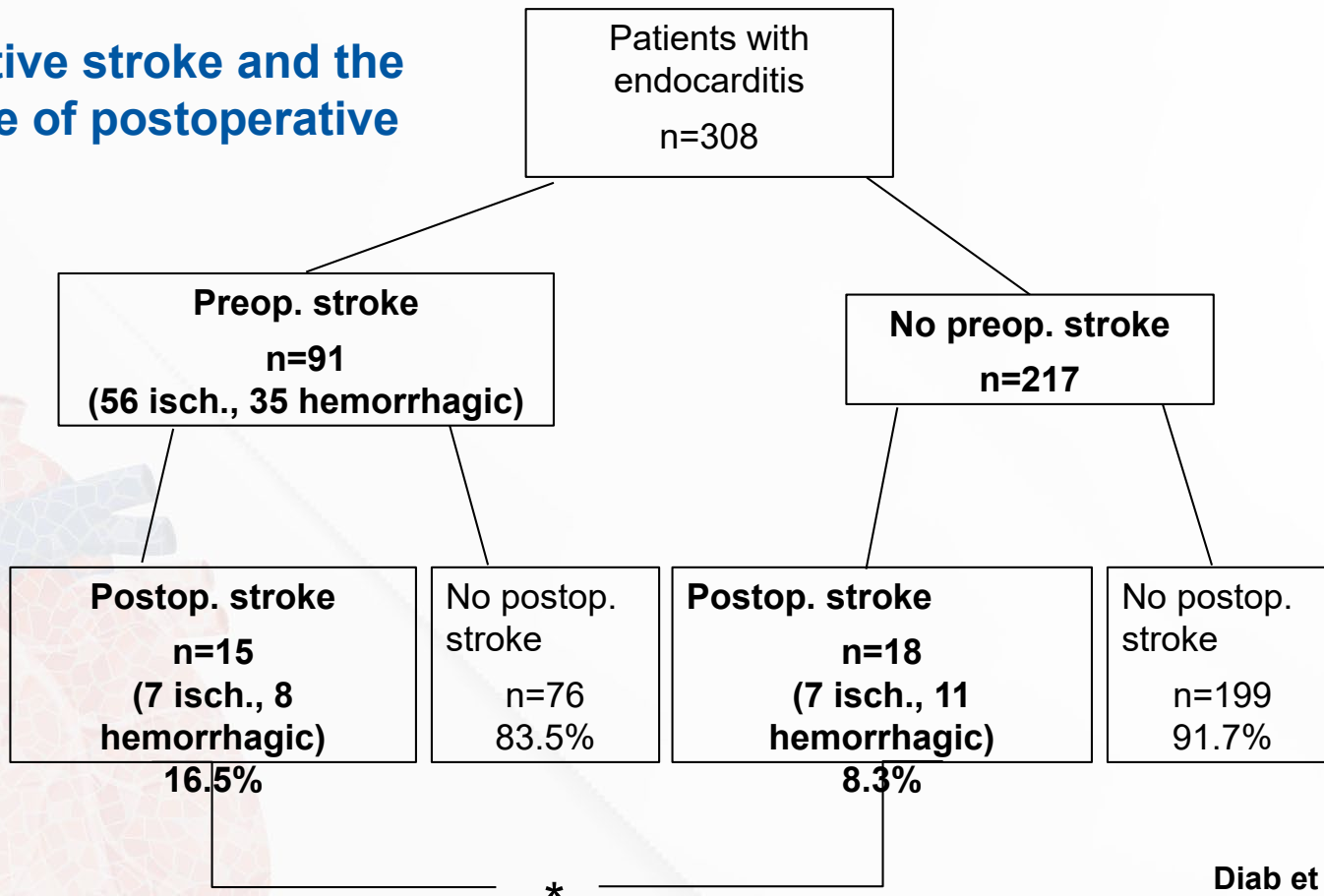
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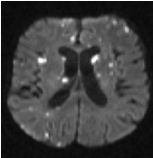
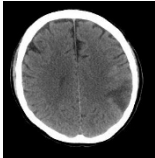
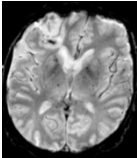
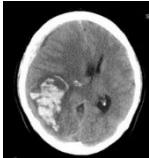
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Tel: +49-364-19322901; fax: +49-364-19322902; e-mail: doenst@med.uni-jena.de (T. Doenst).



Preoperative stroke and the occurrence of postoperative stroke



Relationship between preop. radiological lesions and postoperative stroke

		preOP			
Post-OP					
		Emb (n=56)	Emb + HT (n=17)	Emb+M B (n=15)	ICB (n= 3)
	Emb	4	0	2	1
	Emb+HT	2	1	1	0
	Emb+M B	1	0	0	0
	ICB	1	2	0	0

Cite this article as: Diab M, Musleh R, Lehmann T, Sponholz C, Pletz MW, Franz M *et al.* Risk of postoperative neurological exacerbation in patients with infective endocarditis and intracranial haemorrhage. *Eur J Cardiothorac Surg* 2021;59:426–33.

Risk of postoperative neurological exacerbation in patients with infective endocarditis and intracranial haemorrhage

Mahmoud Diab ^a, Rita Musleh^{a,b}, Thomas Lehmann^c, Christoph Sponholz ^d, Mathias W. Pletz^e,
Marcus Franz ^f, P. Christian Schulze^f, Otto W. Witte ^b, Klaus Kirchhof^g,
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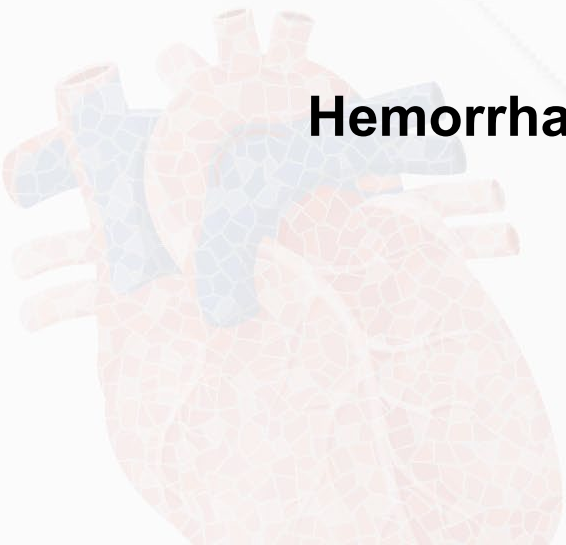
Types of ICH

Intracerebral hemorrhage

Subdural hemorrhage

Subarachnoid hemorrhage

Hemorrhagic transformation of embolic infarcts



IE surgery in patients with pre-op ICH

Table 2: Neurological and radiological characteristics of patients with pre-ICH and their surgical timing

Patients with pre-ICH (n = 34)

Stroke	23 (68)
Asymptomatic ICH	11 (32)
Type of ICH	
Cerebral haemorrhage	5 (15)
Subdural haemorrhage	2 (6)
Subarachnoid haemorrhage	2 (6)
Haemorrhagic infarct	21 (62)
Mixed	4 (12)
Presence of meningitis	1 (3)
Presence of cerebral abscess	2 (6)
Presence of encephalopathy	6 (18)
Time from ICH to surgery	
≤7 days	21 (62)
8–14 days	5 (15)
15–28 days	3 (9)
≥29 days	3 (9)
Unknown	2 (6)

Data are given as n (%).

ICH: intracranial haemorrhage.

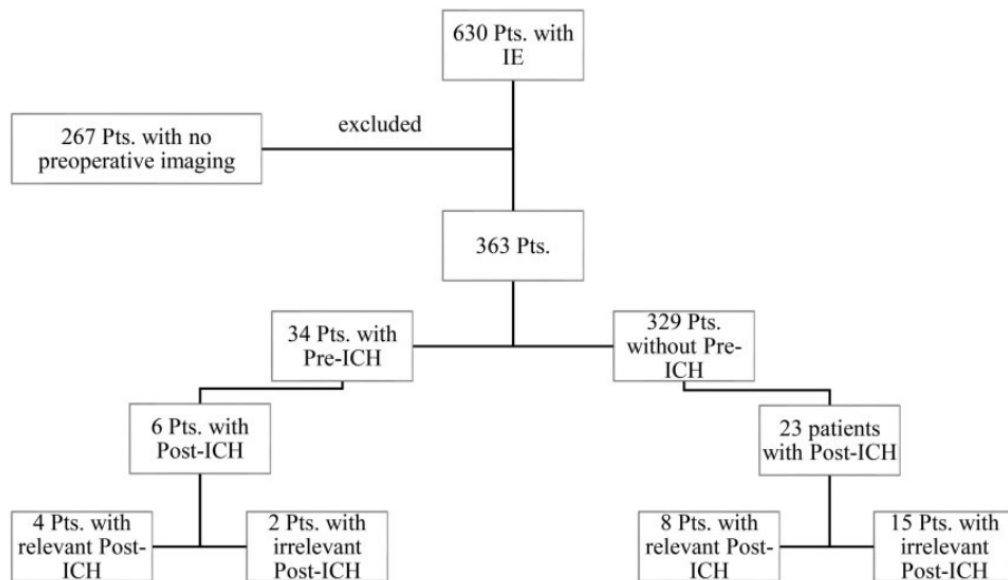


Figure 1: Flow chart of the distribution of the whole patient population in the study. ICH: intracranial haemorrhage; IE: infective endocarditis; Pts: patients

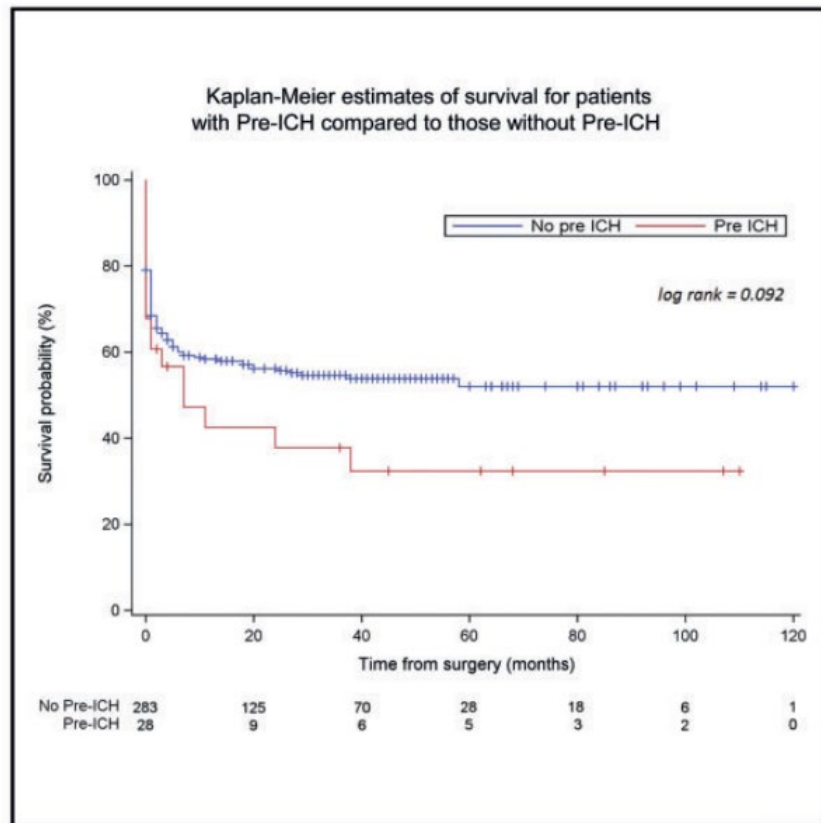


IE surgery in patients with pre-op ICH

Multivariable Analysis:

ICH not related to 30d mortality
(OR 1.02, 95%CI: 0.43-2.40, $p=0.96$)

ICH not related to
neurological deterioration
(OR 1.10, 95%CI: 0.44-2.73, $p=0.84$)





CLINICAL RESEARCH

Intracranial haemorrhage in infective endocarditis



Hémorragie intracrânienne dans l'endocardite infectieuse

Erwan Salaun^{a,*}, Anissa Touil^a, Sandrine Hubert^{a,b},
Jean-Paul Casalta^{a,b}, Frédérique Gouriet^{a,b},
Emmanuelle Robinet-Borgomano^c, Emilie Doche^c,
Nadia Laksiri^c, Caroline Rey^c, Cécile Lavoute^a,
Sébastien Renard^a, Hervé Brunel^d,
Anne-Claire Casalta^a, Julie Pradier^a,
Jean-François Avierinos^a, Hubert Lepidi^{a,b},
Laurence Camoin-Jau^{b,e}, Alberto Riberi^{a,b},
Didier Raoult^b, Gilbert Habib^{a,b}

^a Cardiology Department, la Timone Hospital, AP-HM, boulevard Jean-Moulin, 13005 Marseille, France

^b MEPHI, IRD, IHU-Méditerranée Infection, Aix Marseille University, AP-HM, 13005 Marseille, France

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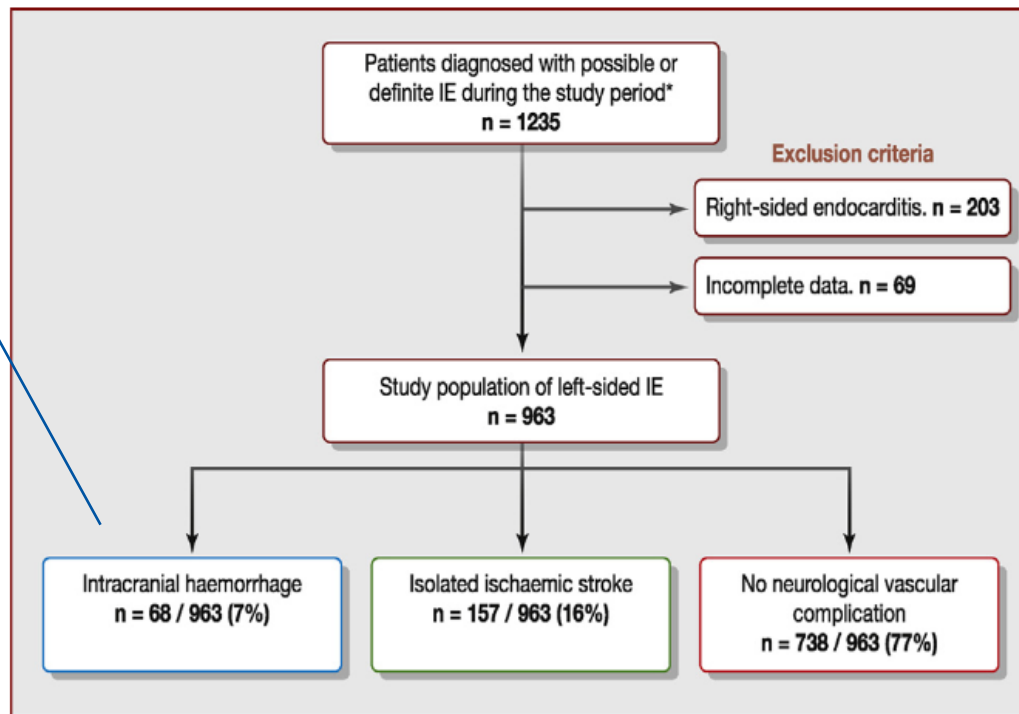
CLINICAL RESEARCH

Intracranial haemorrhage in infective endocarditis



60 patients with ICH and indication for surgery (88%)

38 were operated (63%)

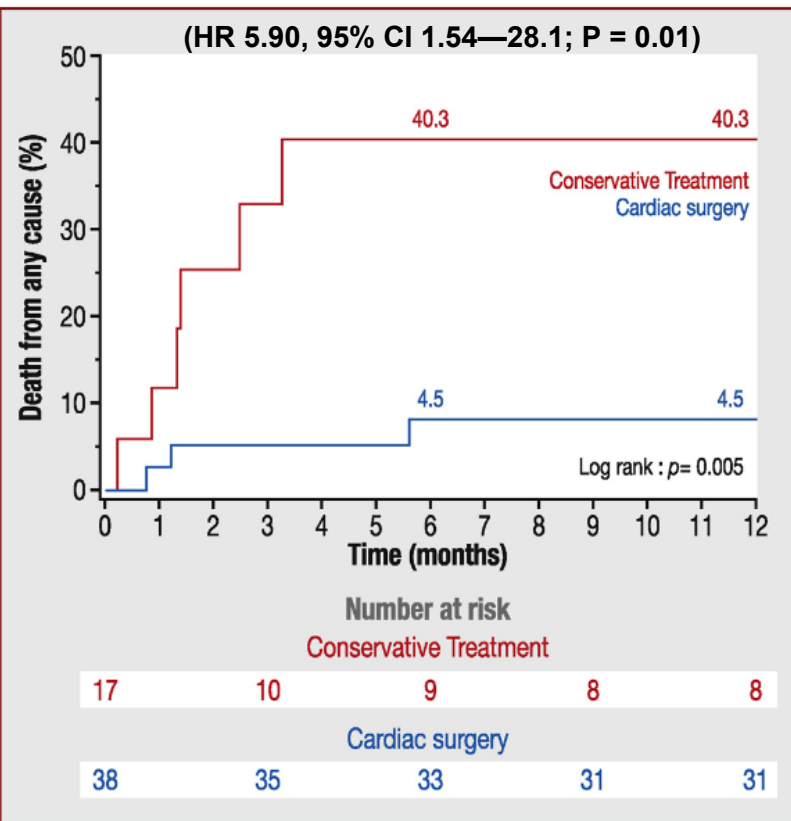


Intracranial haemorrhage in infective endocarditis



No neurological deterioration in surgical patients

„Earliest Patient“ operated after 15 days.





Journal of the American Heart Association

Volume 11, Issue 10, 17 May 2022

<https://doi.org/10.1161/JAHA.121.024401>



SYSTEMATIC REVIEW AND META-ANALYSIS

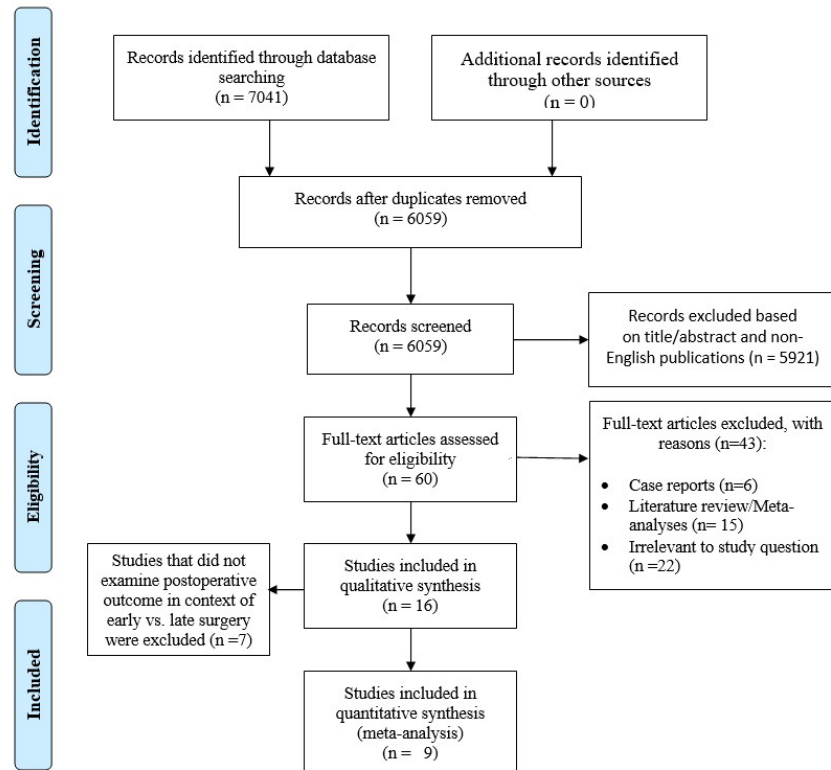
Surgical Timing in Patients With Infective Endocarditis and With Intracranial Hemorrhage: A Systematic Review and Meta-Analysis

Rita Musleh, MD  ; Peter Schlattmann, MD, MSc  ; Túlio Caldonazo, MD; Hristo Kirov, MD; Otto W. Witte, MD  ; Torsten Doenst, MD  ; Albrecht Günther, MD  * ; Mahmoud Diab, MD  *



Results

- We identified 16 studies including 355 patients
- Nine studies examined the impact of surgical timing (early vs. late)
- Only one study examined the fate of IE-patients with ICH who were treated conservatively despite of surgical indication
 - higher mortality in the conservative group





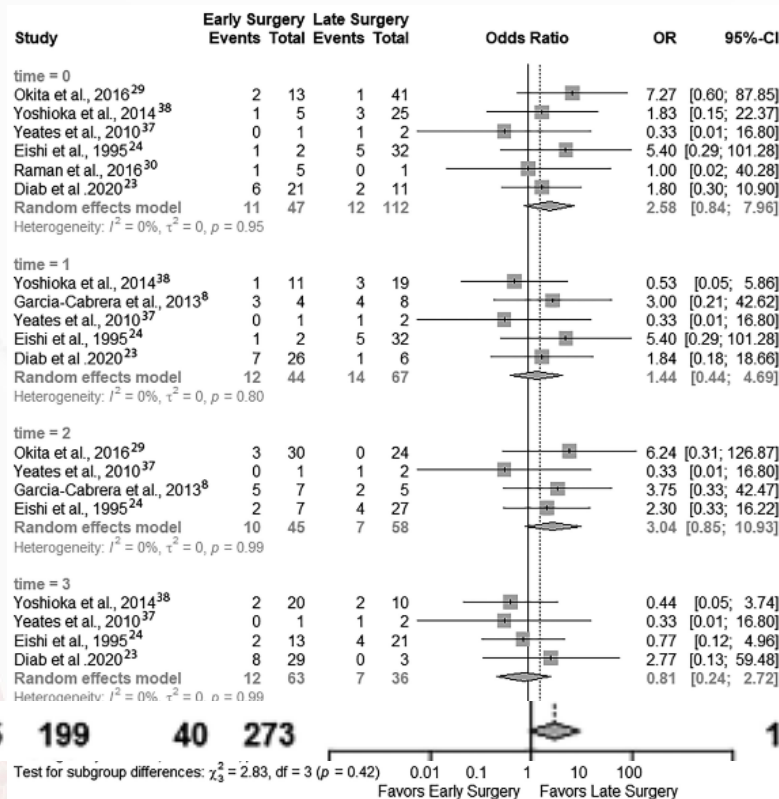
- Except for one, all single center studies
- Low patient numbers
- All studies retrospective

Table 2. Literature Review Presenting the Postoperative Outcomes in the Context of the Surgical Timing in the 9 Studies Included in the Final Quantitative Analysis

Literature (year)	Patients with IE and with Pre-ICH, n	Interval ICH-surgery	Outcomes/conclusions
Diab (2020) ²⁹	34	<7 d (n=21)	Risk of postoperative neurological exacerbation in patients with IE and with ICH might be overestimated. Postoperative neurological deterioration was higher in patients with IE and with Pre-ICH operated on within 7 d; however, the difference was not significant ($P=0.24$). Pre-ICH was not an independent predictor for postoperative neurological deterioration or hospital mortality in patients with IE ($P=0.84$).
		8–14 d (n=5)	
		15–28 d (n=3)	
		>28 d (n=2)	
		Unknown (n=2)	
Salaun (2018) ⁷	38	<28 d (n=17)	No neurological deterioration regardless of the surgical timing.
		Overall median of 34 d (n=38)	Higher mortality in conservatively treated patients with Pre-ICH ($P=0.005$).
Kume (2018) ²⁶	25	<14 d (n=17)	There was no difference in the postoperative bleeding rate and mortality between patients who had surgery within or after 14 d from the onset of ICH (log-rank $P=0.904$). Intracranial mycotic aneurysm is associated with ICH after valve surgery ($P=0.002$).
		>14 d (n=8)	
Okita (2016) ²⁰	54	<7 d (n=13)	Although statistically insignificant, early surgery (within 7 d) had higher incidence of hospital deaths in patients with ICH ($P=0.22$).
		8–21 d (n=17)	
		>21 d (n=24)	
Raman (2016) ²⁹	6	≤10 d <7 d (n=5)	No neurological deterioration regardless of the surgical timing.
Yoshioka (2014) ³⁴	30	8–14 d (n=6)	No neurological deterioration or hemorrhage expansion, regardless of surgery timing (even when operated on within 2 wk). Only 2 patients with new postoperative ectopic asymptomatic hemorrhage. Four patients died because of organ and heart failure.
		15–28 d (n=9)	
		>28 d (n=10)	
Garcia-Cabrera (2013) ⁸	12	<14 d (n=4)	Higher mortality and neurological deterioration associated with early surgery within 2 wk. Outcome according to surgical timing: 4 patients within the first 2 wk (75% mortality, 50% new ICH), 3 patients operated on within the third week (66% mortality, 33% new ICH), and 5 cases operated on after 3 wk (40% mortality, 20% new ICH).
		14–21 d (n=3)	
		21 d (n=5)	
Yeates (2010) ³⁶	3	Median of 5.8 wk (3–60 d) with 1 of 3 patients operated <1 wk	No neurological deterioration regardless of the surgical timing.
Eishi (1995) ²³	34	<1 d (n=1)	Neurological deterioration is not clearly related to the surgical timing. No neurological deterioration in patients operated on 2–28 d after ICH, but 19% exacerbation in patients operated on >4 wk. Six patients died, with 1 neurological death in the 1 patient operated on within 24 h.
		2–28 d (n=12)	
		>28 d (n=21)	

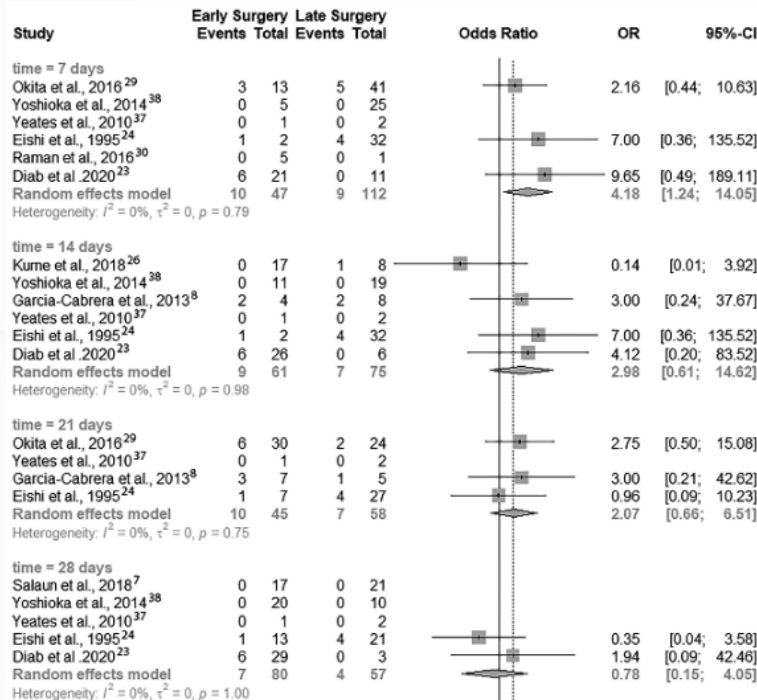


30-Day Mortality





Neurological Deterioration

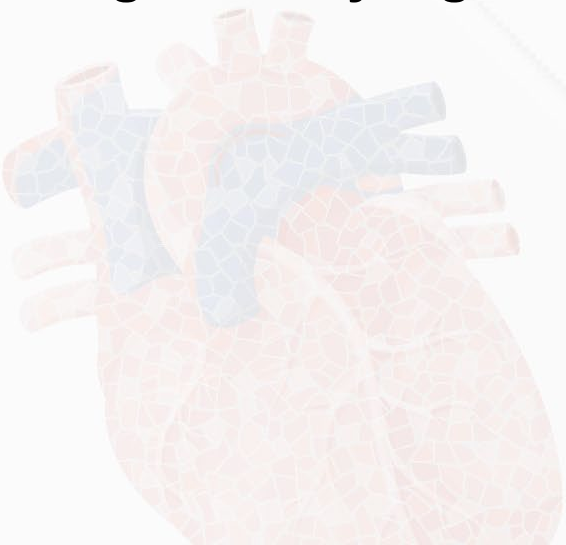


Favors Early Surgery Favors Late Surgery



Summary

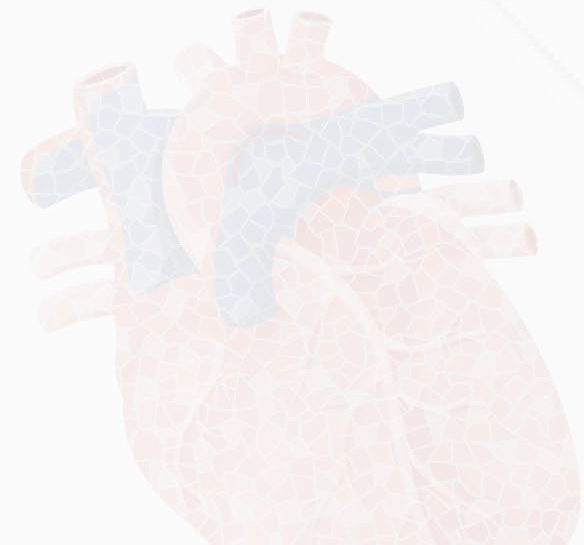
Cardiac surgery for IE within 30 days of ICH was not associated with significantly higher mortality, but with significantly increased rates of neurological deterioration.





What do we make of it ?

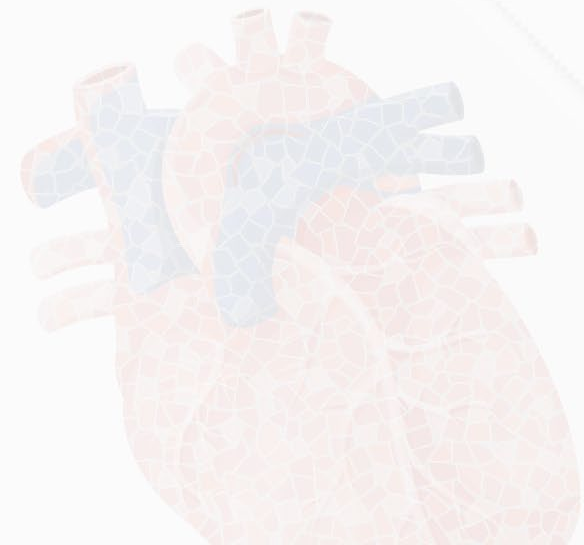
Evidence is conflicting
Only retrospective studies



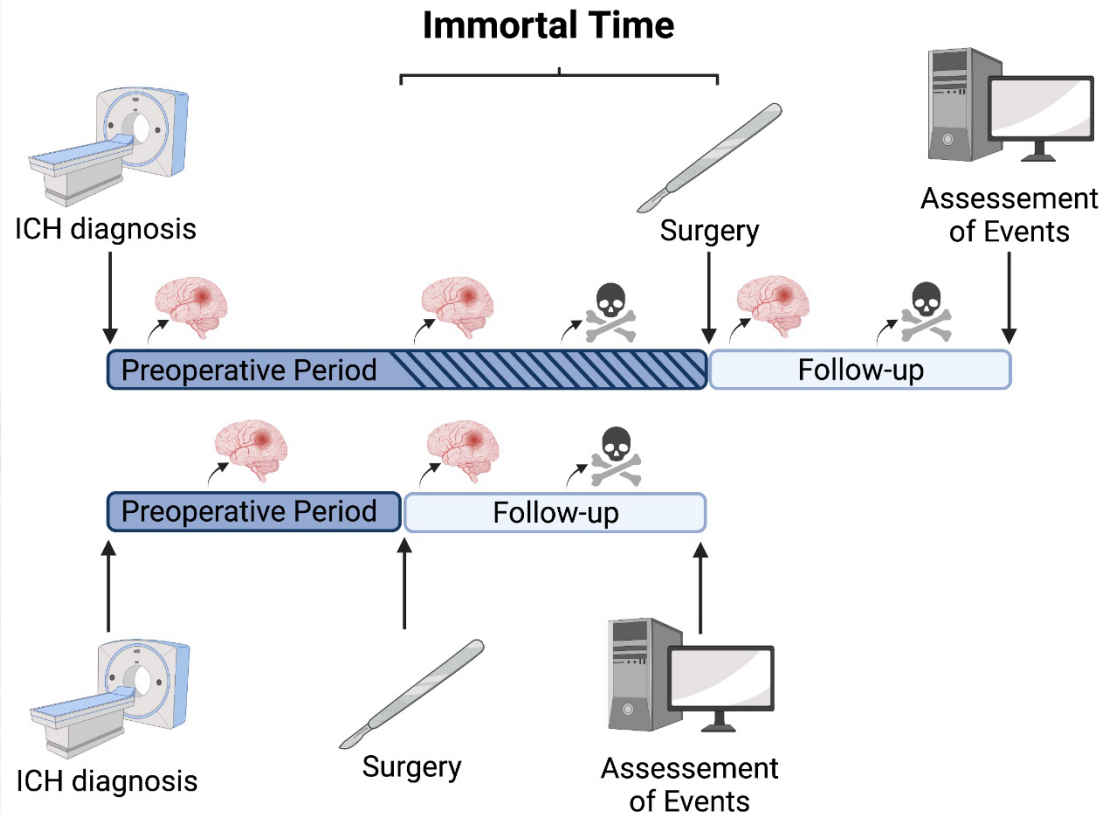


What do we make of it ?

Evidence is conflicting
Only retrospective studies
Immortal-time bias

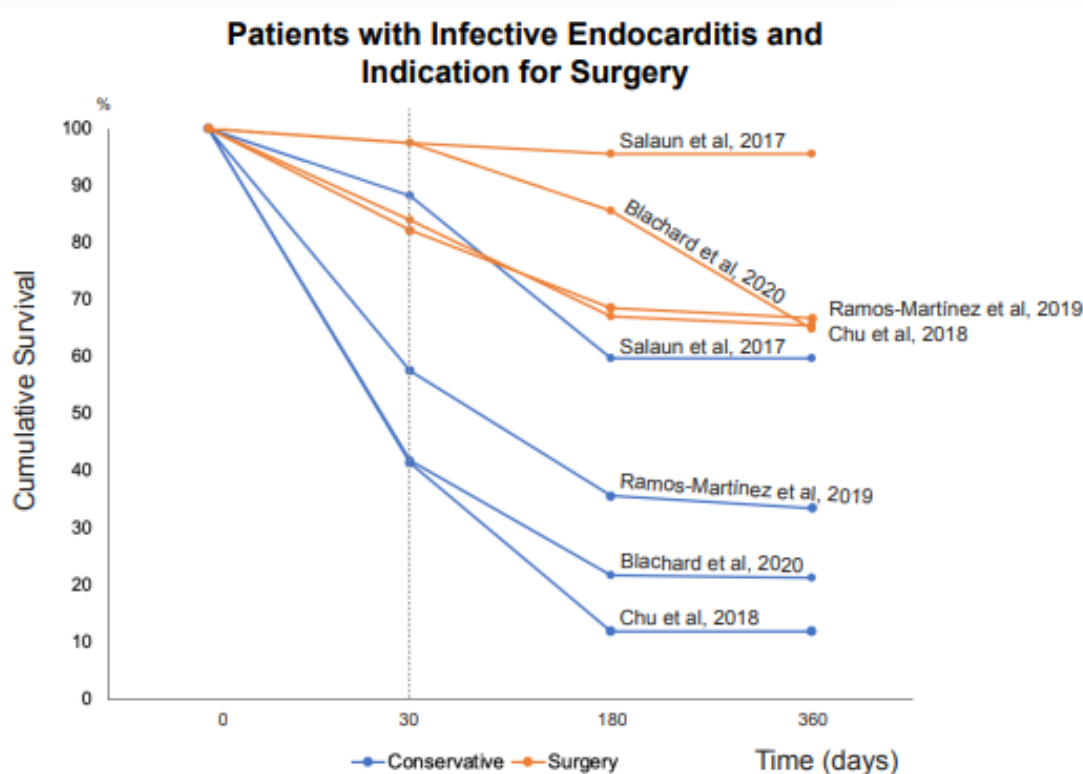


Immortal Time Bias – underestimated in retrospective studies



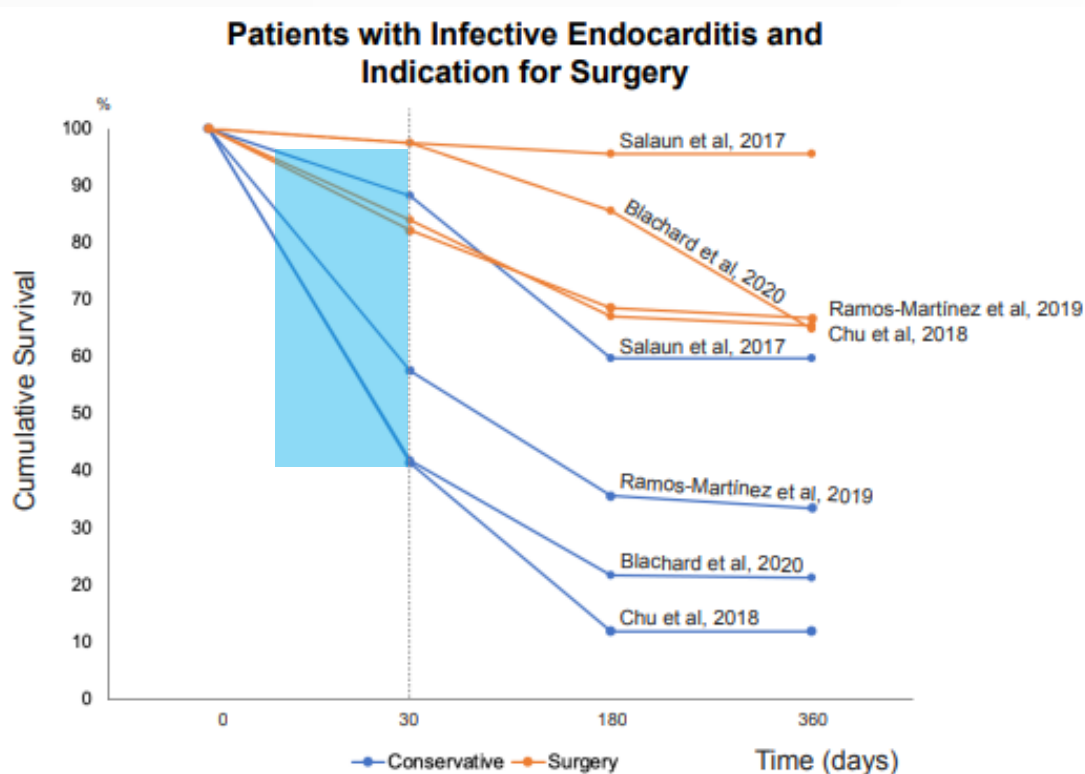


Potential impact of Immortal-Time Bias on interpretation of results





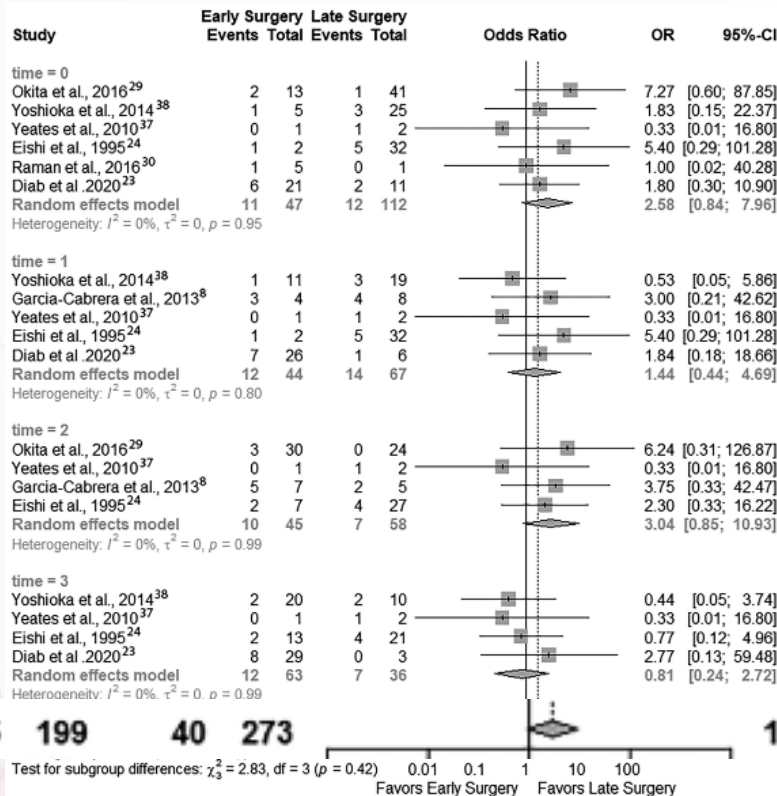
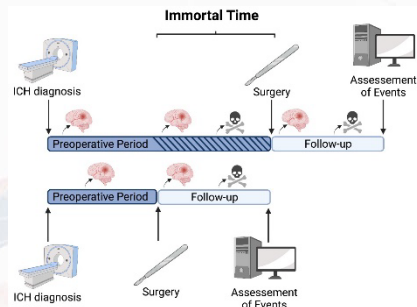
Potential impact of Immortal-Time Bias on interpretation of results





30-Day Mortality

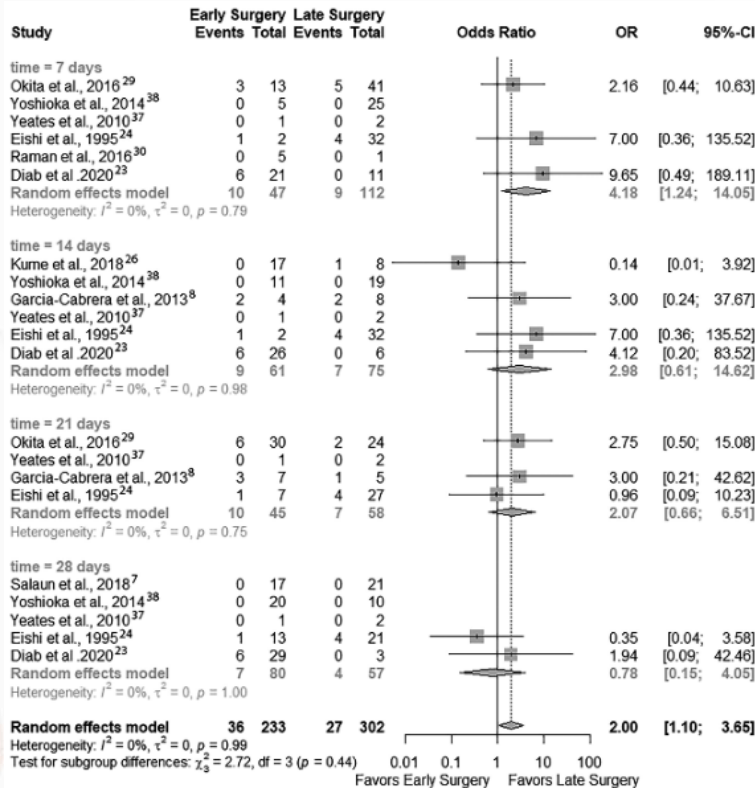
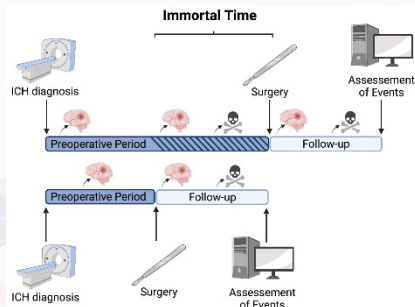
Not considered -
effect unknown





Neurological Deterioration

Not considered -
effect unknown



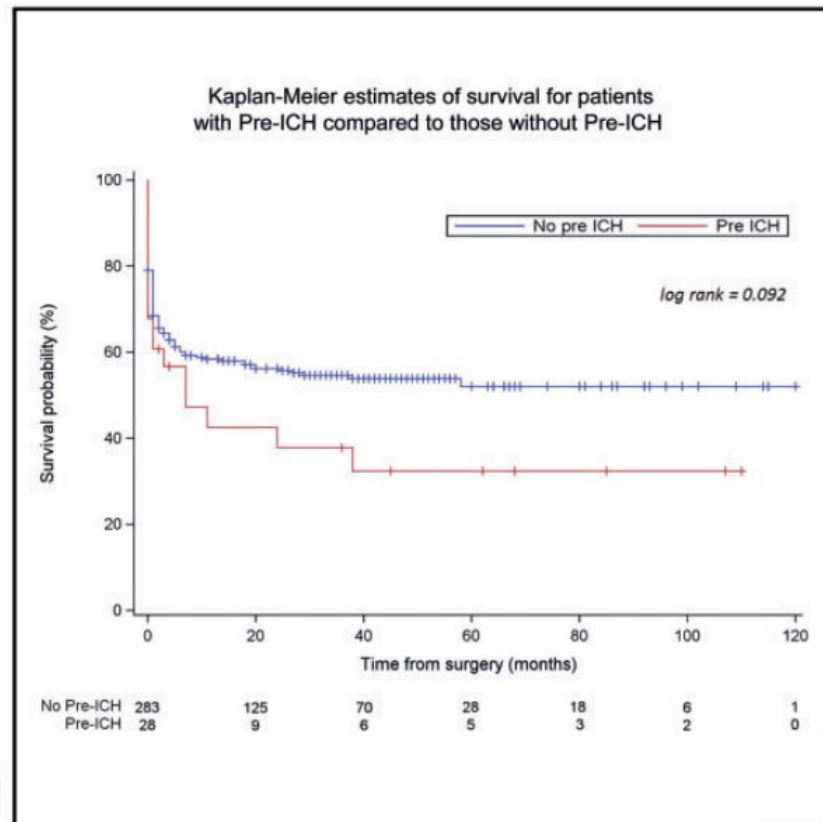


IE surgery in patients with pre-op ICH

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(OR 1.02, 95%CI: 0.43-2.40, p=0.96)

ICH not related to
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(OR 1.10, 95%CI: 0.44-2.73, p=0.84)



IE surgery in patients with pre-op ICH

Impact of post-operative anticoagulation management

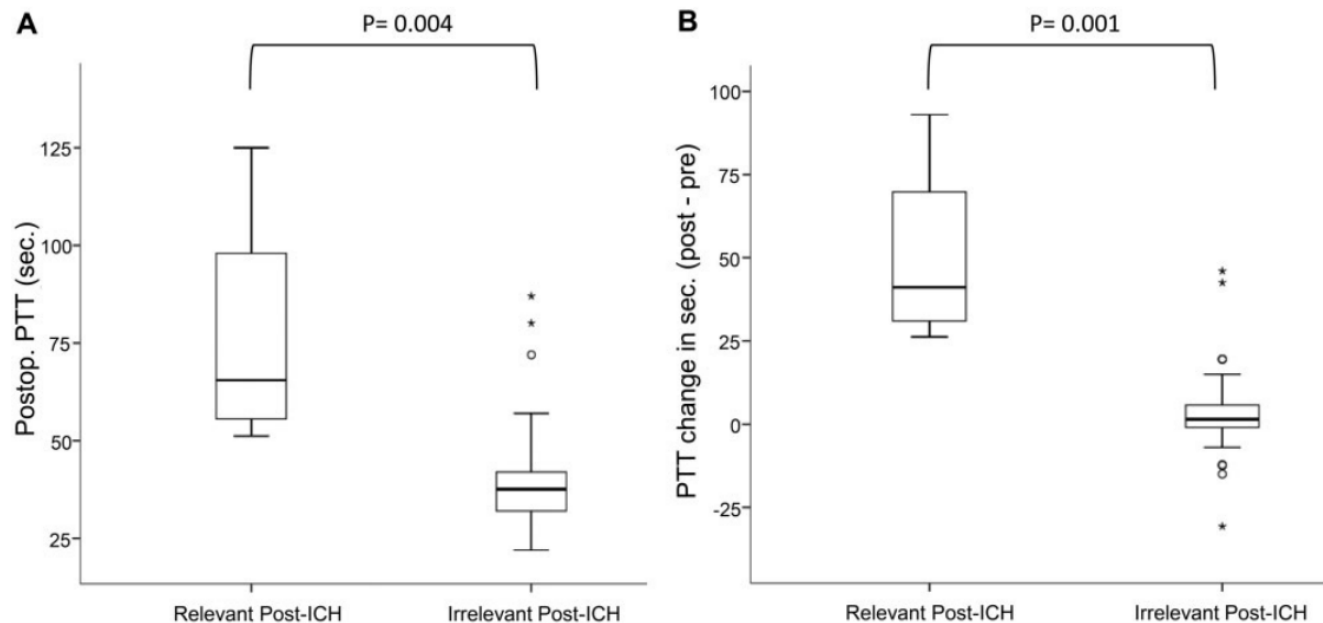


Figure 2: Changes in PTTs among patients with and without relevant post-ICH. Postoperative PTT in 2 cohorts representing patients with ($n = 4$) and without ($n = 30$) relevant post-ICH (maximal postoperative PTT given in s). **(A)** Postoperative PTT showed median (interquartile range) of 65.5 (53.4–111.5) in the relevant post-ICH group compared with 37.6 (31.9–43.5) in the group without relevant post-ICH. The difference is significant ($P = 0.004$). **(B)** Change in PTT between preoperative and postoperative values with a median (interquartile range) of 41 (31.0–69.8) in the relevant post-ICH group compared with 1.5 (1.0–5.7) in the group without relevant post-ICH ($P = 0.001$). ICH: intracranial haemorrhage; postop: postoperative; PTT: partial thromboplastin time.



Conclusions

- Intracranial hemorrhage may not be as dangerous as commonly expected.
- ICH may or **may not** be associated with mortality and/or neurological deterioration.
- An immortal time bias may camouflage the truth. We need prospective (randomized) evidence.
- Based on the available data, post-op heparin management may play an important role.



Thank you for your attention

