SOLACI CACI'24
BUENOS AIRES HILTON
BUENOS AIRES, ARGENTINA
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ICBA Instituto Cardiovascular

Balloon Pulmonary Angioplasty for Chronic Thromboembolic Pulmonary Hypertension: Has It Become Common?

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ICBA, Instituto Cardiovascular de Buenos Aires

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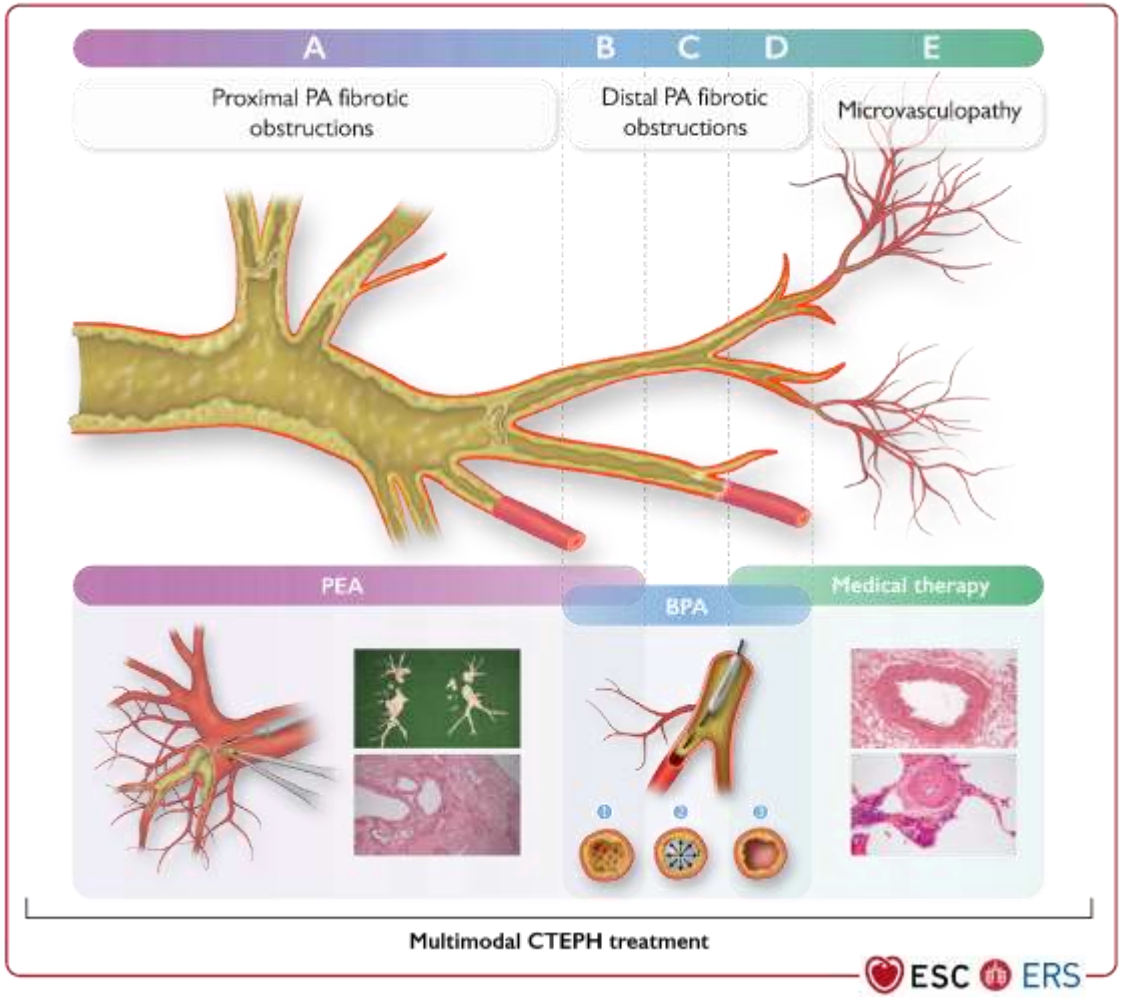
¿Qué opciones tenemos para el tratamiento?



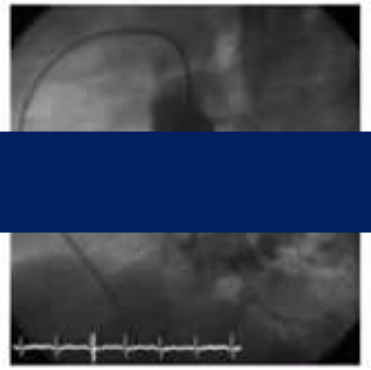
Humbet M et al; European Heart Journal (2022) 00, 1–114

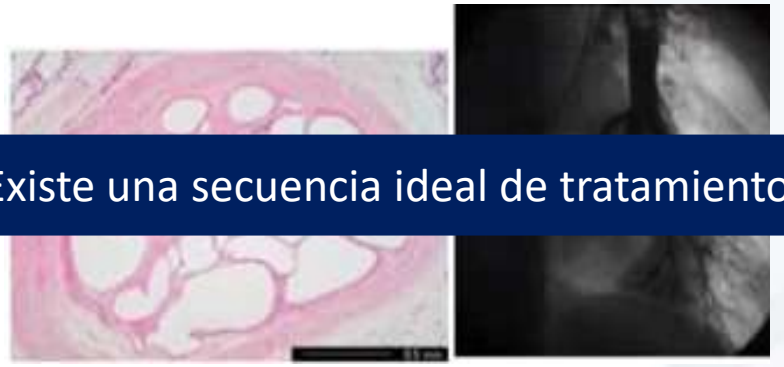
¿Qué estamos tratando?

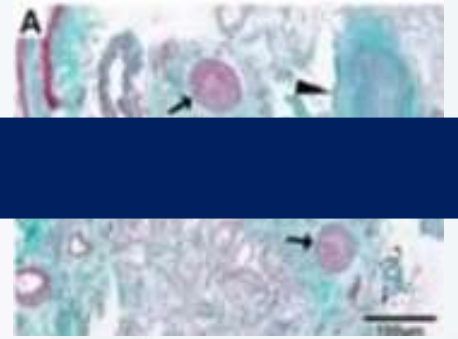
Alteración fibrótica de arterias lobares o segmentarias proximales

Alteración fibrótica de arterias segmentarias distales o subsegmentarias

Afectación microvascular o vasculopatía pulmonar







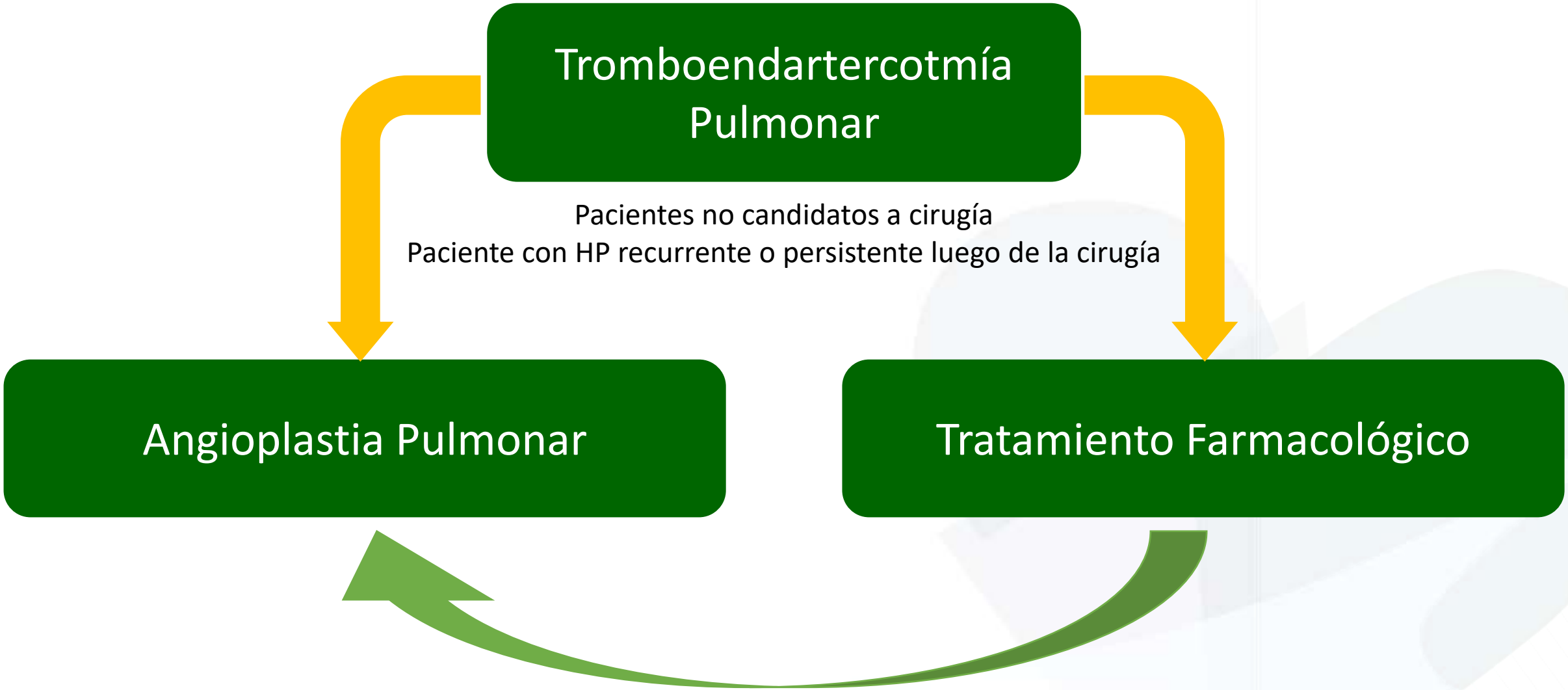
¿Existe una secuencia ideal de tratamiento?

Tromboendartercotmía Pulmonar

Angioplastia Pulmonar

Tratamiento Farmacológico

¿Por dónde empezar?



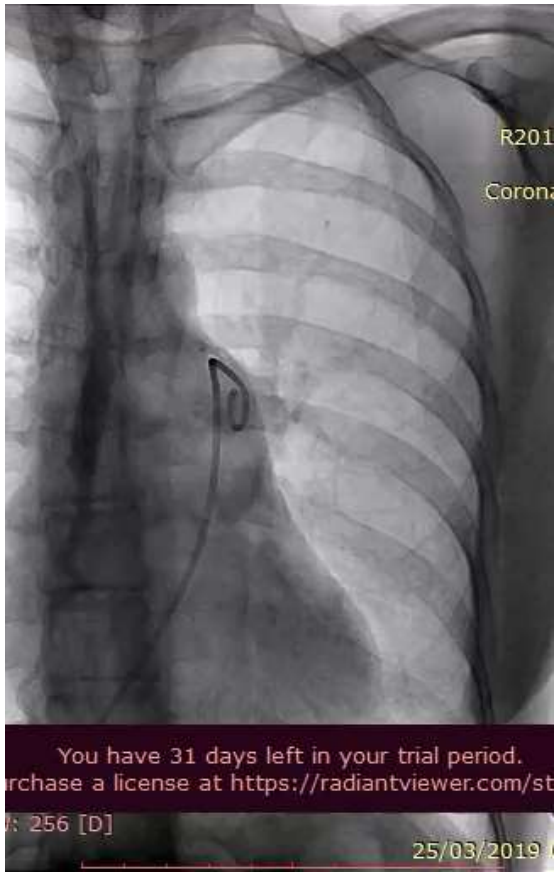
Caso Clínico

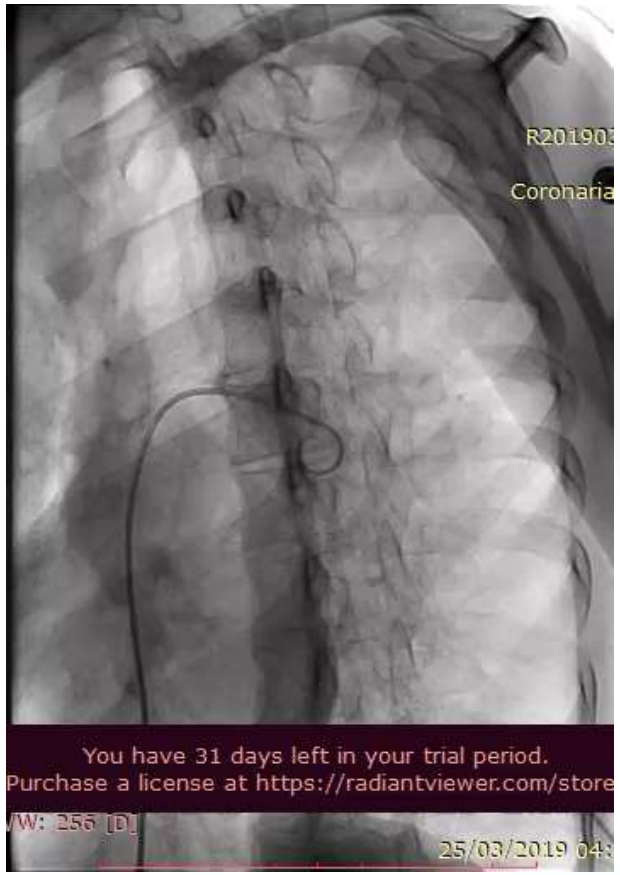
Mujer 40aa → Disnea → HP → V/Q → CCD → AngioPulmonar

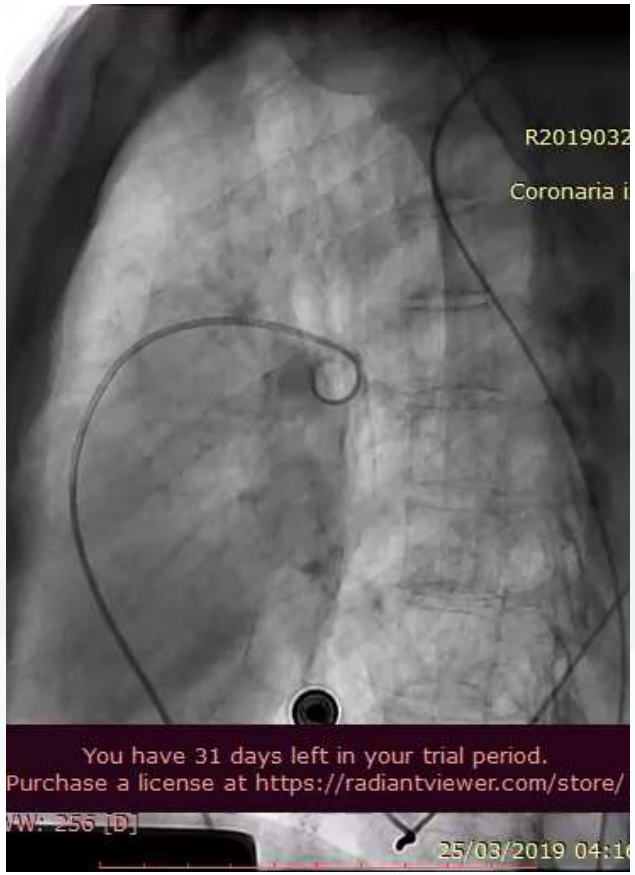
Caso Clínico

	Sat O_2	Presiones
Aurícula Derecha (mmHg)	64%	5
Ventrículo Derecho (mmHg)	65%	75/0 (6PFD)
Arteria Pulmonar (mmHg)	64%	89/34 (52)
Wedge (mmHg)		6
Aorta (mmHg)	96%	105/72 (88)
Volumen Minuto		2,98 L/min
Índice Cardiaco		2,19 L/min/m^2
RVS		2228 Dynas.seg.cm^{-5} 28 UW
RVP		1235 Dynas.seg.cm^{-5} 15 UW
SVO_2		64%

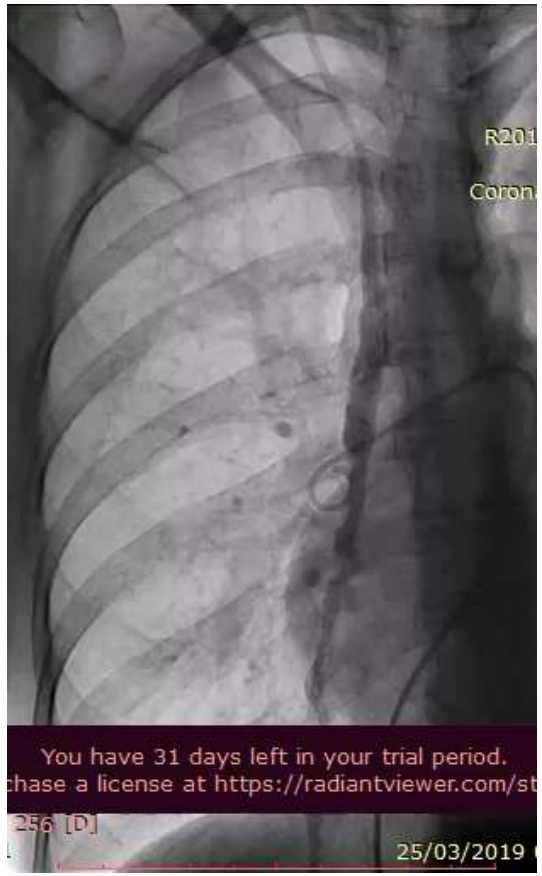
Caso Clínico

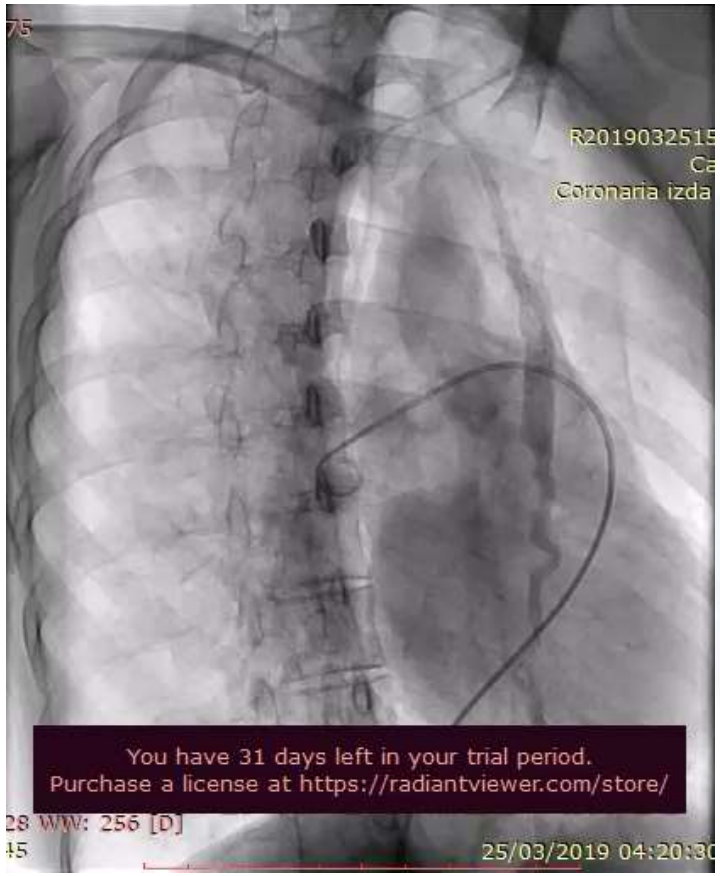


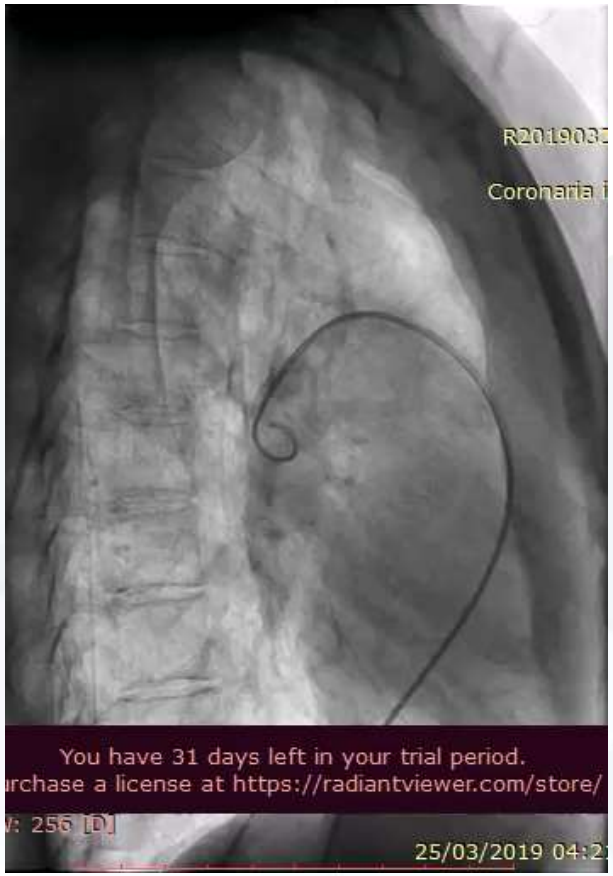




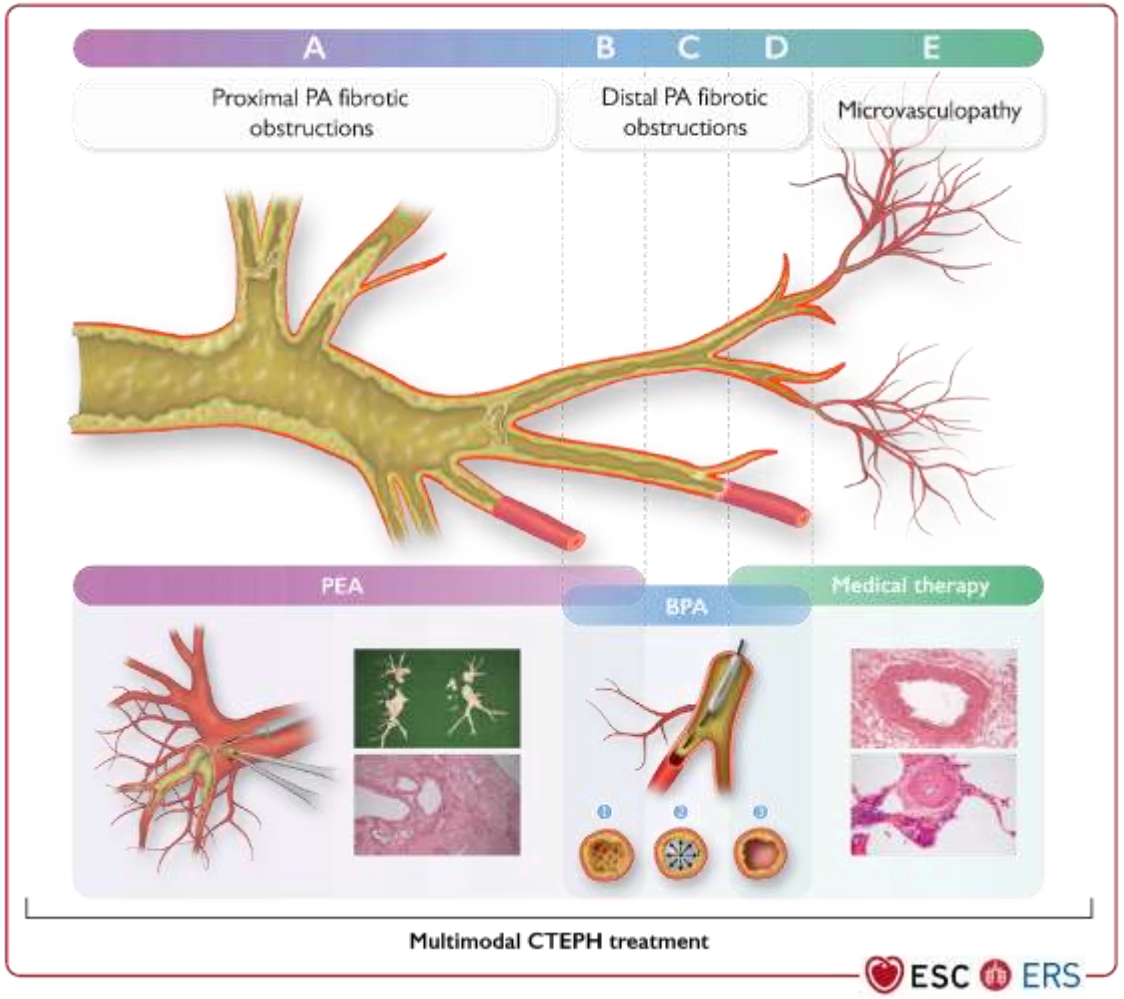
Caso Clínico





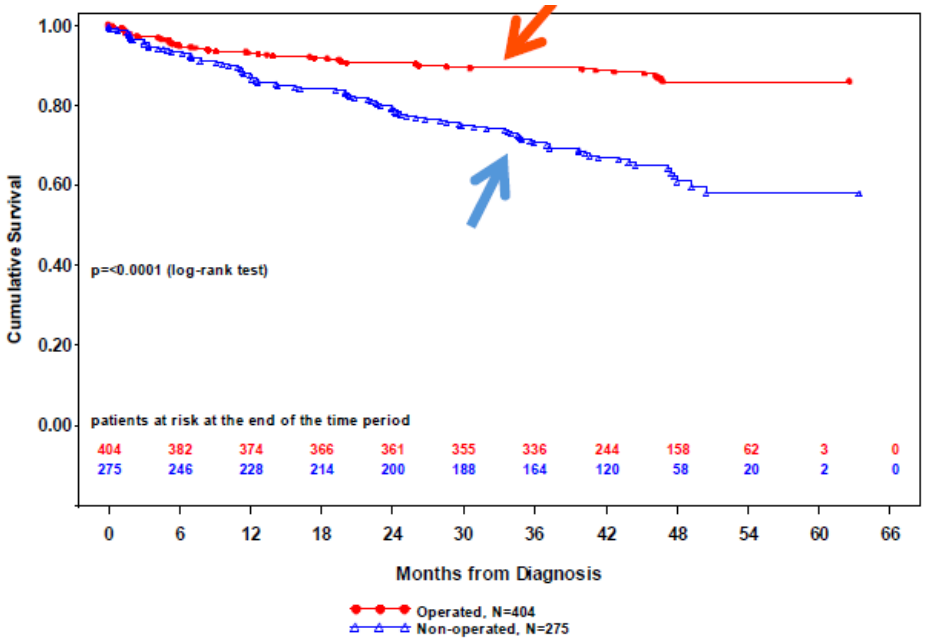


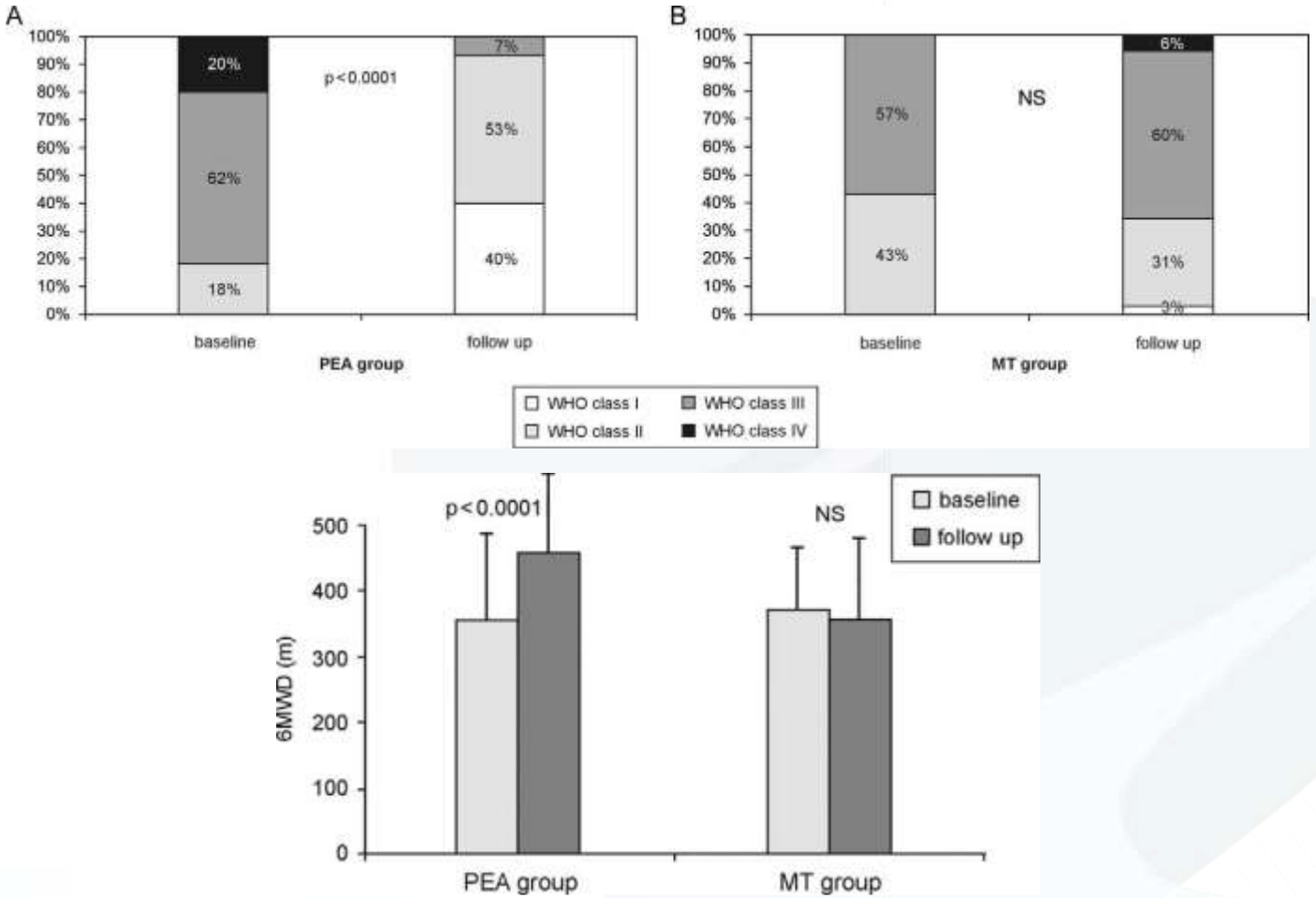
¿Qué opciones tenemos para el tratamiento?



Humbet M et al; European Heart Journal (2022) 00, 1–114

Tromboendarterectomía Quirúrgica



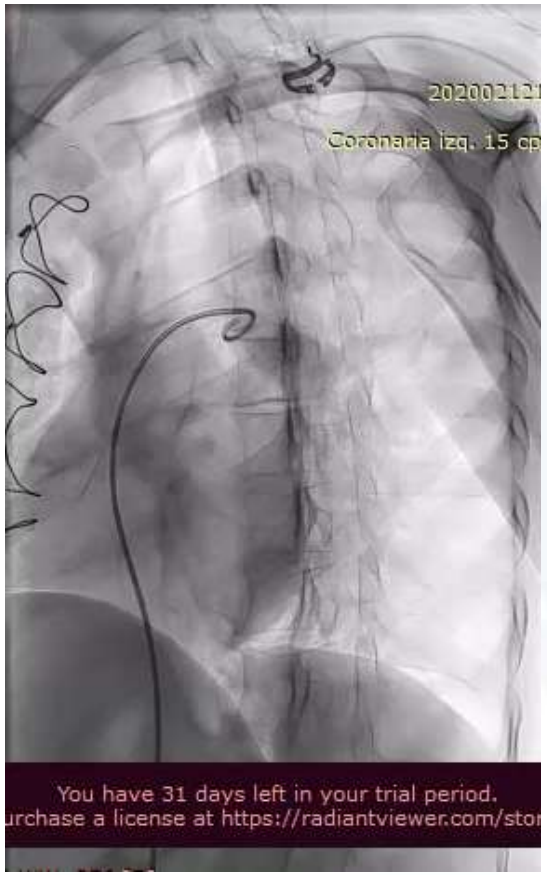


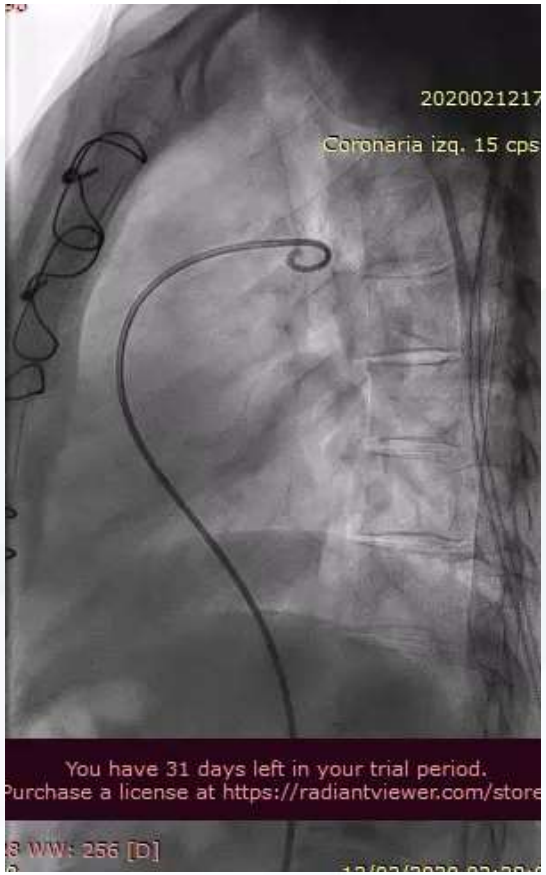
Simonneau G et al. Am J Respir Crit Care Med 2013;187:A5365
Wiesteska M et al; Clin Appl Thromb Hemost. 2016 Jan;22(1):92-9

Caso Clínico – 6 meses POP

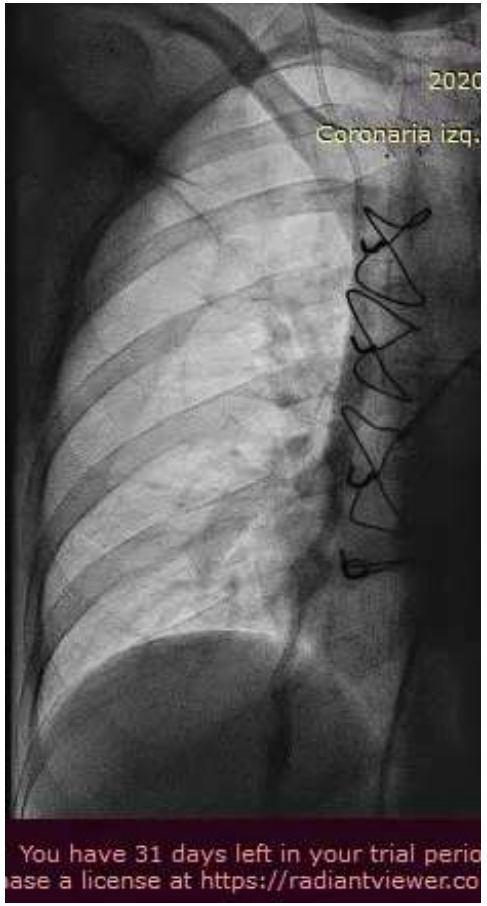
	25/03/19	23/12/19 PostCx
Aurícula Derecha (mmHg)	5	5
Ventrículo Derecho (mmHg)	75/0 (6PFD)	60/01 (11 PFD)
Arteria Pulmonar (mmHg)	89/34 (52)	57/17 (34)
Wedge (mmHg)	6	6
Aorta (mmHg)	105/72 (88)	90/70 (76)
Volumen Minuto	2,98 L/min	2,50 L/min
Índice Cardiaco	2,19 L/min/m^2	1,86 L/min/m^2
RVS	2228 Dynas.seg.cm^{-5} 28 UW	2272 Dynas.seg.cm^{-5} 28 UW
RVP	1235 Dynas.seg.cm^{-5} 15 UW	768 Dynas.seg.cm^{-5} 10 UW
SVO_2	64%	47%

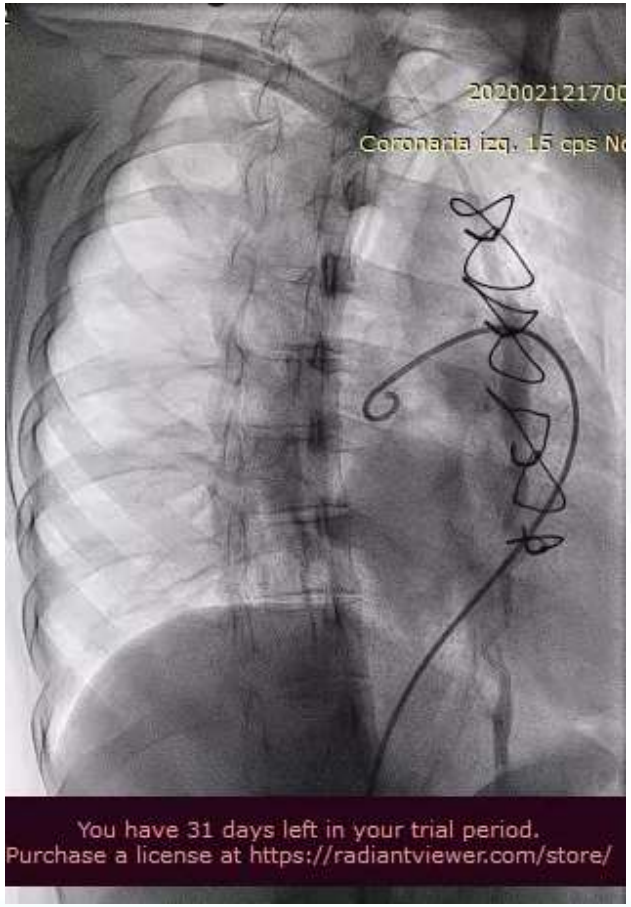
Caso Clínico – 6 meses POP



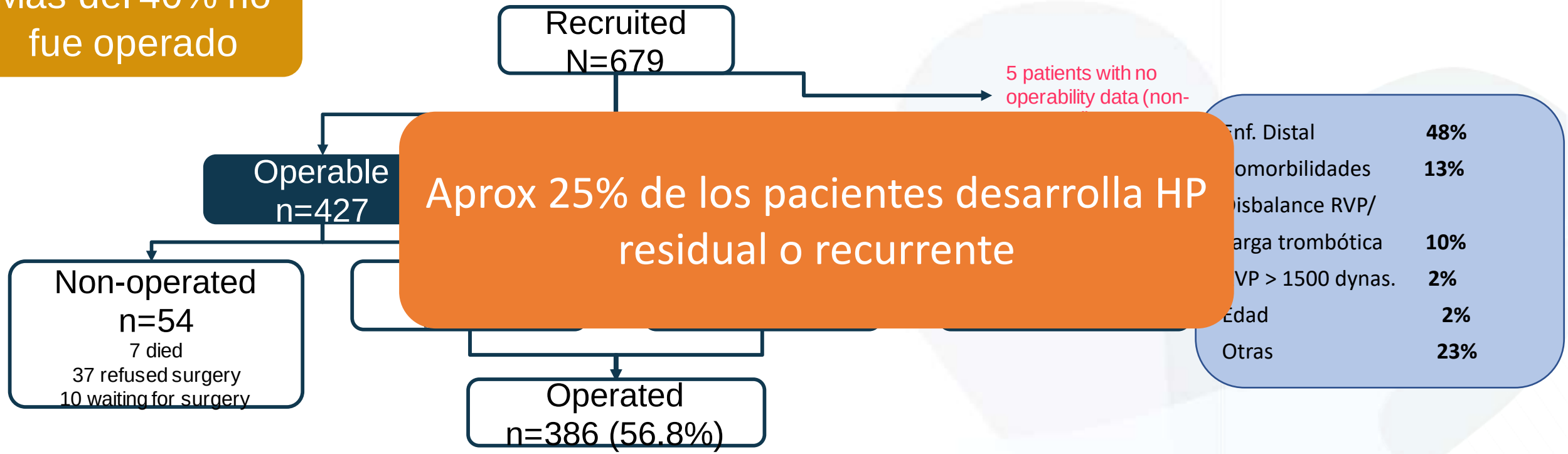


Caso Clínico – 6 meses POP





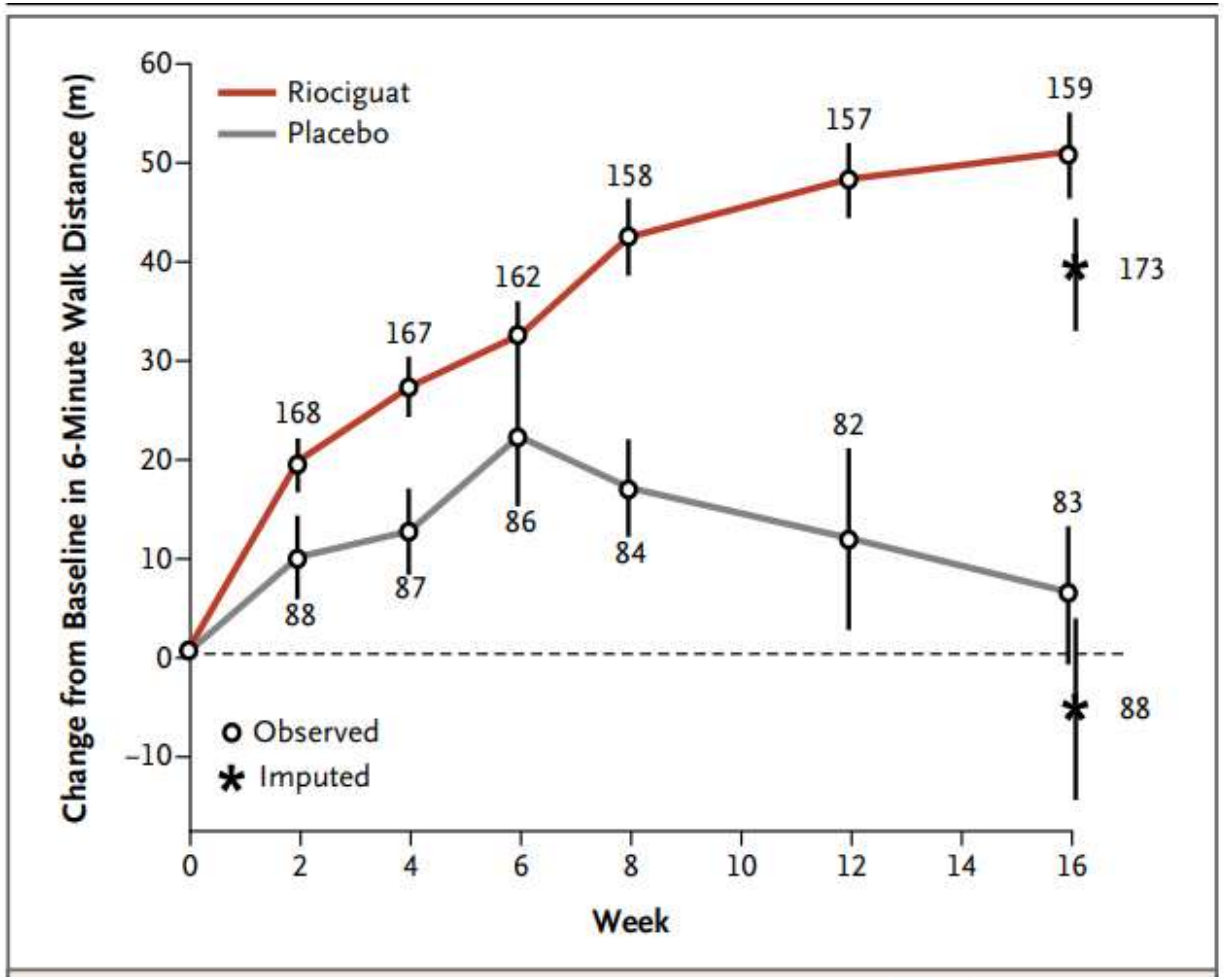
Mas del 40% no fue operado

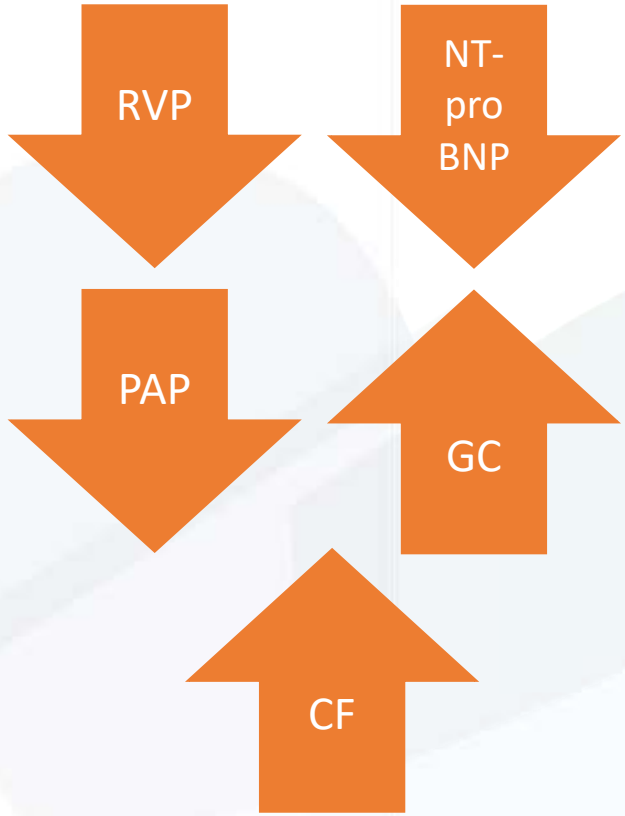


Aprox 25% de los pacientes desarrolla HP residual o recurrente

Pepke-Zaba J et al. Circulation 2011;124:1973–1981
Hsieh WC et al. J Thorac Cardiovasc Surg 2018;156:1275–1287

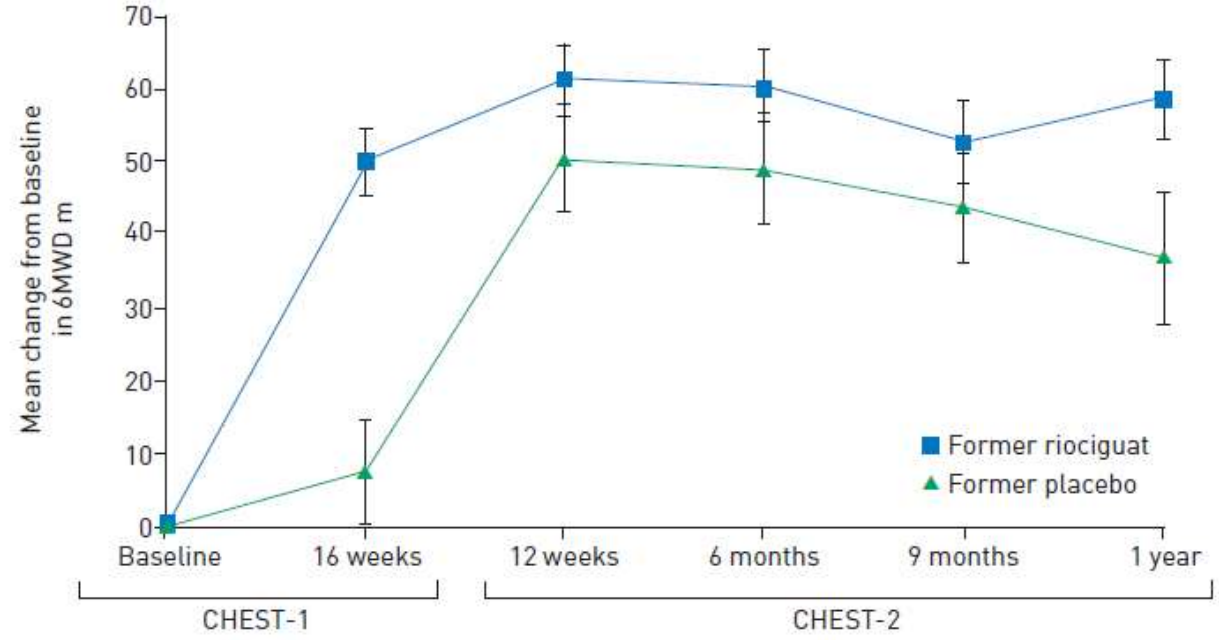
Tratamiento farmacológico – Riociguat





Ghofrani HA, et al. N Engl J Med. 2013 Jul 25;369(4):319-29

Tratamiento farmacológico – Riociguat

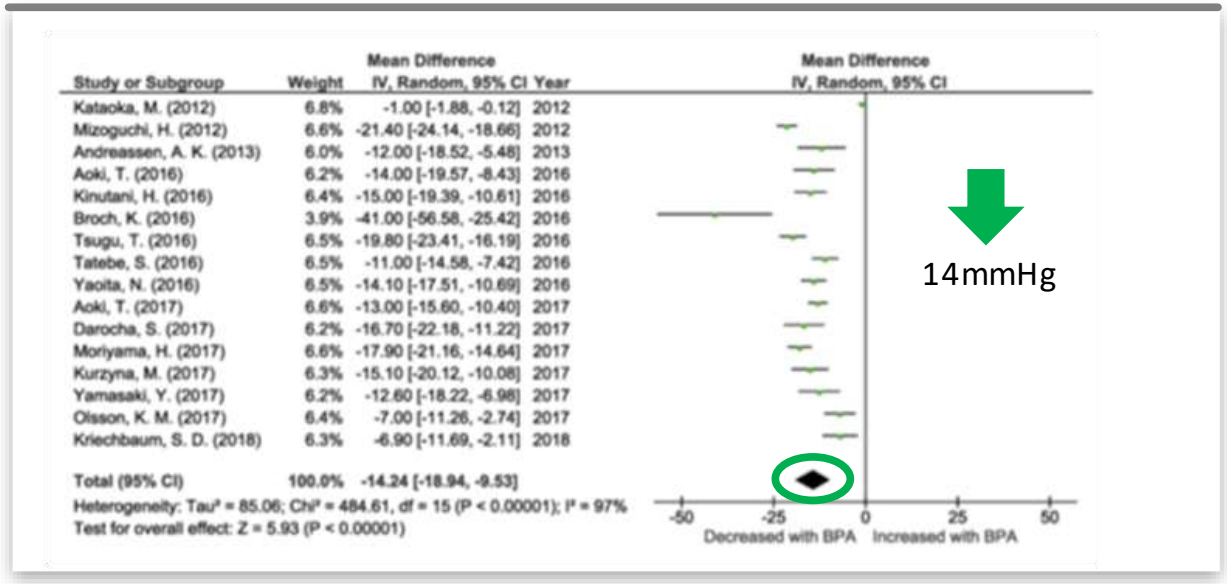


Mean 6MWD absolute values m						
Former riociguat	345	396	406	406	400	411
Placebo	360	368	414	411	408	405
Patients n						
Former riociguat	155	154	145	143	143	114
Placebo	82	81	75	75	72	58

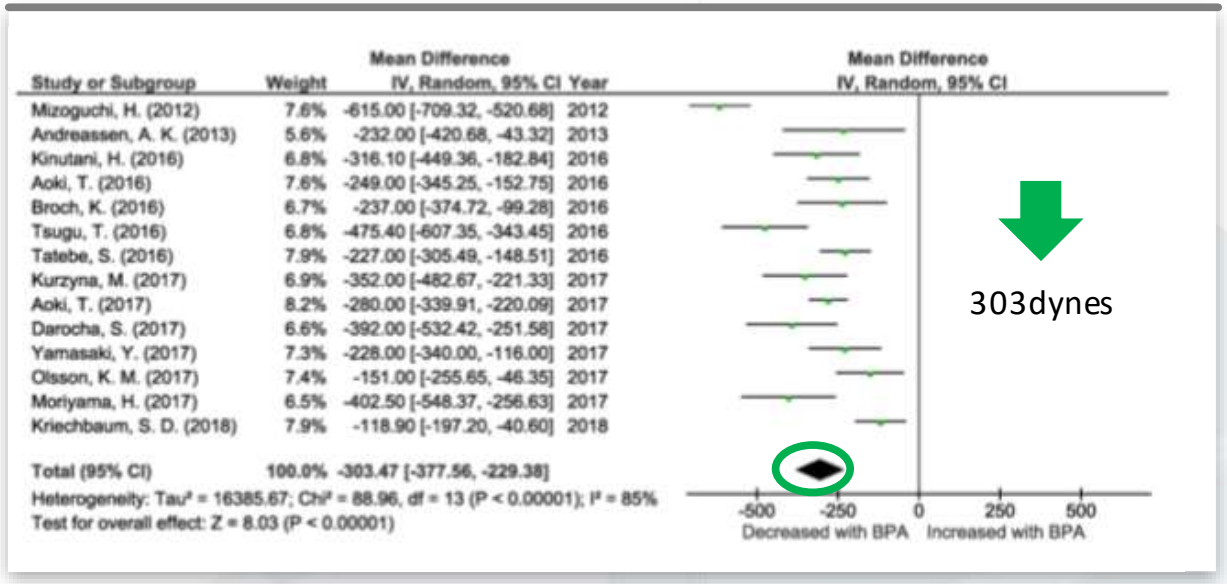
Simonneau G, et al. Eur Respir J. 2015 May;45(5):1293-302

Angioplastia pulmonar con balón

mPAP



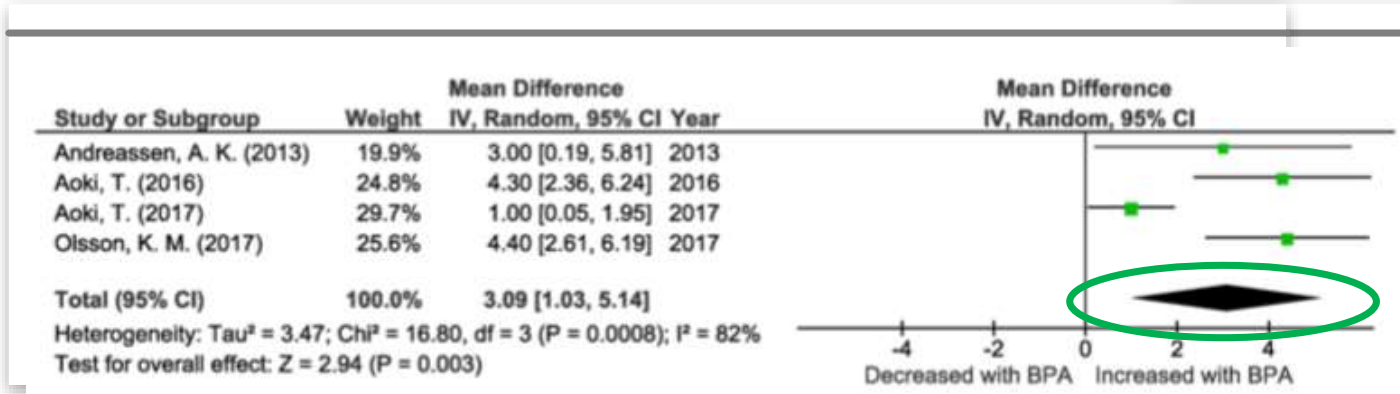
PVR



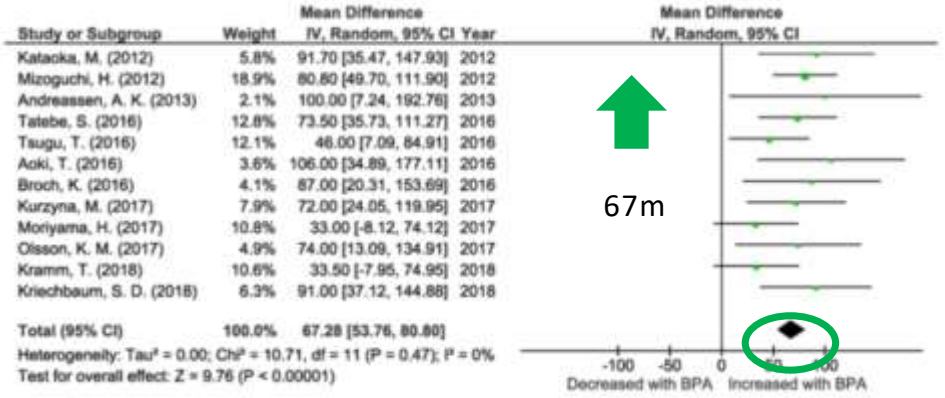
Khan MS et al. IKhan MS et al. IJCard 2019

Angioplastia pulmonar con balón

O_2 Sat

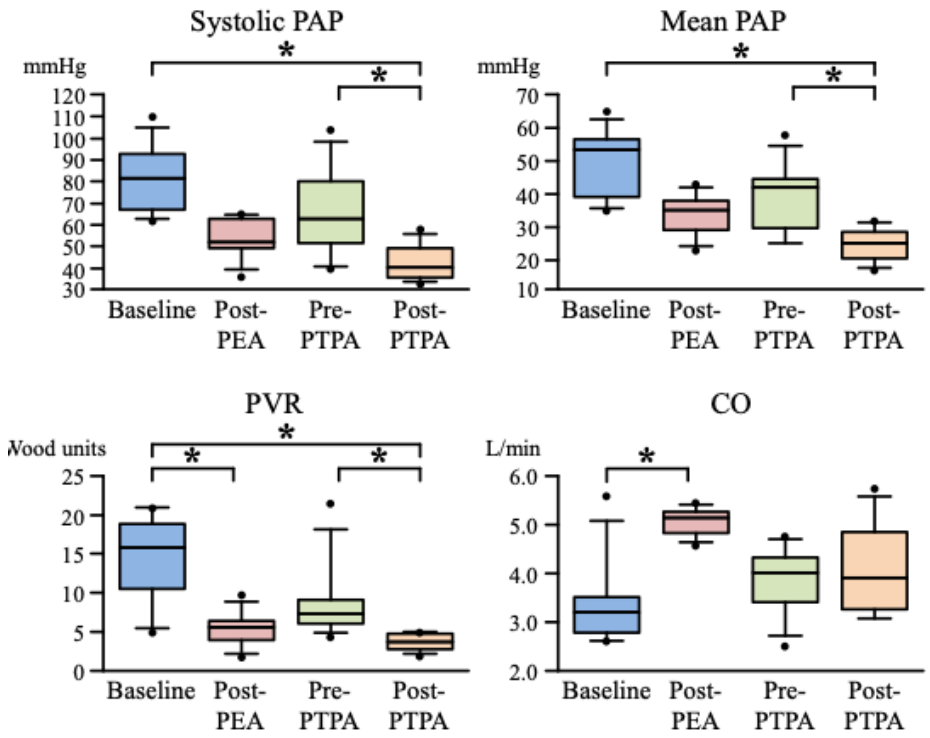


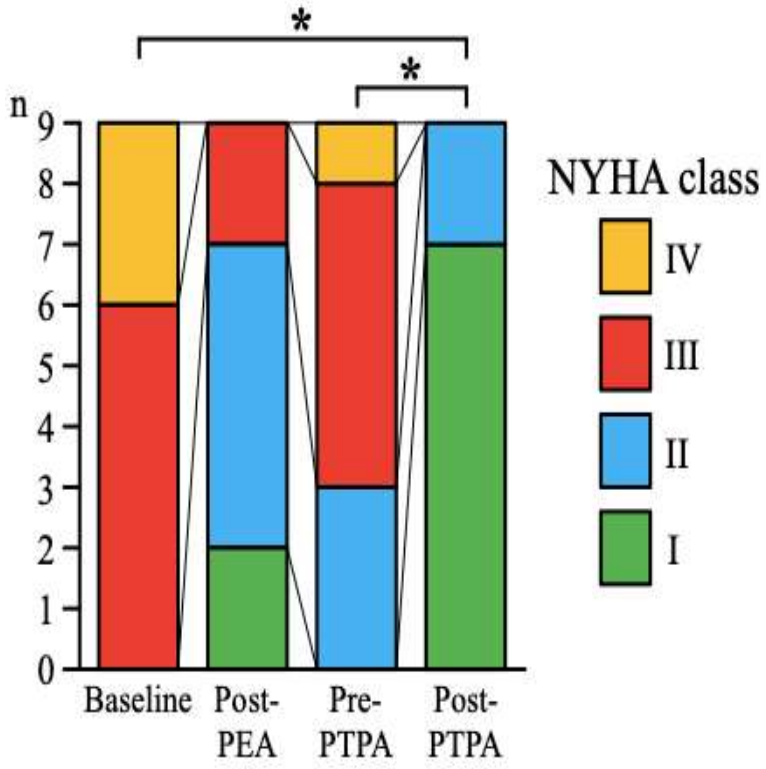
6-MWD



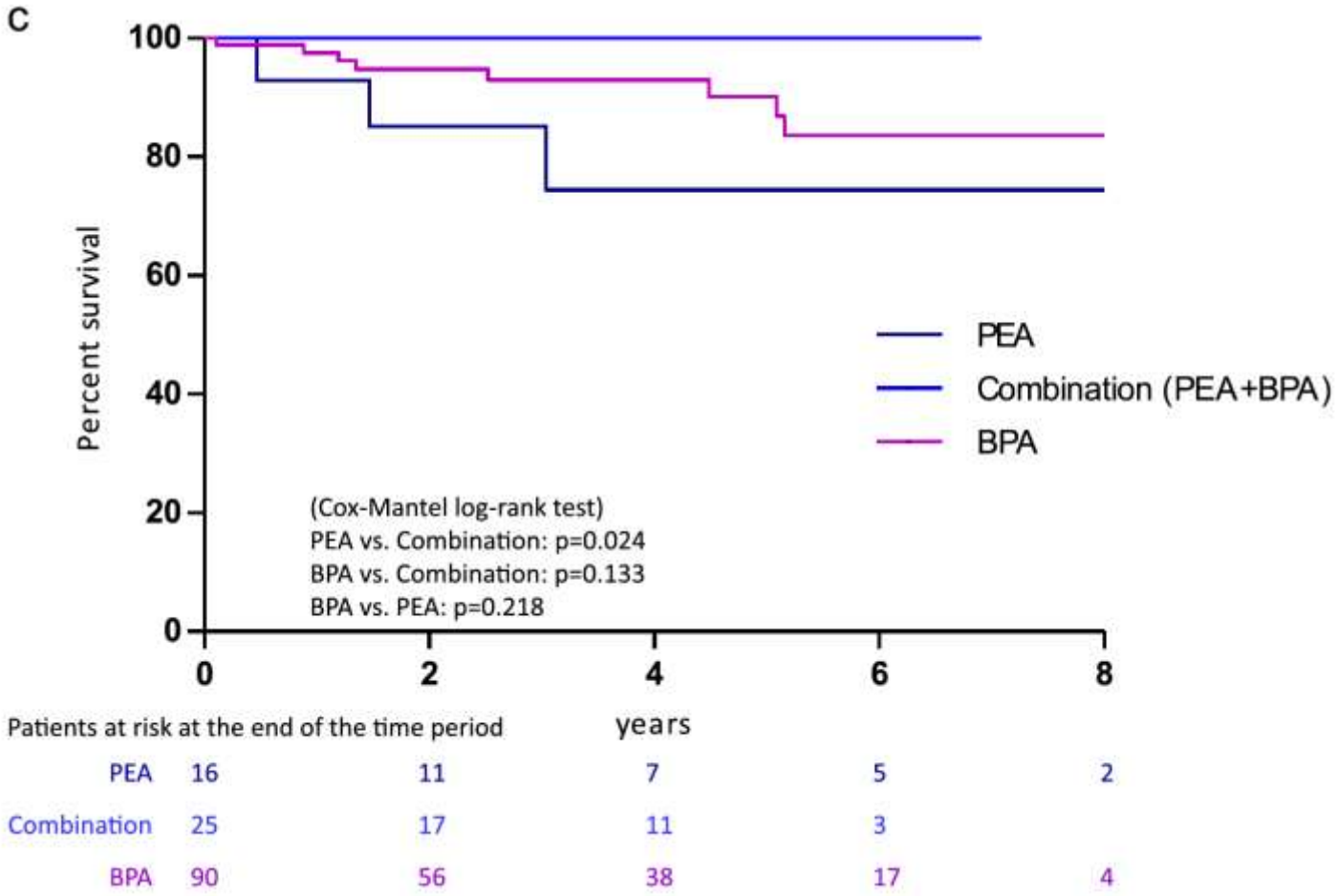
Khan MS et al. IKhan MS et al. IJCard 2019

Angioplastia pulmonar con balón Post PEA





Angioplastia pulmonar con balón Post PEA



Taniguchi Y et al. International Journal of Cardiology 326 (2021) 170–177

APB vs PEA

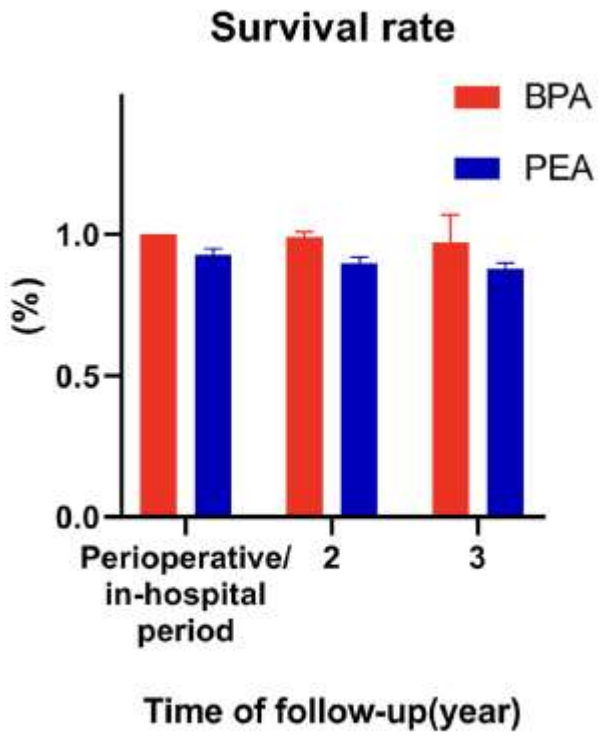


Fig. 4 The histogram of survival rate at different follow-up times after BPA and PEA

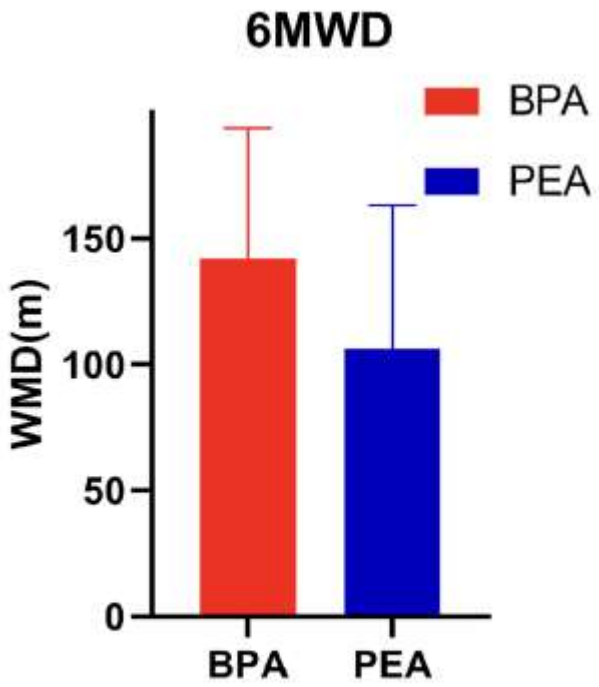


Fig. 5 The histogram of 6MWD at 1–6 months after BPA and PEA

Zhang L et al. Heart Failure Reviews volume 26, pages897–917 (2021)

¿Cuál es el último recurso?

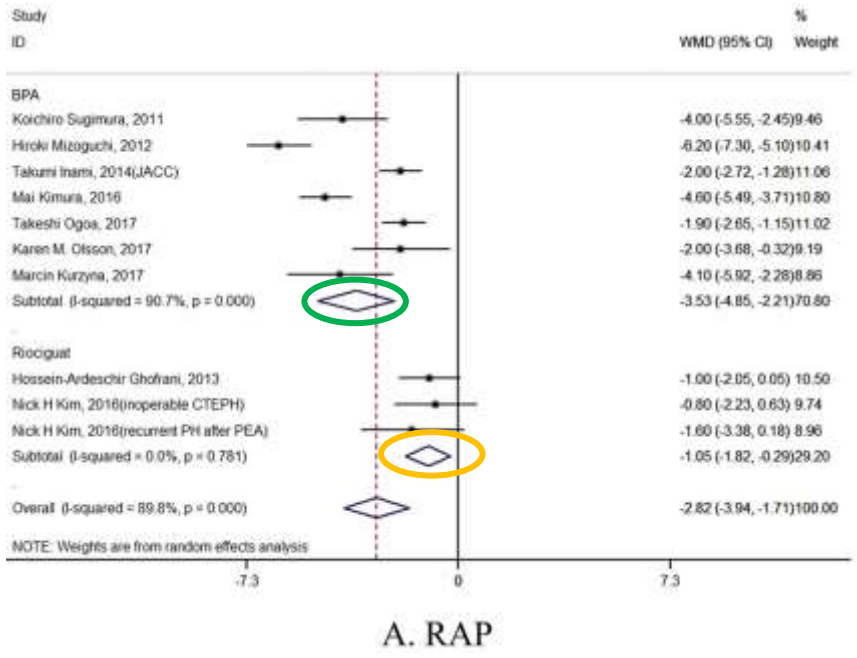
¿Cuál es el último recurso?

Endarterectomia quirúrgica

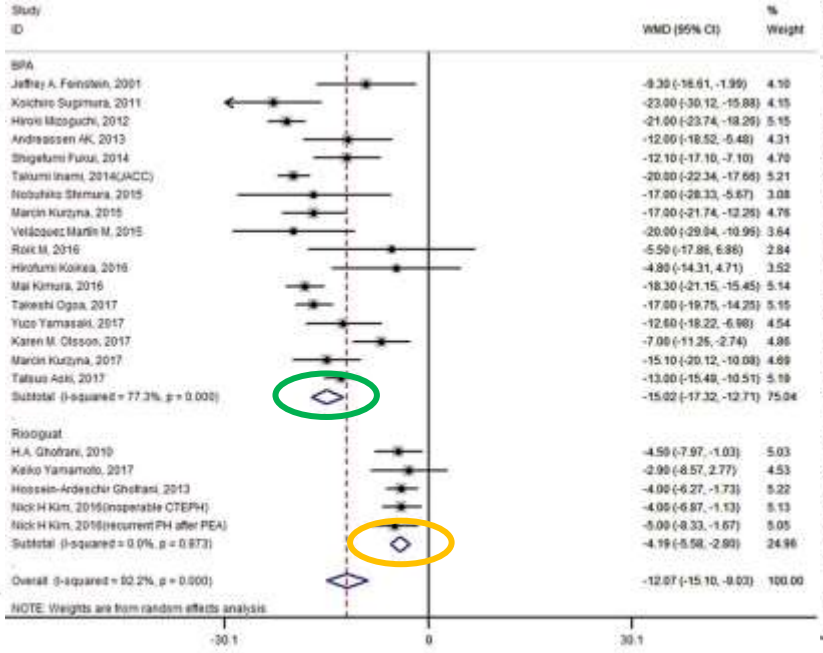
+

Angioplastia Pulmonar con balón

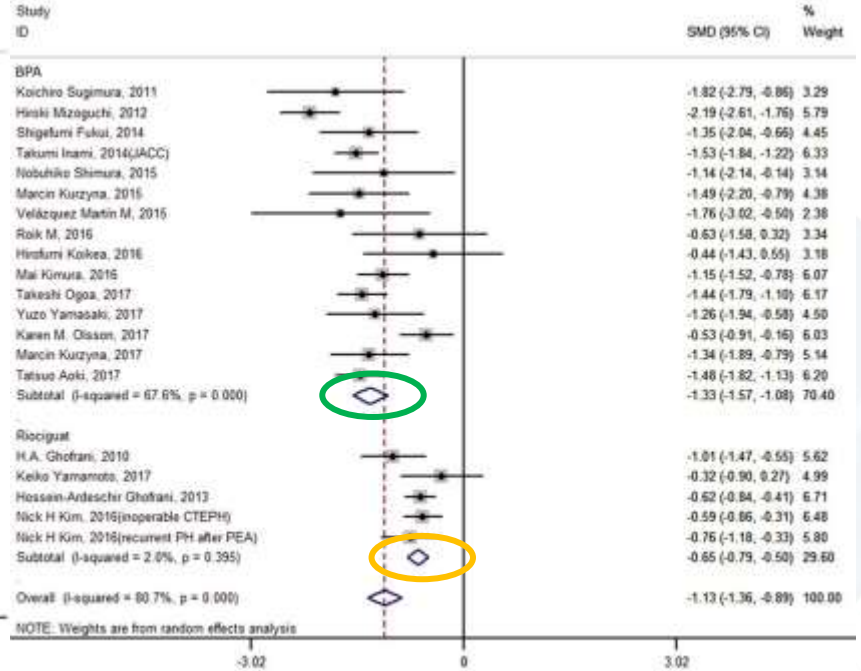
Tratamiento Farmacológico VS APB



A. RAP



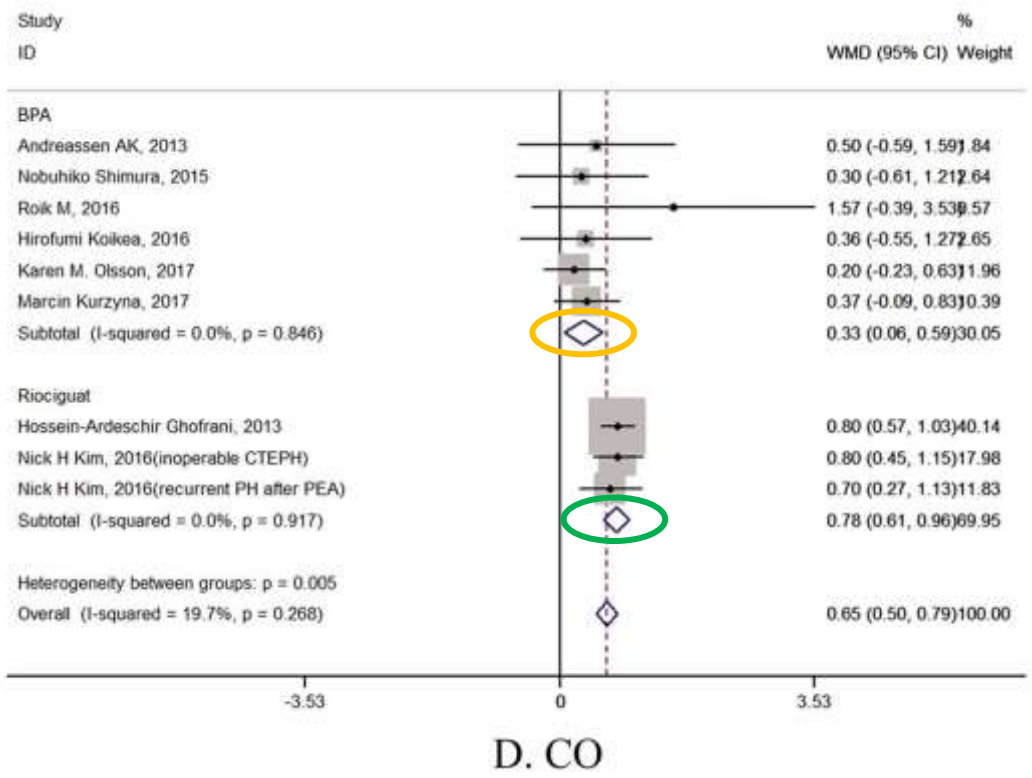
B. mPAP



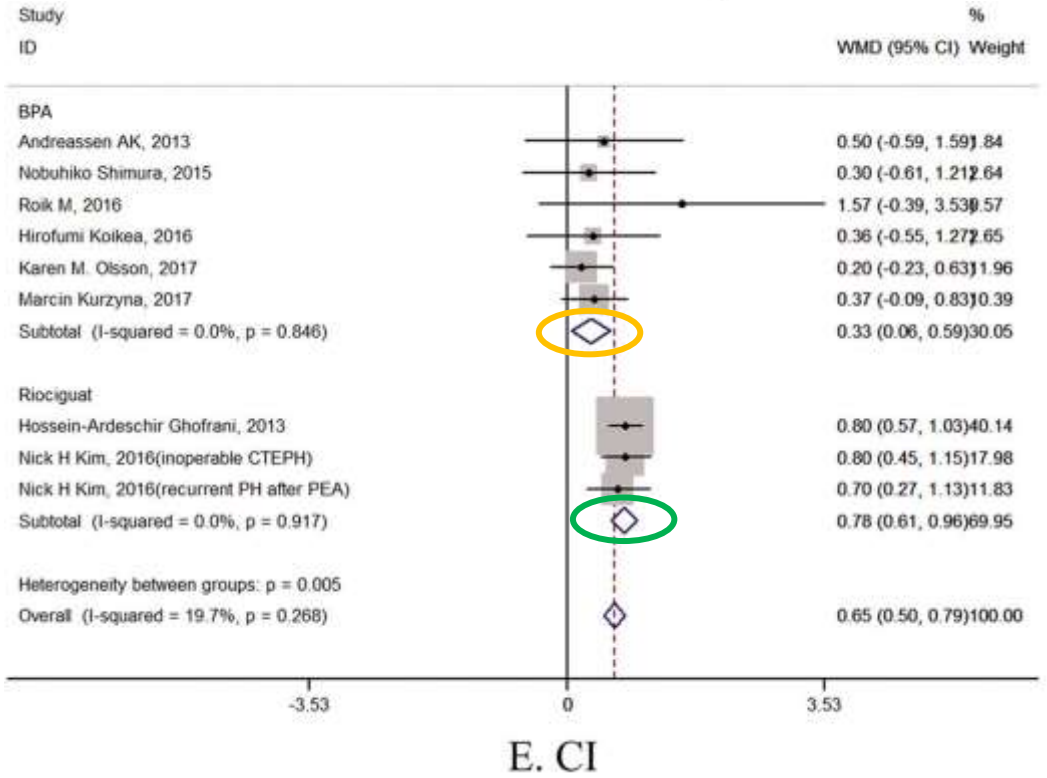
C. PVR

Wang W, et al. Clin Cardiol. 2019 Aug;42(8):741-752

Tratamiento Farmacológico VS APB



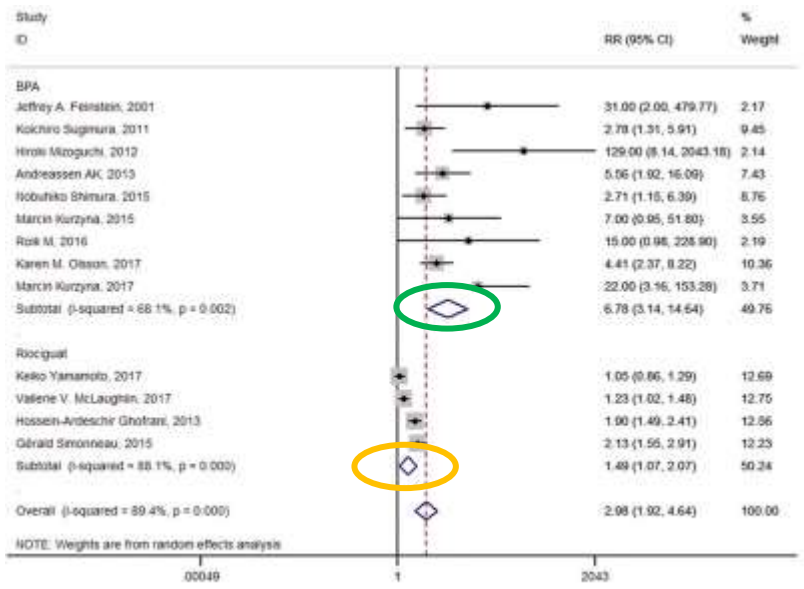
D. CO



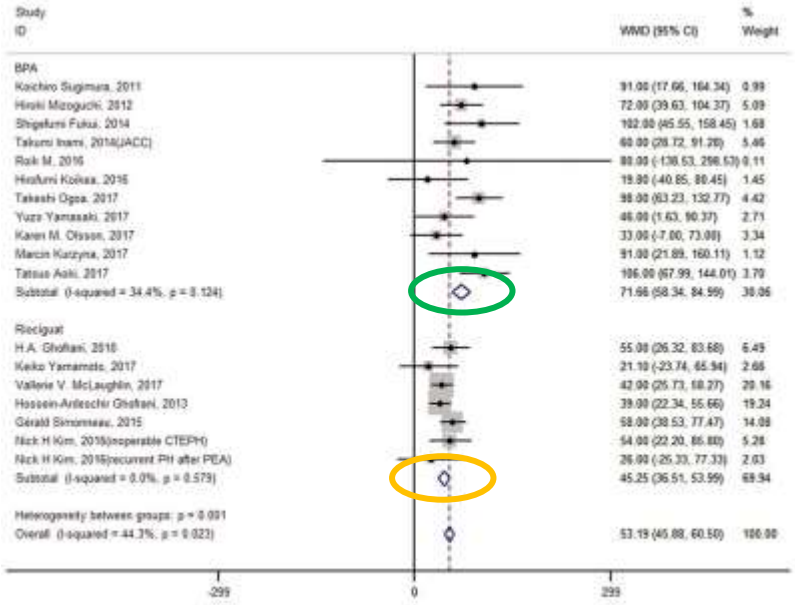
E. CI

Wang W, et al. Clin Cardiol. 2019 Aug;42(8):741-752

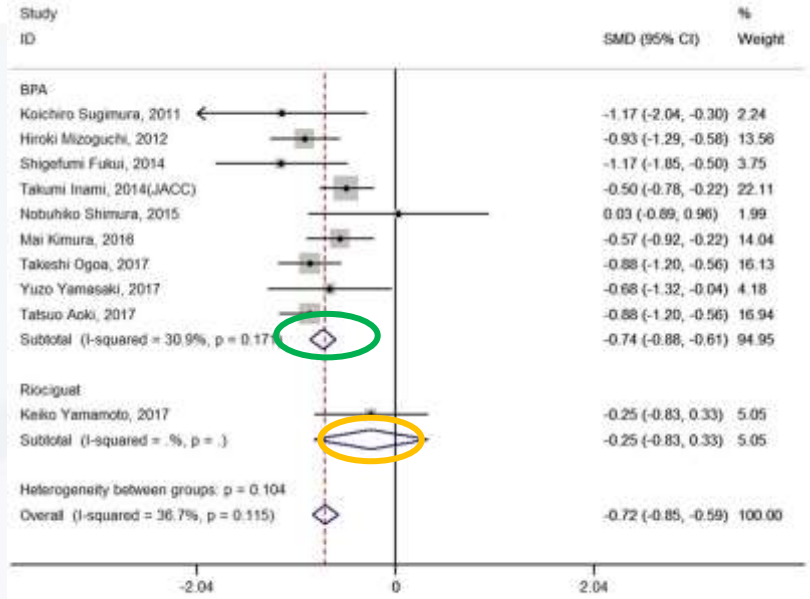
Tratamiento Farmacológico VS APB



A. NYHA functional class



B. 6MWD

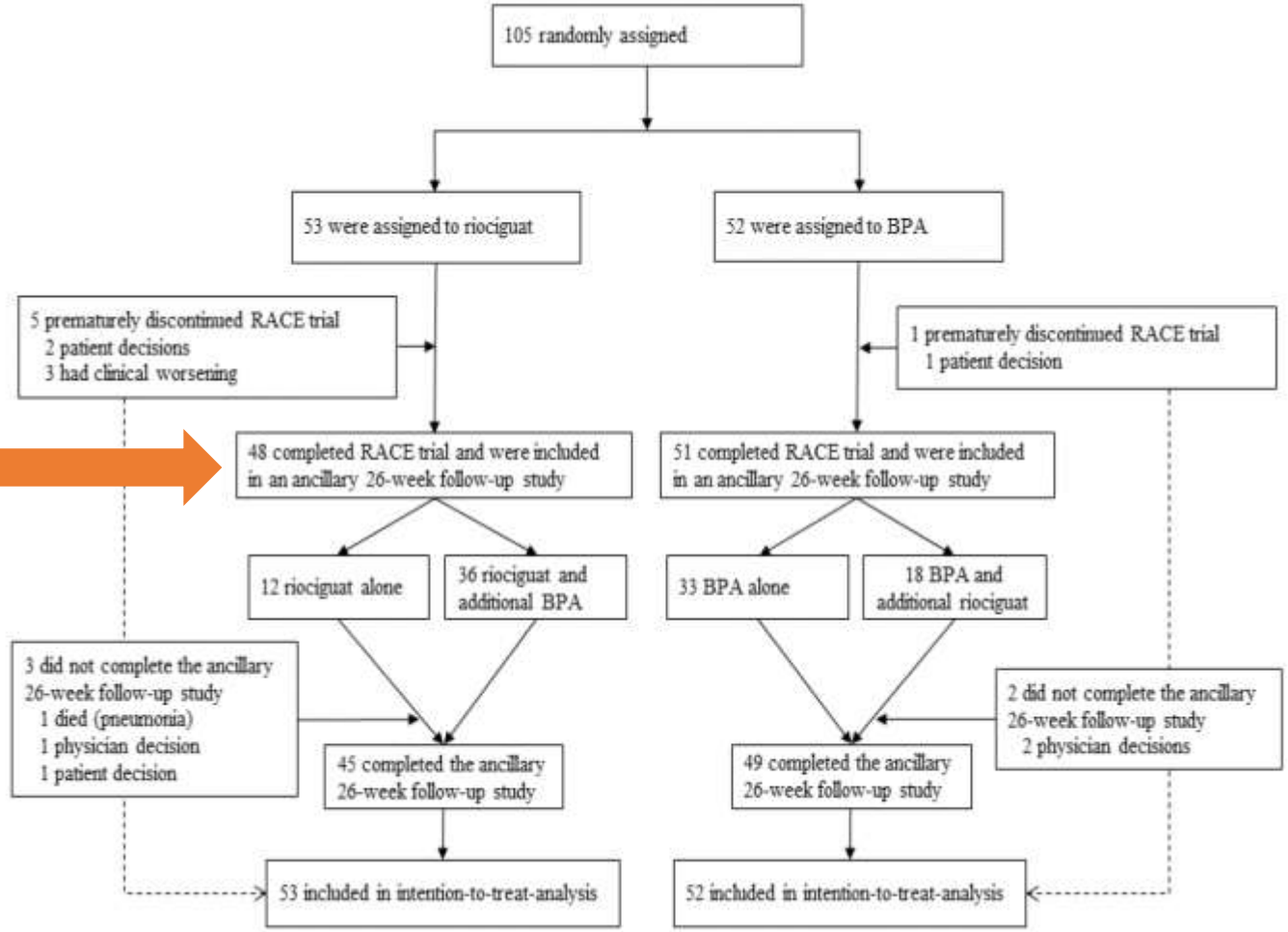


C. BNP

Wang W, et al. Clin Cardiol. 2019 Aug;42(8):741-752

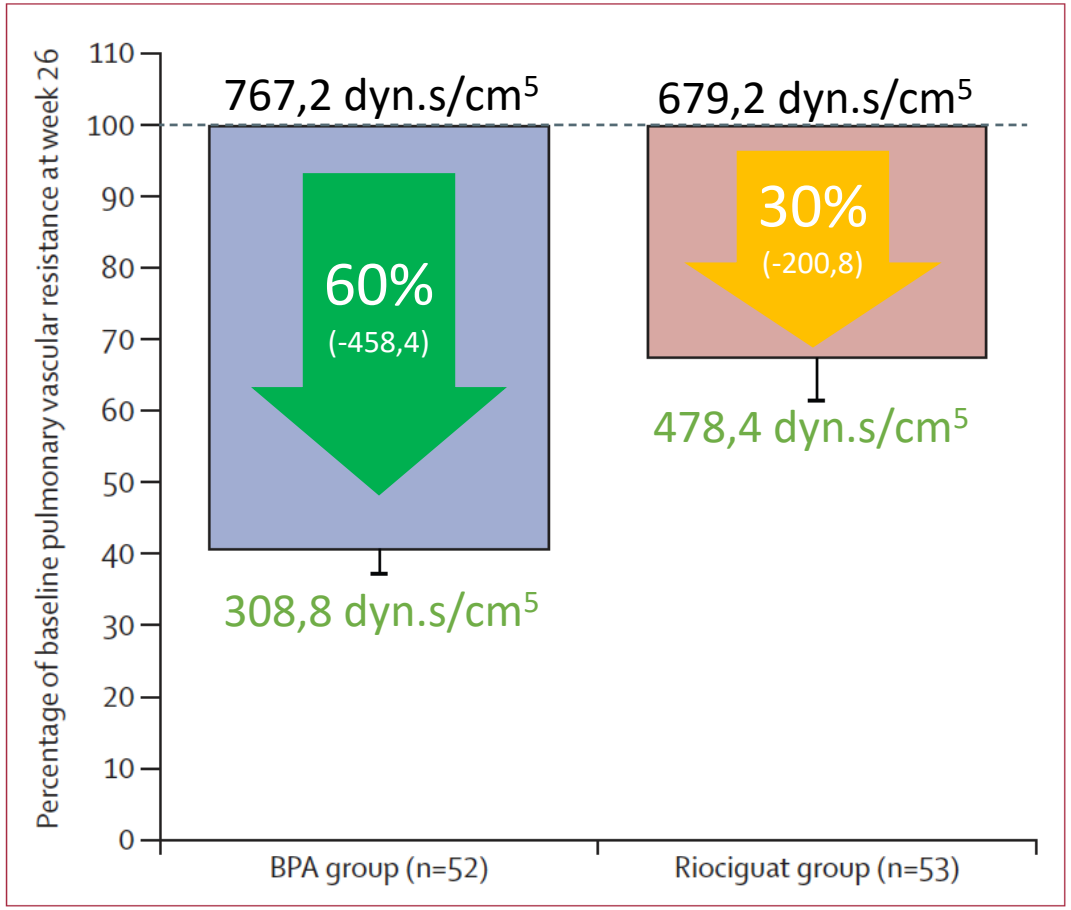
Estudio RACE

WHO FC =>II
RVP >320 dyn.s/cm^5



Jais X, Brenot P, et al. Lancet Respir Med. 2022 Aug 1;S2213-2600(22)00214-4

Estudio RACE – endpoint primario



Jais X, Brenot P, et al. Lancet Respir Med. 2022 Aug 1;S2213-2600(22)00214-4

Estudio RACE – endpoint secundario

	BPA group			Riociguat group			Treatment effect (95% CI)	p value
	Number of patients	Baseline	Change	Number of patients	Baseline	Change		
Secondary endpoints								
6-min walk distance, m	52	379·9 (103·3)	50·3 (8·64)	52	389·7 (123·6)	44·1 (8·64)	6·14‡ (–18·12 to 30·40)	0·62
Borg dyspnoea score	52	3·7 (1·62)	–1·18 (0·26)	50	3·2 (1·65)	0·52 (0·27)	–1·70‡ (–2·44 to –0·95)	<0·0001
WHO functional class	52	12 (23%) in cl 38 (73%) in clas 2 (4%) in class IV	46 (88%) improved; 6 (12%) unchanged; 0 worsened	53	10 (19%) i 43 (81%) in in class IV	26 (49%) improved; 26 (49%) unchanged; 1 (2%) worsened	9·45 (3·2 to 27·2)	<0·0001
NT-proBNP, pg/mL	44	1886·7 (2369·7	–1534·2 (2314·4)	45	1455·3 (170	–422·2 (1429·0)	..	..
Geometric mean (95% CI)*, % of baseline	..	..	21·1% (16·0–28·0)	..	..	57·4% (43·5–75·6)	0·37† (0·25 to 0·55)	<0·0001
Clinical worsening	52	..	0	53	..	3 (6%)	..	0·072¶

88%
81%
49%
29%

Data are mean (SD) or n (%), unless stated otherwise. BPA=balloon pulmonary angioplasty. NT-proBNP=N-terminal pro-brain natriuretic peptide. *For pulmonary vascular resistance and NT-proBNP concentration, changes are expressed as a percentage of the baseline value (geometric mean [95% CI]). † The treatment effect expressed as the ratio between the geometric mean of BPA over the geometric mean of riociguat was calculated by analysis of covariance of the ln-transformed week 26 values, including treatment and the ln-transformed baseline values as covariates. ‡The treatment effect expressed as the least-squares mean difference (BPA minus riociguat) was calculated by analysis of covariance for the change from baseline to week 26, including treatment and the baseline value as covariates. §The treatment effect expressed as the odds ratio at week 26 was calculated using a logistic regression, including treatment and WHO functional class at baseline as covariates. ¶p value calculated using the log-rank test.

Estudio RACE – Variables hemodinámicas

	BPA group			Riociguat group			Treatment effect (95% CI)	p value
	Number of patients	Baseline	Change	Number of patients	Baseline	Change		
Haemodynamic variables								
Mean right atrial pressure, mm Hg	51	8·7 (3·9)	−3·3 (4·1)	49	8 (3·4)	−1 (4·1)	−1·85‡ (−3·12 to −0·58)	0·0048
Mean pulmonary artery pressure, mm Hg	51	46·5 (8·4)	−18·7 (9·3)	49	44·7 (10·0)	−5·1 (7·9)	−13·03‡ (−16·19 to −9·86)	<0·0001
Mean pulmonary artery wedge pressure, mm Hg	51	8·7 (2·9)	0·8 (3·4)	49	9·8 (3·0)	0·2 (3·4)	−0·049‡ (−1·26 to 1·16)	0·94
Cardiac output, L/min	51	4·2 (0·9)	0·7 (0·9)	49	4·4 (1·2)	1·1 (0·9)	−0·39‡ (−0·75 to −0·03)	0·033

40%

11%

Data are mean (SD) or n (%), unless stated otherwise. BPA=balloon pulmonary angioplasty. NT-proBNP=N-terminal pro-brain natriuretic peptide. *For pulmonary vascular resistance and NT-proBNP concentration, changes are expressed as a percentage of the baseline value (geometric mean [95% CI]). † The treatment effect expressed as the ratio between the geometric mean of BPA over the geometric mean of riociguat was calculated by analysis of covariance of the ln-transformed week 26 values, including treatment and the ln-transformed baseline values as covariates. ‡The treatment effect expressed as the least-squares mean difference (BPA minus riociguat) was calculated by analysis of covariance for the change from baseline to week 26, including treatment and the baseline value as covariates. §The treatment effect expressed as the odds ratio at week 26 was calculated using a logistic regression, including treatment and WHO functional class at baseline as covariates. ¶p value calculated using the log-rank test.

Table 2: Study endpoints

Estudio RACE – Información de seguridad

	BPA group (n=52)	Riociguat group (n=53)
Patients with ≥1 adverse event	33 (63%)	38 (72%)
Patients with ≥1 serious adverse event	26 (50%)	14 (26%)
Patients with ≥1 treatment-related serious adverse event	22 (42%)	5 (9%)
Most frequent adverse events (≥3 patients in either group)		
Gastro-oesophageal reflux	0	10 (19%)
Dizziness	1 (2%)	9 (17%)
Haemoptysis	8 (15%)	0
Headache	0	8 (15%)
Vomiting	0	8 (15%)
Cough	0	7 (13%)
Lung injury	8 (15%)	0
Peripheral oedema	4 (8%)	6 (11%)
Dyspepsia	0	6 (11%)
Nausea	0	5 (9%)
Diarrhoea	1 (2%)	5 (9%)
Chest pain	1 (2%)	5 (9%)
Palpitations	3 (6%)	1 (2%)
Epistaxis	2 (4%)	3 (6%)
Lower respiratory tract infection	3 (6%)	2 (4%)
Constipation	0	3 (6%)
Urinary tract infection	3 (6%)	0

Data are n (%). Individual patients could have more than one event. BPA=balloon pulmonary angioplasty.

Table 3: **Safety data**

APB

400 APB

33 eventos en 22 ptes

8%

Jais X, Brenot P, et al. Lancet Respir Med. 2022 Aug 1;S2213-2600(22)00214-4

¿Cuál es el último recurso?

¿Cuál es el último recurso?

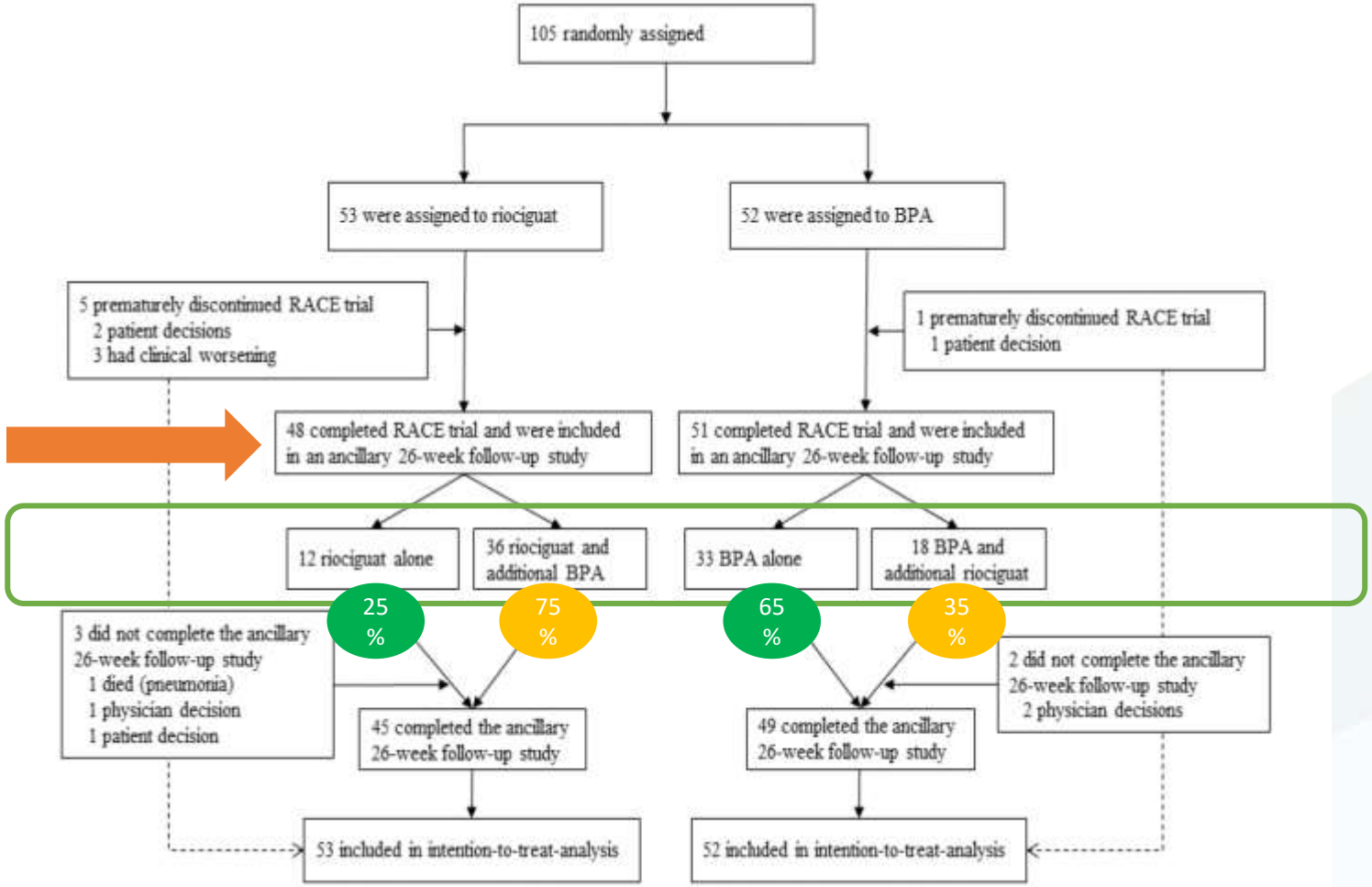
Tratamiento Farmacológico

+

Angioplastia Pulmonar con balón

Estudio RACE

WHO FC =>II
RVP >320 dyn.s/cm^5



Jais X, Brenot P, et al. Lancet Respir Med. 2022 Aug 1;S2213-2600(22)00214-4

Estudio RACE – 52 semanas

APB + Riociguat

Endpoints	n	Cambios
RVP en reposo (dyn.s/cm^5)	52	↓ 35%
TC6M (m)	52	↑ 45.9m
WHO FC	52	↓ 90%
NT-proBNP (pg/mL)	44	↓14.6%

Riociguat + APB

Endpoints	n	Cambios
RVP en reposo (dyn.s/cm^5)	53	↓ 38,6%
TC6M (m)	52	↑ 58,4m
WHO FC	53	↓ 66%
NT-proBNP (pg/mL)	45	↓19,1%

Los SAE relacionados a la APB fue significativamente menor en aquellos pacientes que recibieron tratamiento previo con Riociguat

Jais X, Brenot P, et al. Lancet Respir Med. 2022 Aug 1;S2213-2600(22)00214-4

Estudio RACE

APB → **↓ PMAP** → **↓ obstrucción macro-vascular**

Riociguat → **↑ Gasto Cardíaco** → **↑función VD ↓RVS**

¿Qué dicen las guías?

Recommendations	Class	Level
CTEPH (continued)		
PEA is recommended as the treatment of choice for patients with CTEPH and fibrotic obstructions within pulmonary arteries accessible by surgery	I	B
BPA is recommended in patients who are technically inoperable or have residual PH after PEA and distal obstructions amenable to BPA	I	B
Riociguat is recommended for symptomatic patients with inoperable CTEPH or persistent/recurrent PH after PEA	I	B
Long-term follow-up is recommended after PEA and BPA, as well as for patients with CTEPH established on medical therapy	I	C

Humbet M et al; European Heart Journal (2022) 00, 1–114

¿Qué dicen las guías?

	GRADE			
Recommendations	**Quality of evidence**	**Strength of recommendation**	**Class**	**Level**
In patients with CTEPH who are candidates for BPA, medical therapy should be considered prior to the intervention	Very low	Conditional	**IIa**	**B**

Humbet M et al; European Heart Journal (2022) 00, 1–114

Caso clínico – Resolución

Tromboendarterectomía Pulmonar

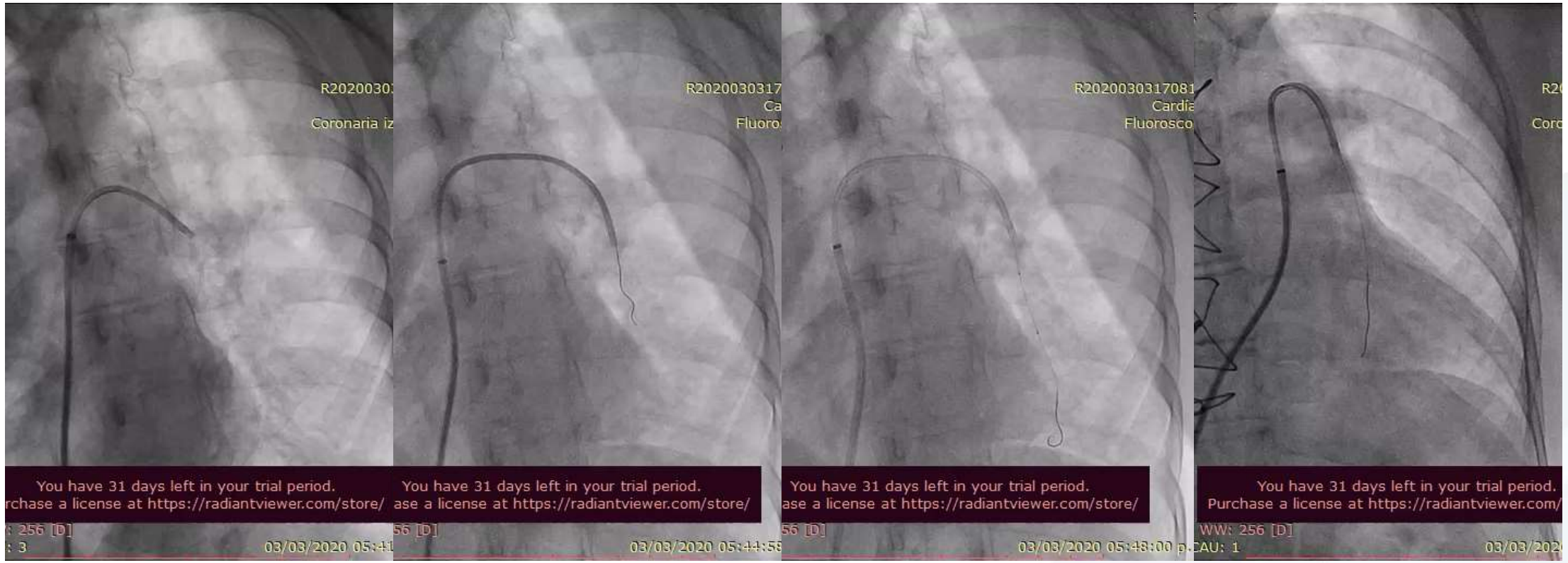
HP Persistente POP

Se decide APB

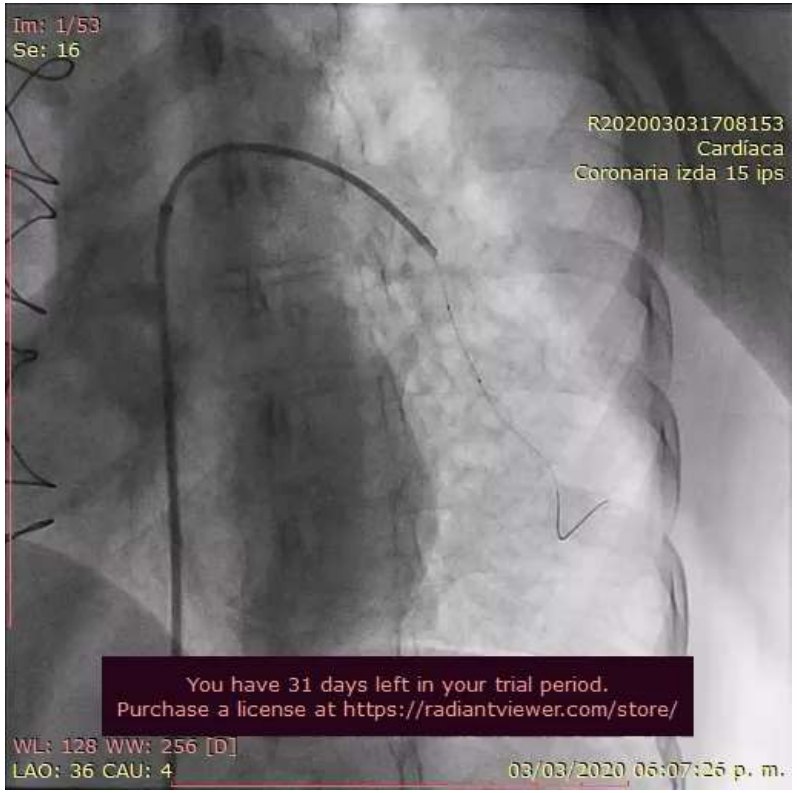
Pretratamiento con Riociguat

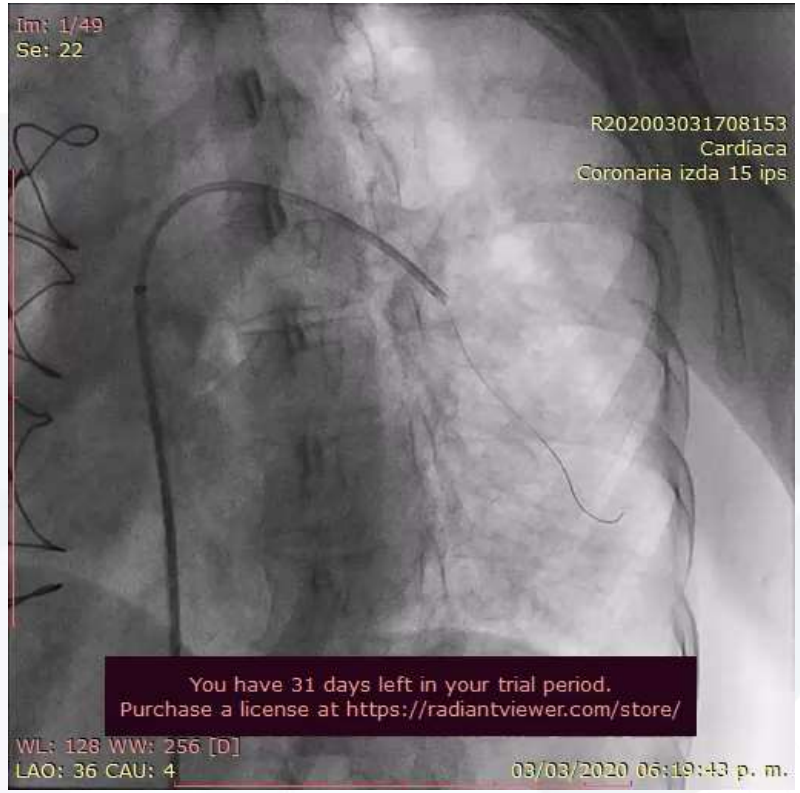
APB x2

Caso clínico – Resolución



Caso clínico – Resolución





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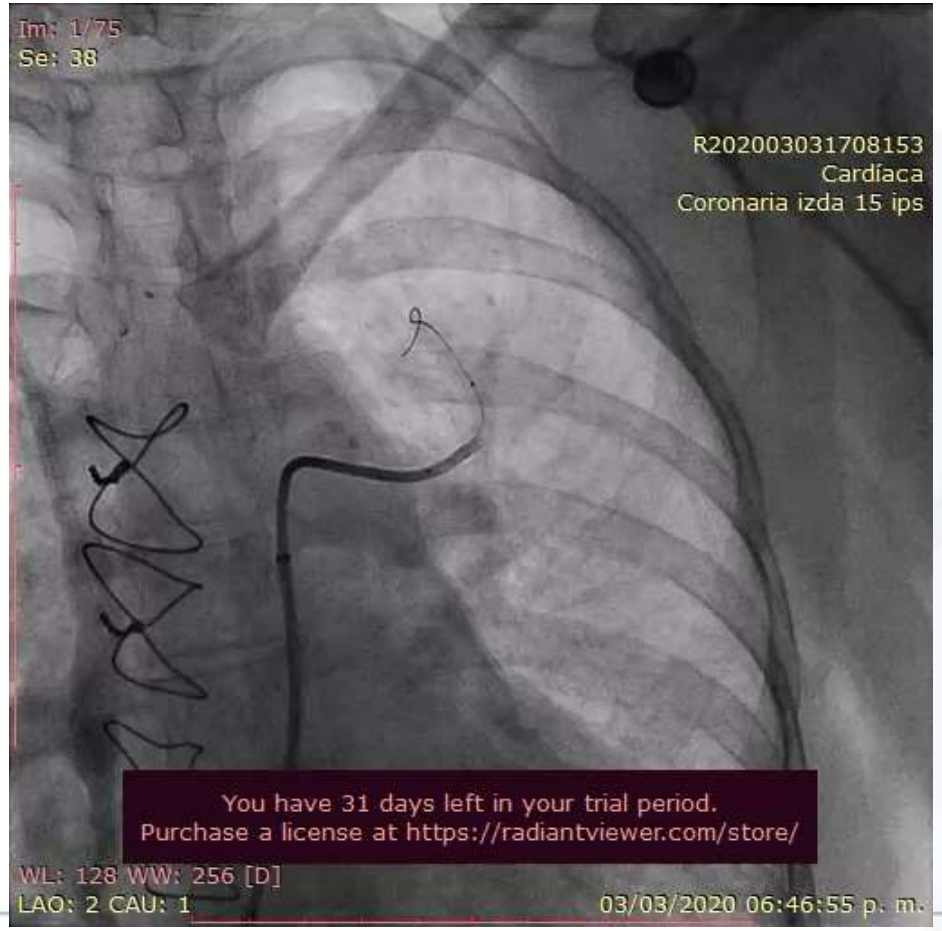

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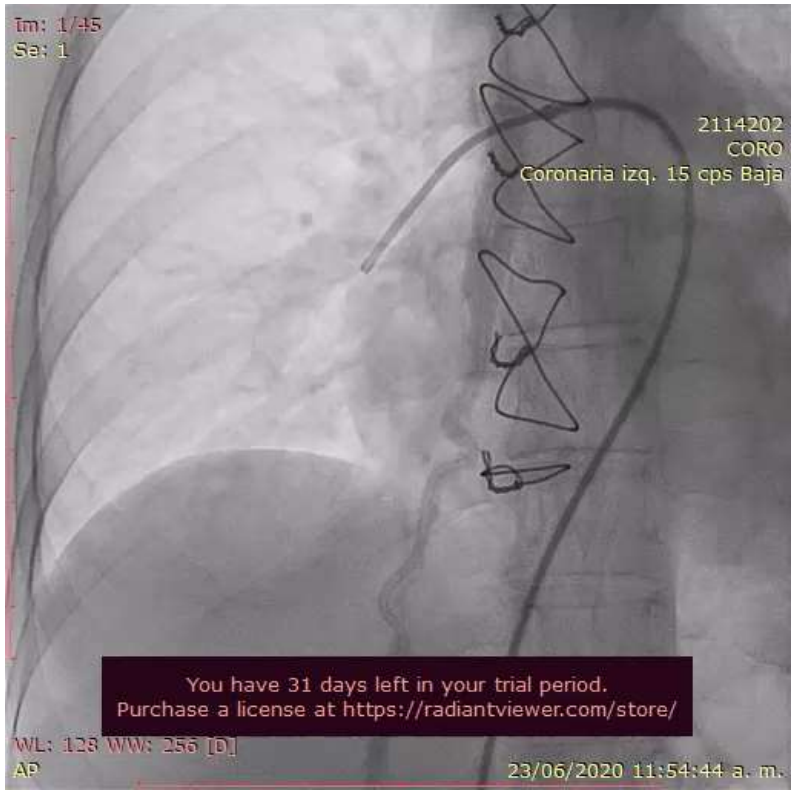

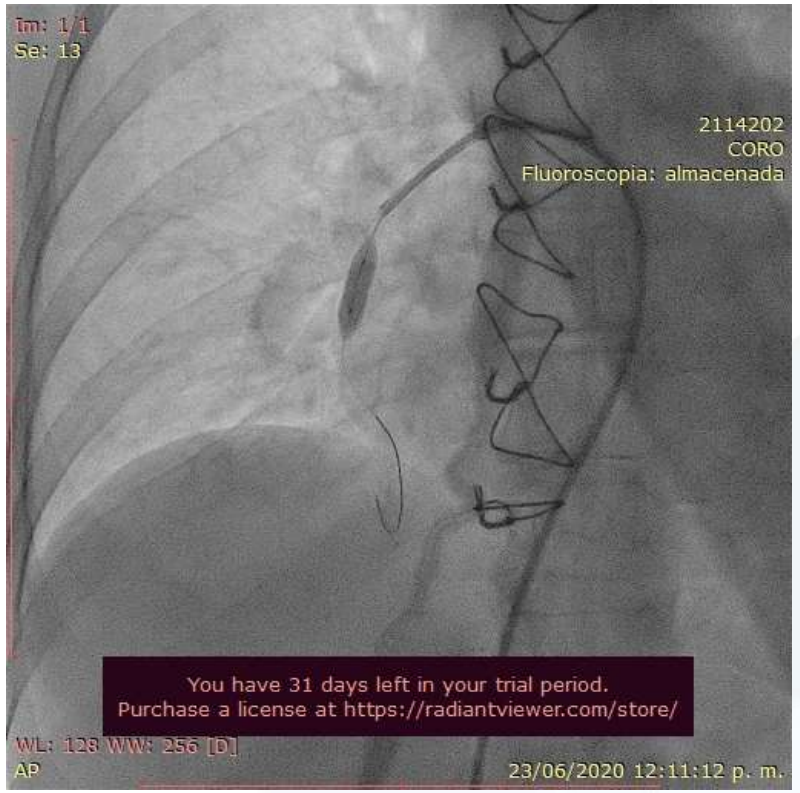

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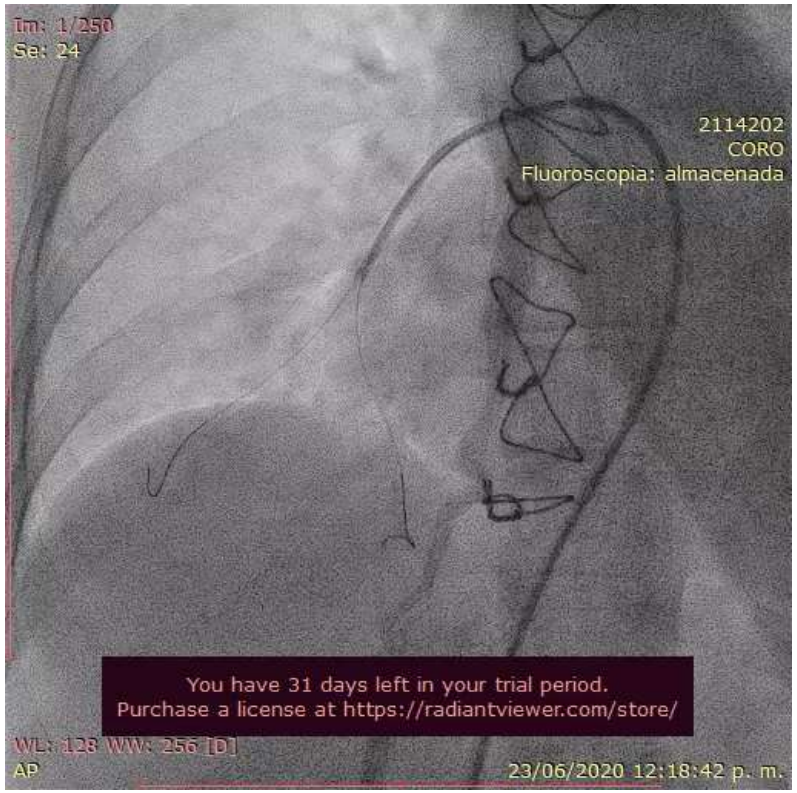

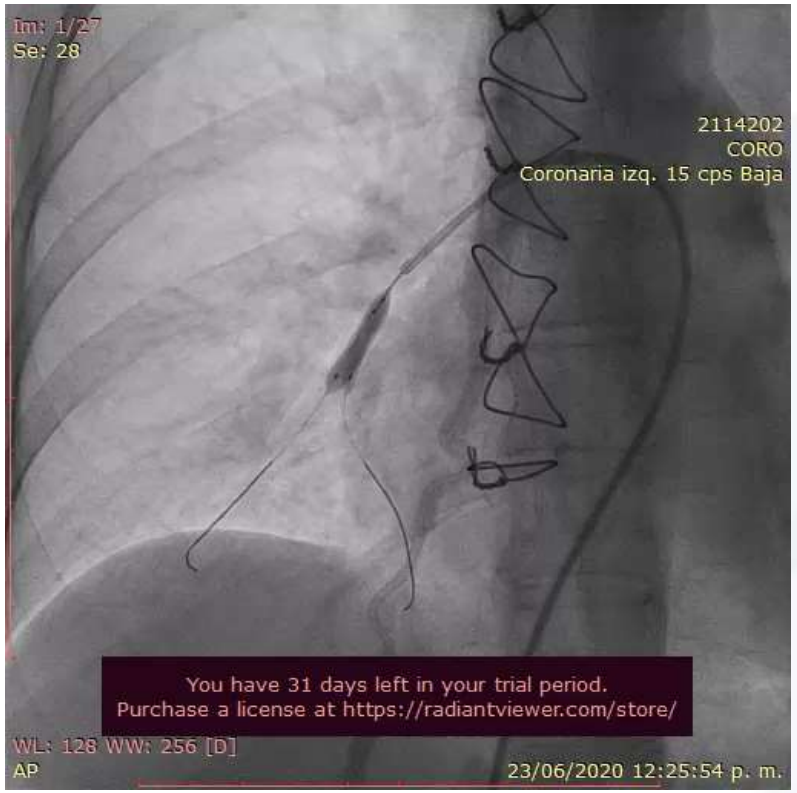

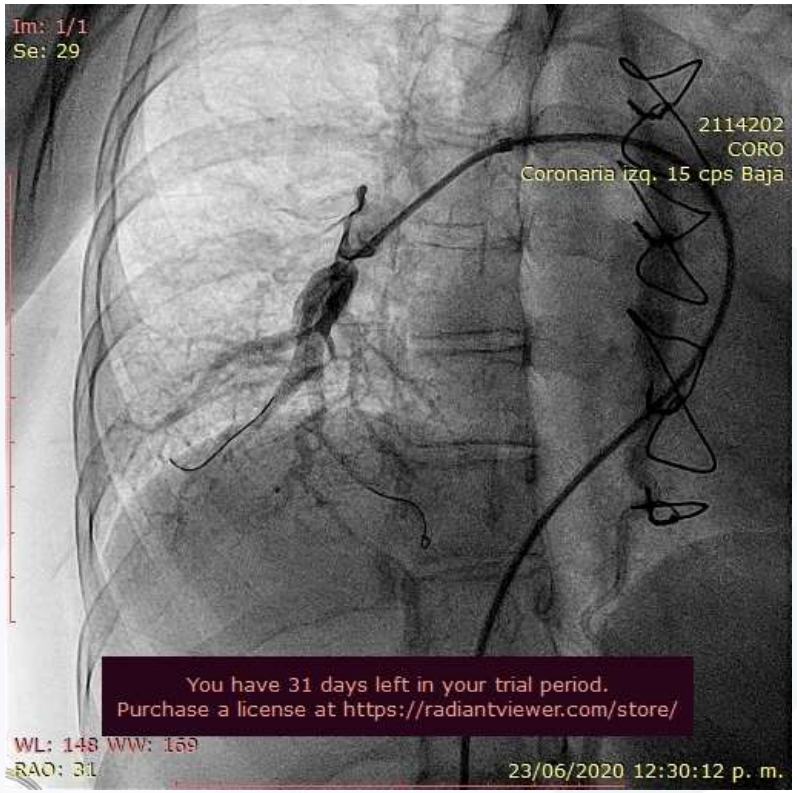

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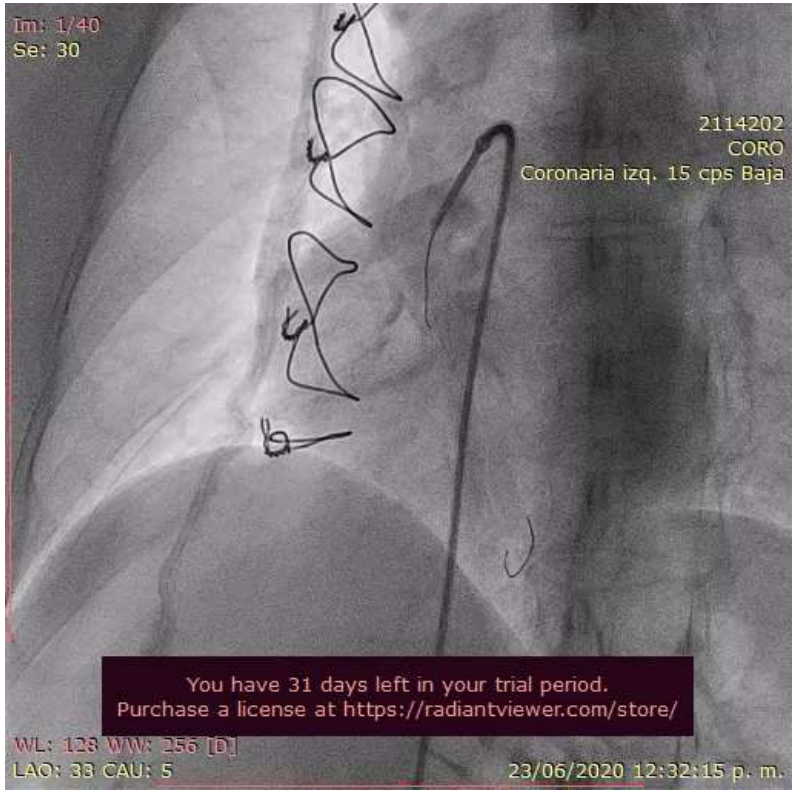
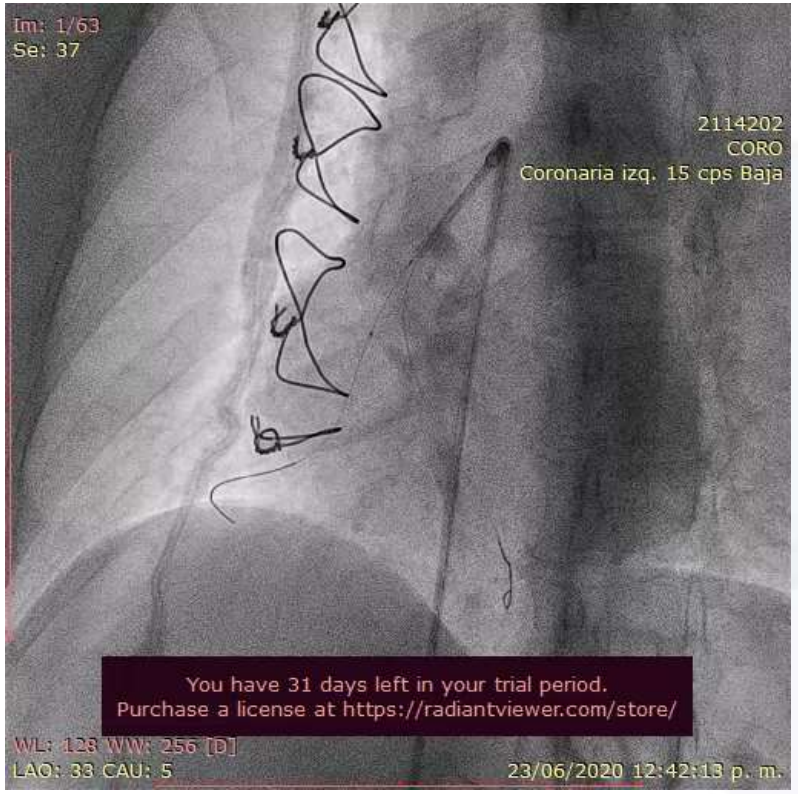
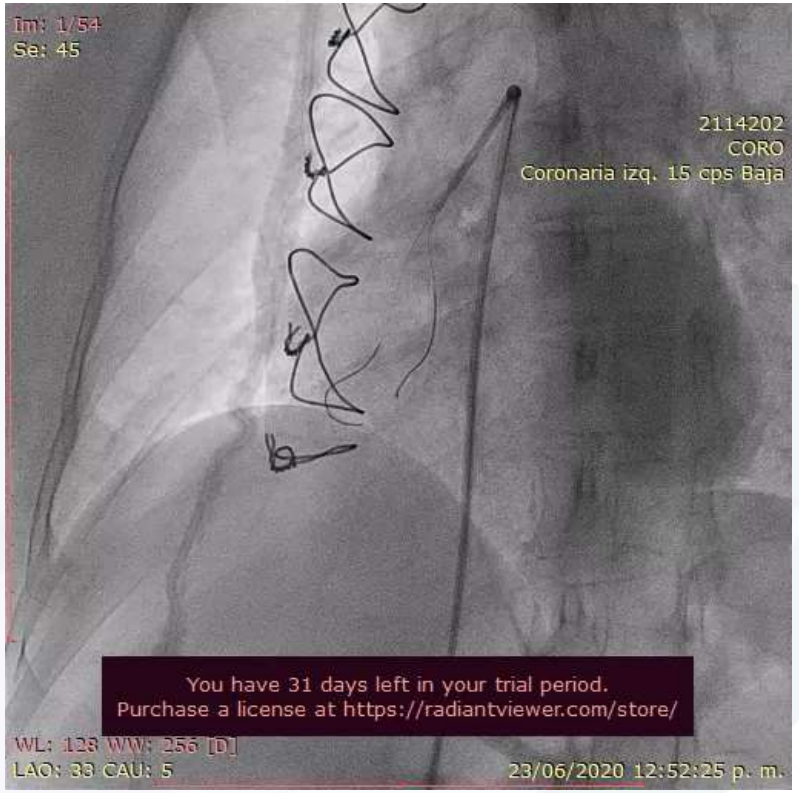
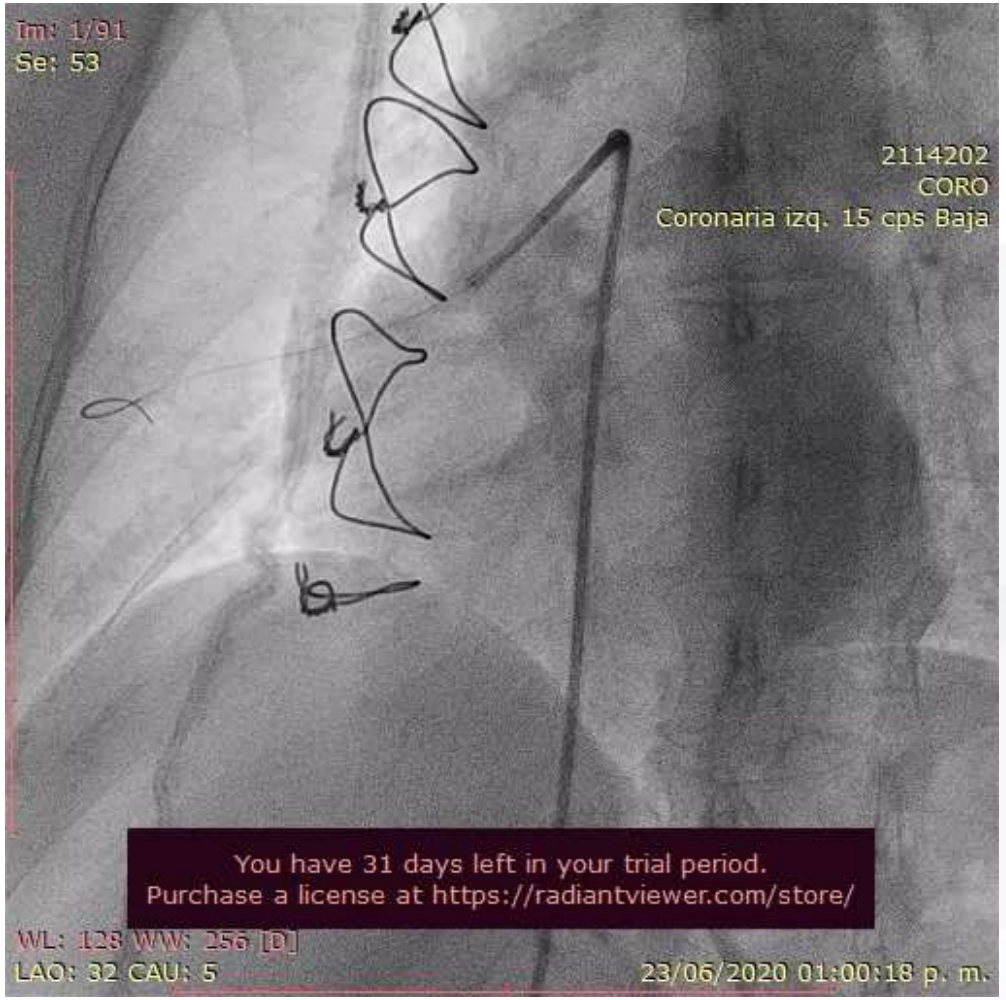






Caso clínico – Resolución



Caso clínico – Resolución

	25/03/19	23/12/19 PostCx	23/06/20 PostAPB I	04/05/2022 PostAPB II
Aurícula Derecha (mmHg)	5	5	2	4
Ventrículo Derecho (mmHg)	75/02 (6PFD)	60/01 (11 PFD)		32/01 (8 PFD)
Arteria Pulmonar (mmHg)	89/34 (52)	57/17 (34)	47/12 (28)	30/10 (17)
Wedge (mmHg)	6	6	4	5
Aorta (mmHg)	105/72 (88)	90/70 (76)	111/52 (72)	100/50 (67)
Volumen Minuto	2,98 L/min	2,50 L/min	2,98 L/min	3,10 L/min
Índice Cardiaco	2,19 L/min/m^2	1,86 L/min/m^2	2,20 L/min/m^2	2,27 L/min/m^2
RVS	2228 Dynas.seg.cm^{-5} 28 UW	2272 Dynas.seg.cm^{-5} 28 UW	1937 Dynas.seg.cm^{-5} 24 UW	1626 Dynas.seg.cm^{-5} 20 UW
RVP	1235 Dynas.seg.cm^{-5} 15 UW	768 Dynas.seg.cm^{-5} 10 UW	644 Dynas.seg.cm^{-5} 8 UW	30 Dynas.seg.cm^{-5} 4 UW
SVO_2	64%	47%	67%	66%

Nuestra experiencia – ICBA (2015-2020)

Variable	
Edad	56aa (30 – 84)
Sexo Femenino	92%
Inoperable	58%
HP Residual	42%

N: 27	Pre APB	Post APB	Delta	Valor P
PAP (media)	52mmHg (IQR 41,5 - 59,5)	39mmHg (IQR 34,2 - 48)	-25%	0,039
RVP	1034Dyne.s.cm-5 (IQR 736 - 1338)	500Dyne.s.cm-5 (IQR 349 - 583)	-51%	0,001
IC	2,09L/min/m2 (IQR 1,7 - 3,1)	2,8L/min/m2 (IQR 2,2 - 3,6)	+34%	0,146
CF I/II/III/IV	0%/17%/42%/42%	8%/75%/17%/0%		0.001

Spaletra,P et al. ICA 2021

Nuestra experiencia – ICBA (2015-2020)

50% pretratados con Riociguat	Delta Pre – Post APB (SIN pre tratamiento)	Delta Pre – Post APB (CON pre tratamiento)	Valor p
PAP (media)	-26%	-24%	NS
RVP	-49%	-55%	NS
IC	+34%	+34%	NS

Eventos Adversos	
Injuria vascular pulmonar mayor	0%
Injuria vascular pulmonar menor	4,7%
Edema de reperfusión menor	33%
Edema de reperfusión mayor	0%
Intubación	0%
Injuria renal aguda	0%
Mortalidad intrahospitalaria	0%

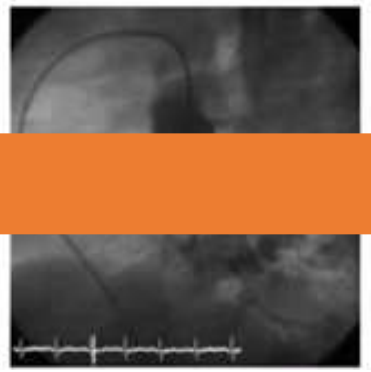
Spaletra,P et al. ICA 2021

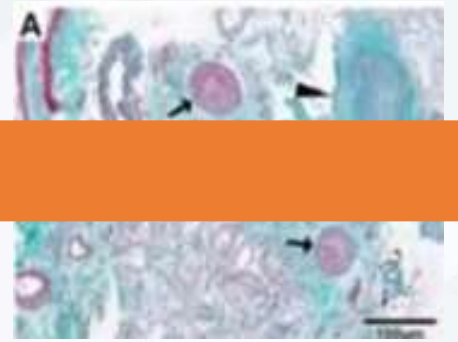
¿Cuál es el último recurso en la HPTEC?

Alteración fibrótica de arterias lobares o segmentarias proximales

Alteración fibrótica de arterias segmentarias distales o subsegmentarias

Afectación microvascular o vasculopatía pulmonar





TERAPIAS SINÉRGICAS O COADYUVANTES

Tromboendartercotmía Pulmonar

Angioplastia Pulmonar

Tratamiento Farmacológico

ICBA Instituto Cardiovascular

¡¡¡Muchas gracias!!!

@pablospaletra