

Radioterapia postoperatoria en el cáncer de próstata

III Congreso Nacional SEOQ

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Indice



1. **Guía Clínica ASTRO/AUA (ago/13).**
2. **Radioterapia de Rescate Precoz**
3. **¿Qué hacer hoy ante un pte. recién operado?**
4. **Ensayos clínicos**

- Int J Radiat Oncol Biol Phys 2013;86 (5): 822-828. Valicenti RK *et al*
- J Urol 2013; 190: 441-449. Thompson IA *et al*

www.auanet.org/education/guidelines/radiation-after-prostatectomy.cfm.

www.redjournal.org/webfiles/images/journals/rob/RAP%20Guideline.pdf.

1. Guía Clínica ASTRO/AUA



Guidelines

Adjuvant and Salvage Radiation Therapy After Prostatectomy: American Society for Radiation Oncology/American Urological Association Guidelines

Richard K. Valicenti, MD, MBA,* Ian Thompson Jr., MD,[†] Peter Albertsen, MD, MS,[‡] Brian J. Davis, MD, PhD,[§] S. Larry Goldenberg, MD,^{||} J. Stuart Wolf, MD,[¶] Oliver Sartor, MD,[#] Eric Klein, MD,^{**} Carol Hahn, MD,^{††} Jeff Michalski, MD, MBA,^{‡‡} Mack Roach III, MD,^{§§} and Martha M. Faraday, PhD^{|||}

Int J Radiat Oncol Biol Phys 2013;86 (5): 822-828. Valicenti RK *et al*

ASTRO:

Valicenti RK (UC-Davis)

Davis BJ (Mayo CI)

Michalsky JF (Whas U)

Roach M III (UCSF)

Hahn C (Duke U)

Adjuvant and Salvage Radiotherapy After Prostatectomy: AUA/ASTRO Guideline

Ian M. Thompson,* Richard K. Valicenti,* Peter Albertsen, Brian J. Davis, S. Larry Goldenberg, Carol Hahn, Eric Klein, Jeff Michalski, Mack Roach, Oliver Sartor, J. Stuart Wolf, Jr. and Martha M. Faraday

From the American Urological Association Education and Research, Inc., Luthicum, Maryland, and the American Society for Radiation Oncology, Fairfax, Virginia

J Urol 2013; 190: 441-449. Thompson IA *et al*

AUA:

Thompson IM (U Texas, St Ant)

Albertsen P (U conn)

Goldenberg SL (U Brit Col, Van , Can)

Klein E (clev CI)

Wolf JS (U Michi)

Sartor O (Tulane U, NwOr)

Faraday MM (Four Oaks)

1. Guía Clínica ASTRO/AUA

Standard: Directive statement that an action <u>should</u> (benefits outweigh risks/burdens) or <u>should not</u> (risks/burdens outweigh benefits) be taken based on Grade A (high quality; high certainty) <u>or B</u> (moderate quality; moderate certainty) evidence
Recommendation: Directive statement that an action <u>should</u> (benefits outweigh risks/burdens) or <u>should not</u> (risks/burdens outweigh benefits) be taken based on Grade C (low quality; low certainty) evidence
Option: Non-directive statement that <u>leaves the decision regarding an action up to the individual clinician and patient because the balance between benefits and risks/burdens appears equal or appears uncertain</u> based on Grade A (high quality; high certainty), B (moderate quality; moderate certainty), or C (low quality; low certainty) evidence
Clinical Principle: a statement about a component of clinical care that is <u>widely agreed upon by urologists or other clinicians</u> for which there may or may not be evidence in the medical literature
Expert Opinion: a statement, achieved by <u>consensus of the Panel</u> , that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence

Terminología AUA:

Grado (fuerza) de Evidencia:

A: E. Aleatorizados u observacionales excepcionalmente consistentes.

B: E. Aleatorizados con debilidades u observacionales de moderada consistencia.

C: E. Observacionales con pocos pacientes, cuyos datos podrían ser confusos.

Grado de certeza: Alto (A), Moderado (B) Bajo (C)

BJU Int 2009; 104: 294- Faraday *et al*

1. Guía Clínica ASTRO/AUA

294 Peer-reviewed estudios

Pub-Med, Embase y Cochrane desde 01.01.90 al 15.12.12

Manuscrito mandado a 75 reviewers de los cuales 44 comentaron

Aprobado finalmente por el Board of Directors de ASTRO y de AUA

Marco clínico para orientar sobre el uso de la RT postoperatoria

1. Guía Clínica ASTRO/AUA. Directrices (1)

1. **CLINICAL PRINCIPLE.** Patients who are being considered for management of localized prostate cancer with radical prostatectomy should be informed of the potential for adverse pathologic findings that portend a higher risk of cancer recurrence and that these findings may suggest a benefit of additional therapy after surgery.

	Overview	Risk factors	%bNED-10 y
8 centers	1983-2000	+ margins	36
<i>Karakiewicz</i>	Med fu 25 mo	ECE, +/- margins	25/46
<i>Urol 2005</i>	bNED 61% at 10 y	SVI, +/- margins	12/20
<i>N=5831</i>	0% adj RT	LNI, +/- margins	14/8
Wash U	1983-2003	Stage cT3	15
<i>Roehl</i>	Med fu 65 mo	Gleason score ≥8	32
<i>J Urol 2004</i>	bNED 68% at 10 y	ECE, +/- margins	53/62
<i>n=3478</i>	6% adj RT	SVI	26
		LN	12
Baylor	1983-1998	+margins	36
<i>Hull</i>	Med fu 47 mo	ECE alone	71
<i>J Urol 2002</i>	bNED 75% at 10 y	SVI	37
<i>n=1000</i>	0% adj treatment	LN	7
U Chicago	1994-2004	+/- margins	60/90
<i>Orvieto</i>	Mean fu 76 mo	SVI	~50
<i>BJU 2006</i>	bNED 86% at 10 y		
<i>n=996</i>	0% adj treatment		

(≤50% highlighted)

SVI, EPE
Mg+



pT3 y Mg+

1. Guía Clínica ASTRO/AUA. Directrices (1)

Table 8: 15-Year Biochemical Recurrence-Free Survival (%)
in Men Treated with Radical Prostatectomy in the PSA era (adapted from Mullins 2012)

Pathology Finding	Pathological Gleason Score		
	3 + 3	3 + 4	≥ 4 + 3
Organ-confined	99	86	79
No EPE; Margin +	94	75	67
EPE; Margin -	89	72	41
EPE; Margin +	75	45	27 (at 14 years)
SVI	39	39	15

Table 9: 15-Year Metastatic Recurrence-Free Survival (%)
in Men Treated with Radical Prostatectomy in the PSA era (adapted from Mullins 2012)

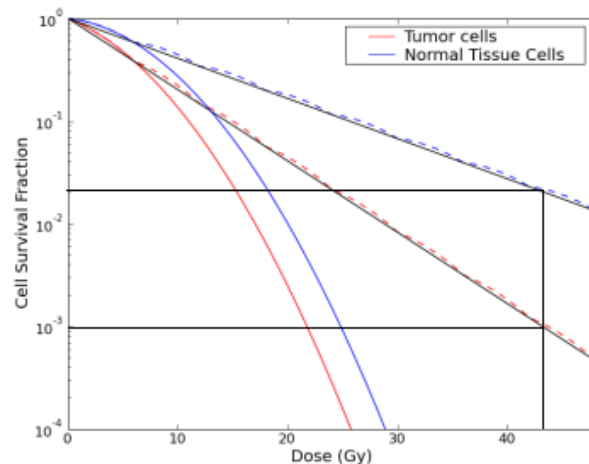
Pathology Finding	Pathological Gleason Score		
	3 + 3	3 + 4	≥ 4 + 3
Organ-confined	100	98	92
No EPE; Margin +	100	100	50
EPE; Margin -	100	97	75
EPE; Margin +	100	88	73
SVI	86	93	38

EPE – extraprostatic extension; SVI – seminal vesicle invasion

J Urol 2012; 188(6): 2219-24. Mullins JK *et al.* -4400 PRR y MdSg **10 a.** (h 29 a)-

1. Guía Clínica ASTRO/AUA. Directrices (2)

2. **CLINICAL PRINCIPLE.** Patients with adverse pathologic findings including seminal vesicle invasion, positive surgical margins, and extraprostatic extension **should be informed that adjuvant radiotherapy, compared to radical prostatectomy only, reduces the risk of biochemical (PSA) recurrence, local recurrence, and clinical progression of cancer.** They should also be informed that the impact of adjuvant radiotherapy **on subsequent metastases and overall survival is less clear,** one of two randomized controlled trials that addressed these outcomes indicated a benefit but the other trial did not demonstrate a benefit. However, the other trial was not powered to test the benefit regarding metastases and overall survival.



La especificidad de la RT radica en que explota la capacidad de **reparación** que tiene la célula sana **del daño subletal** radioinducido y de la que carece, en gran medida, la célula tumoral.

1. Guía Clínica ASTRO/AUA. Directrices (3)

3. **STANDARD.** Physicians should offer adjuvant radiotherapy to patients with adverse pathologic findings at prostatectomy including seminal vesicle invasion, positive surgical margins, or extraprostatic extension because of demonstrated reductions in biochemical recurrence, local recurrence, and clinical progression. (Body of Evidence Strength Grade A)

1. **SWOG 8794.** JUrol 2009; 181: 965-962. Thompson IM *et al*
2. **EORTC 22911.** Lancet 2012; 380:2018-2027. Bolla M *et al*
3. **ARO 96-02/AUO.** J Clin Onc 2009; 27: 2924-2930. Wiegel T *et al*

1. Guía Clínica ASTRO/AUA. Directrices (3)

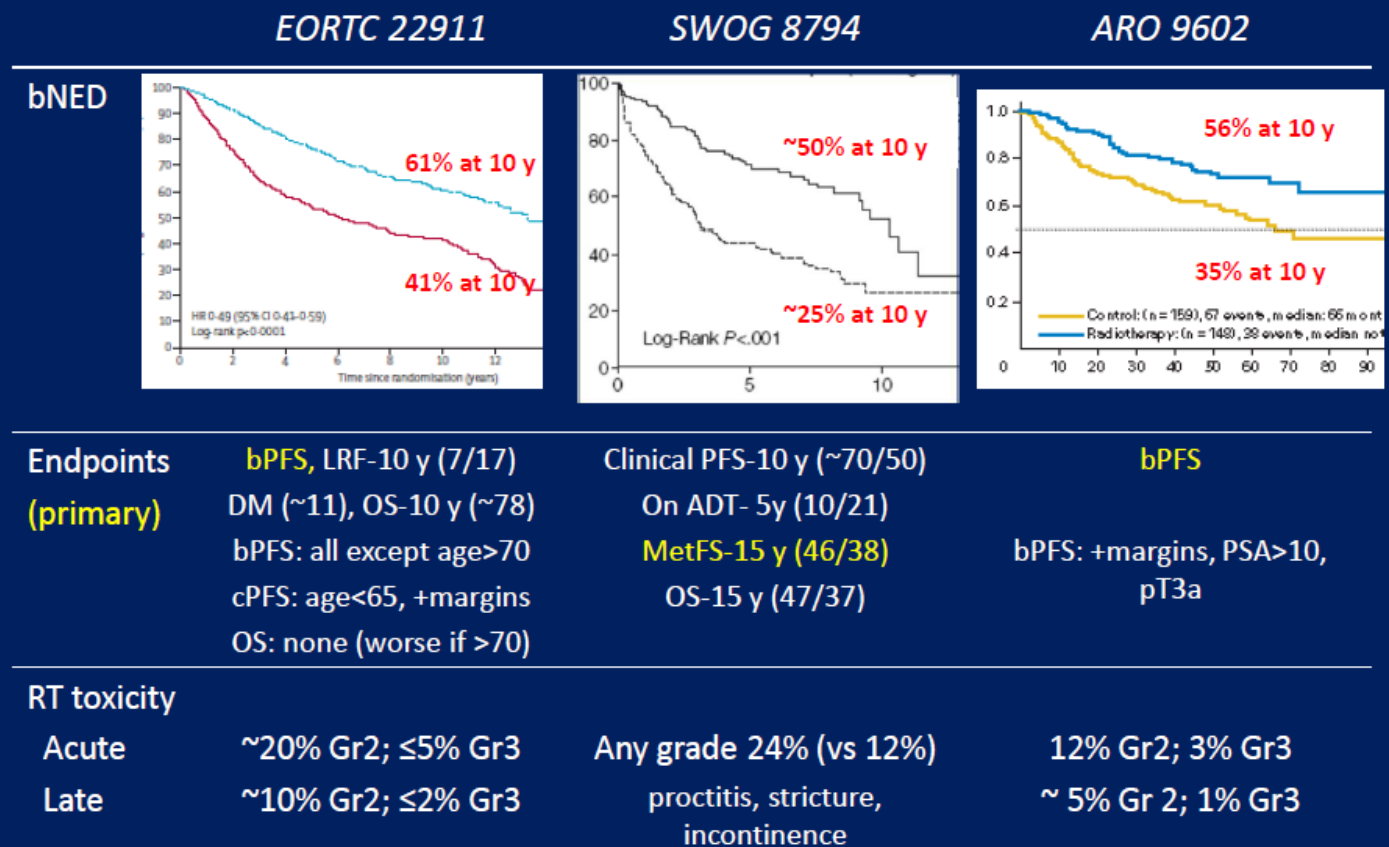
Randomized trials: adj RT vs obs

	<i>EORTC 22911</i> <i>Bolla Lancet 2012</i>	<i>SWOG 8794</i> <i>Thompson J Urol 2009</i>	<i>ARO 9602</i> <i>Wiegel JCO 2009/ GU ASCO 13</i>
Eligibility	pT2-3N0 ece, svi, or psm	pT2-3N0 ece, svi, or psm	pT3N0 ece, svi, psm
Patients	n=1005 1992-2001 Age 65 y Med preop PSA 12 Postop PSA ≤0.2 in 90%	n=425 1988-1997 Age 65 y Med preop PSA ~10 Postop PSA <0.2 in 66%	n=307 1997-2004 Age 65 y Median preop PSA ~9 Postop PSA ≤0.2 in 100%
RT techniques	60 Gy Conventional Prostate bed Within 4 mo	60-64 Gy Conventional Prostate bed Within 4 mo	60 Gy 3D conformal Prostate bed Within 3 mo
Median fu	10.6 y	11.5 y	9.3 y

1. Guía Clínica ASTRO/AUA. Directrices (3)

Fallo Bioquímico

Randomized trials: adj RT vs obs



1. Guía Clínica ASTRO/AUA. Directrices (3)

Fallo Bioquímico

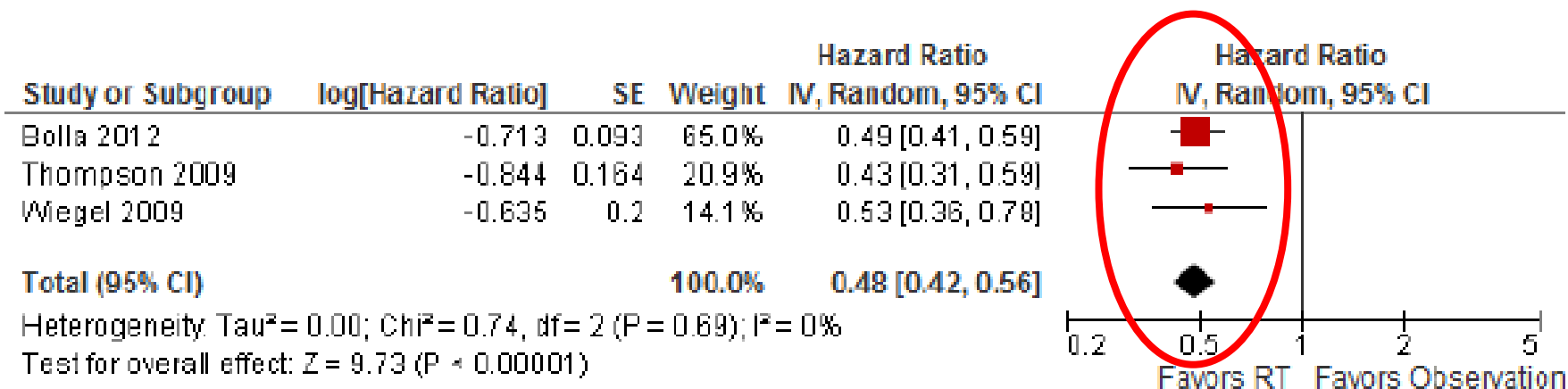
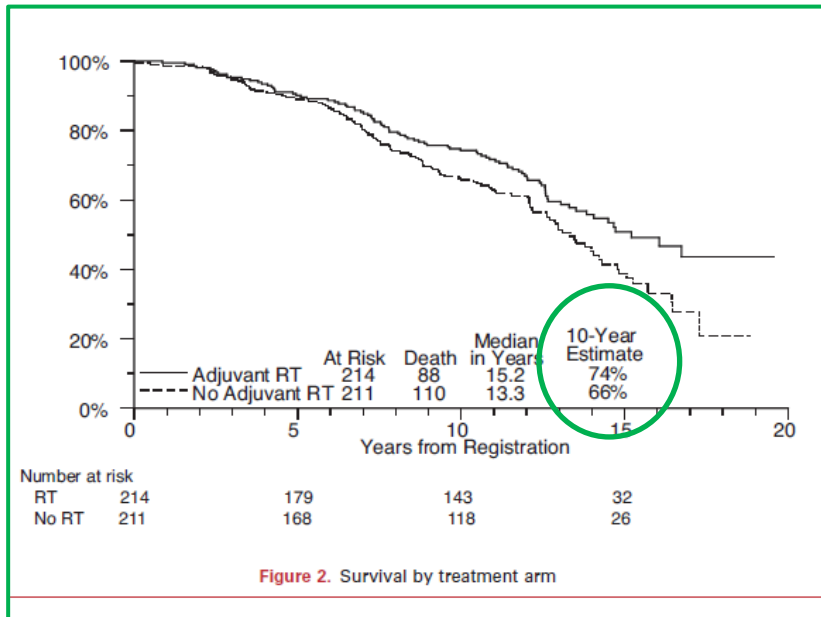


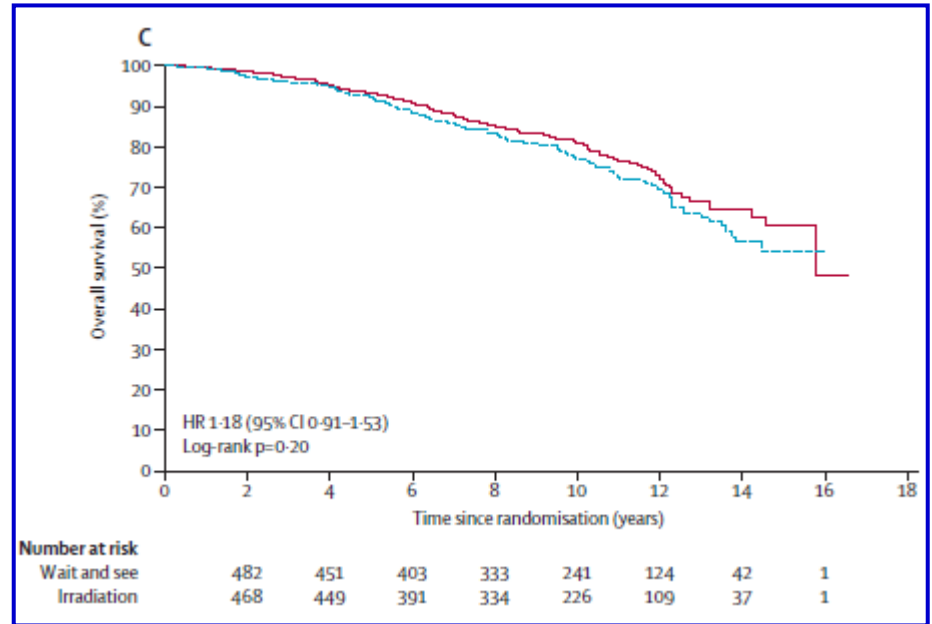
Figure 1: Meta-analysis of biochemical recurrence data from SWOG 8794 (Thompson 2009), EORTC 22911 (Bolla 2012), and ARO 96-02 (Wiegel 2009).

1. Guía Clínica ASTRO/AUA. Directrices (3)

Supervivencia Global



SWOG 8794



EORTC 22911

1. Guía Clínica ASTRO/AUA. Directrices (3)

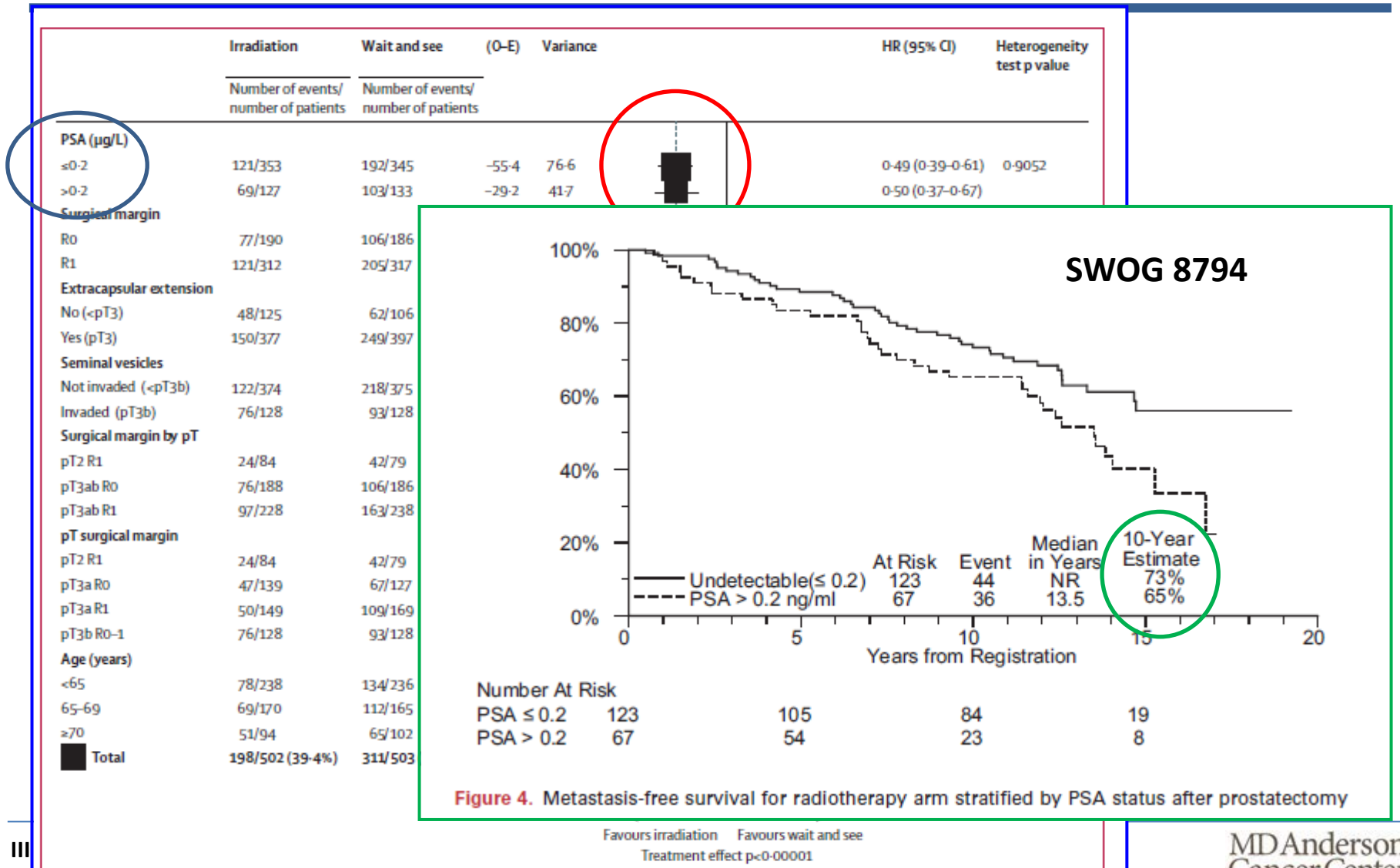


Figure 2: Effects of baseline factors on biochemical progression-free survival

1. Guía Clínica ASTRO/AUA. Directrices (4)

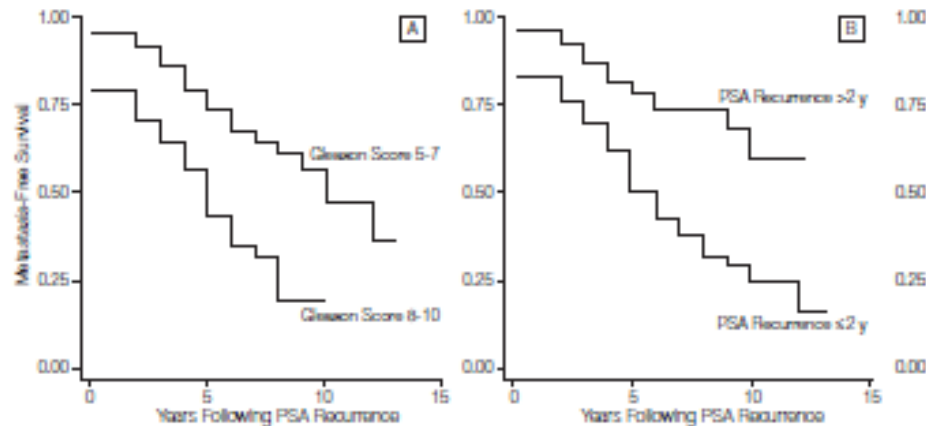
4. CLINICAL PRINCIPLE. Patients should be informed that the development of a PSA recurrence after surgery is associated with a higher risk of development of metastatic prostate cancer or death from the disease. Congruent with this clinical principle, physicians should regularly monitor PSA after radical prostatectomy to enable early administration of salvage therapies if appropriate.

- JAMA 1999; 281: 1591-1597. Pound CR *et al*
- JAMA 2005; 294: 433-439. Freedland SJ

- J Urol 2004; 171: 2221-2225. Albertsen PC *et al*

1. Guía Clínica ASTRO/AUA. Directrices (4)

Figure 3. Actuarial Likelihood of Metastasis-Free Survival in 304 Men With Prostate-Specific (PSA) After Radical Prostatectomy



A, Based on Gleason scores in the radical prostatectomy specimen ($P < .001$). B, Based on years until initial biochemical specific antigen doubling time (PSADT) ($P < .001$).

1594 JAMA, May 5, 1999—Vol 281, No. 17

©1999 American

Table 3. Estimate of the Risk of Prostate Cancer–Specific Survival After Biochemical Recurrence Following Radical Prostatectomy

Prostate-Specific Antigen Doubling Time, mo	Risk Estimate, % (95% Confidence Interval)			
	Recurrence >3 y After Surgery		Recurrence ≤3 y After Surgery	
	Gleason Score <8	Gleason Score ≥8	Gleason Score <8	Gleason Score ≥8
5-y Estimate				
≥15.0	100 (98 to 100)	99 (98 to 99)	99 (96 to 100)	98 (90 to 100)
9.0-14.9	99 (70 to 100)	98 (75 to 100)	97 (76 to 100)	94 (63 to 99)
3.0-8.9	97 (81 to 100)	94 (74 to 99)	91 (67 to 98)	81 (46 to 95)
<3.0	92 (70 to 98)	83 (52 to 96)	74 (37 to 93)	51 (19 to 82)
10-y Estimate				
≥15.0	98 (96 to 100)	96 (93 to 98)	93 (90 to 98)	86 (61 to 96)
9.0-14.9	95 (75 to 99)	90 (58 to 98)	85 (49 to 97)	69 (30 to 92)
3.0-8.9	84 (62 to 94)	68 (37 to 89)	55 (25 to 82)	26 (7 to 62)
<3.0	59 (29 to 83)	30 (10 to 63)	15 (3 to 53)	1 (<1 to 55)
15-y Estimate				
≥15.0	94 (87 to 100)	87 (79 to 92)	81 (57 to 93)	62 (32 to 85)
9.0-14.9	86 (57 to 97)	72 (35 to 92)	59 (24 to 87)	31 (7 to 72)
3.0-8.9	59 (32 to 81)	30 (10 to 63)	16 (4 to 40)	1 (<1 to 51)
<3.0	19 (5 to 51)	2 (<1 to 38)	<1 (<1 to 26)	<1 (<1 to 2)

Mediana de M1: 8 años; GS 8-10: en 5 a; GS 5-7: en 10 a.

Fallo bioq <2 años: M1 en 5 a; >2 años: en >10 a.

PSADT <10 meses: M1 en 5 a; si >10 meses: M1 >10 años. M1 → † en 5 a (2-12).

PSADT <10-12 meses: El 50% † en 10-13 años.

1. Guía Clínica ASTRO/AUA. Directrices (5)

5. **RECOMMENDATION.** Clinicians should define biochemical recurrence as a detectable or rising PSA value after surgery that is ≥ 0.2 ng/ml with a second confirmatory level ≥ 0.2 ng/ml.

- Evidencia grado C (observacionales)
- Ya establecido en documento previo de AUA (www.auanet.org/content/media/psa09.pdf)
- Se entiende que existe un 8.8% de falsos positivos (1).
- No se está seguro si límites de corte más bajos podrían suponer sobretratamientos.
- El cálculo de PSADT con PSAs ultrasensibles dan valores marcadamente diferentes (2)
- Sin embargo, un PSA ultrasensible que se eleva puede ser considerado válido para tomar decisiones de rescate, sobretodo si alto riesgo de recurrencia (Mg+, pT3).

(1) Urology 2003; 61:380-385. Shinghal R *et al*

(2) J Urol 2011; 186: 2228-2232. Reese A *et al*

1. Guía Clínica ASTRO/AUA. Directrices (6)

6. **OPTION.** A **restaging evaluation** in the patient with a PSA recurrence may be considered. (Body of Evidence Strength Grade C)

	Recommended?	Comment
Ultrasound and biopsy	No	Moderate sensitivity only; only evaluates prostate bed
CT abdomen/pelvis	No	Low sensitivity with low PSA
Bone scan	<i>If PSA >10, PSADT <6 mo, velocity >0.5</i>	Low sensitivity with low PSA; indeterminate findings possible

MDACC M·E

RM + Gld difusión-dinámico (con antena endorectal, espectroscopía >70-80% sens/esp...).

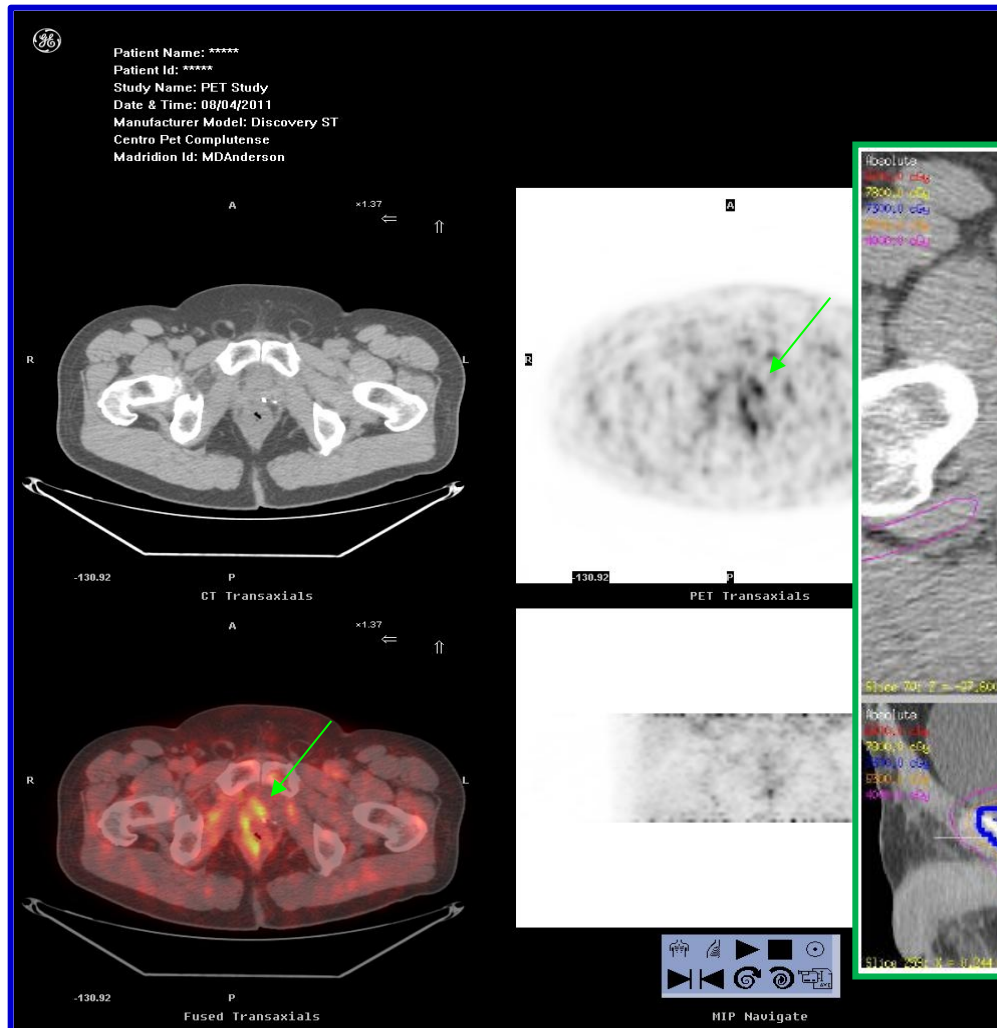
- Siempre.

PET-TC-Colina. (**GGÓsea** como referencia basal, o PSAV >0.5ng/mL/mes o PSADT <6meses)

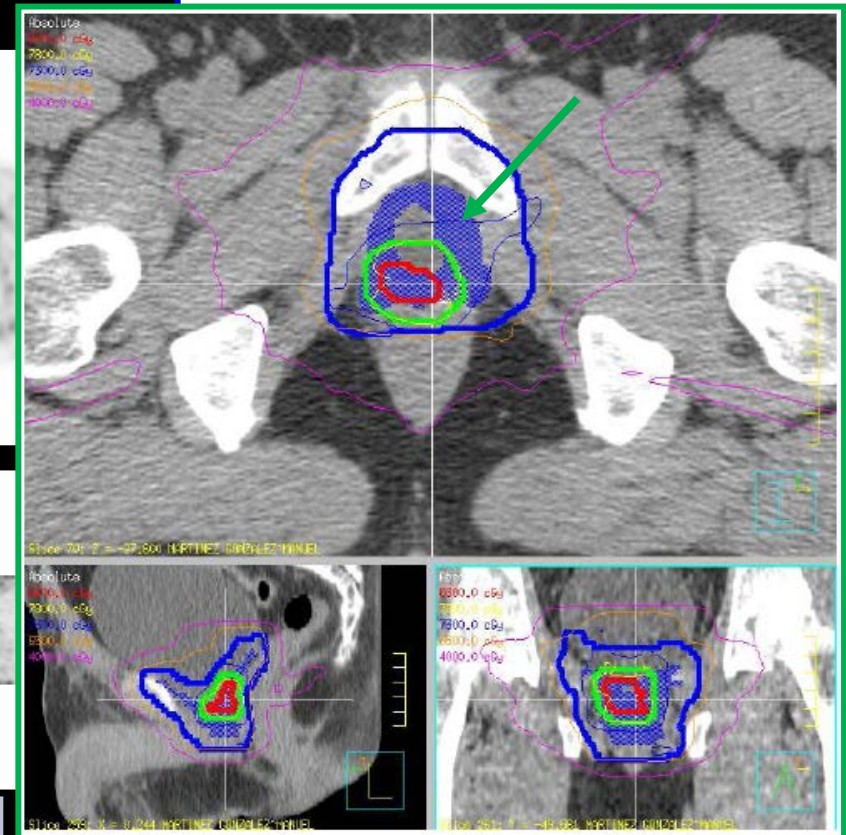
- Si PSA > 1-1.5 ng/ml
- Si PSADT < 6 meses.

Adapted from: Beresford, Clin Onc 2010

1. Guía Clínica ASTRO/AUA. Directrices (6)

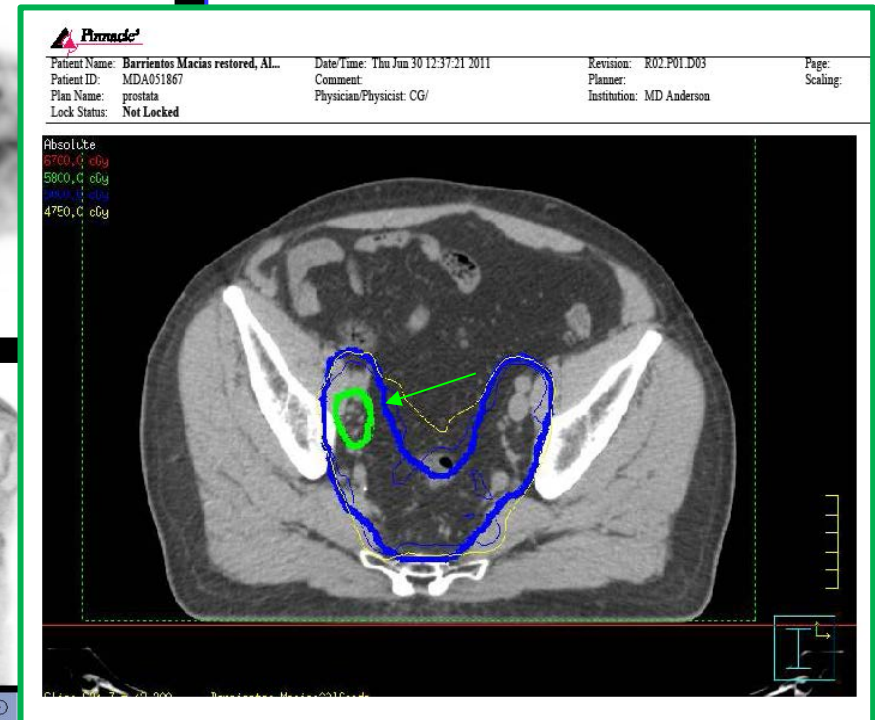
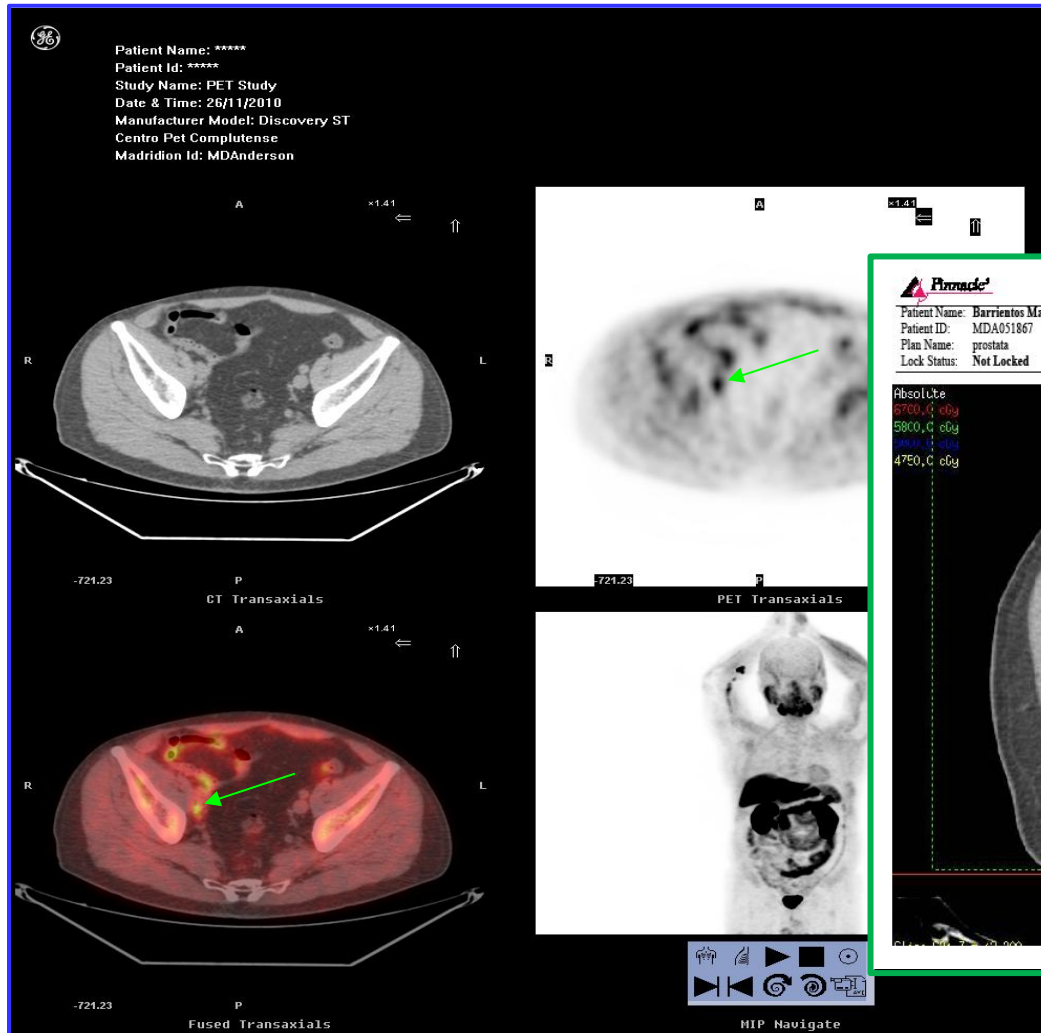


#Caso: R Local



1. Guía Clínica ASTRO/AUA. Directrices (6)

#Caso: R. Regional



1. Guía Clínica ASTRO/AUA. Directrices (7)

7. **RECOMMENDATION.** Physicians should offer salvage radiotherapy to patients with PSA or local recurrence after radical prostatectomy in whom there is no evidence of distant metastatic disease. (Body of Evidence Strength Grade C)

Mayo Clinic (1987-03) #2657 pts bF: #856 (32%) RT de rescate; MedSg (tRT): 5.9 a:

- Redujo el riesgo de RLocal en casi 90% (HR 0.13);
- Retrasó de ADT del 20% (HR 0.81) y
- Redujo la progresión sistémica en 75% (HR 0.24).
- No diferencias en OS

J Urol 2009; 182 (6): 2708-2715. Boorjian SA et al

Johns Hopkins (1982-04): #397 (no RT), #160 (RT sola) #78 (RT+ADT); MedSeg(tRT): 6 a.

- Redujo el número de muertes por PCa 3 veces: 89 (no RT) y 19 y 8 (RT± ADT)
- Incluso en PSADT <6 meses. En >6 meses si Mg+ y GS8-10.

JAMA 2008; 299: 2760-2769. Trock BJ et al

1. Guía Clínica ASTRO/AUA. Directrices (7)

Aunque, en casos más extremos, balance (ya que Fallo Bioquímico \neq Fallo Clínico) entre:

Expectativa de vida e Hª Natural (Direct #4)

Eficacia-Toxicidades (Direct #9).

1. Guía Clínica ASTRO/AUA. Directrices (7)

Expectativa de Vida:

The image displays two overlapping browser windows. The top window shows the 'Prostate Cancer Nomogram' page from nomograms.mskcc.org. The bottom window shows the 'Comorbidity Index and Score of Charlson et al.' calculator from www.medal.org. The calculator interface includes a list of conditions on the left and a grid of radio buttons for selecting the severity of each condition. The results section at the bottom shows a weighted index of comorbidity of 2, a combined condition and age-related score of 5, and an estimated 10-year survival of 21%.

Condition	none	without end organ damage	with end organ damage
AIDS?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Cerebrovascular disease?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Chronic pulmonary disease?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Congestive heart failure?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Connective tissue disease?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Dementia?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Hemiplegia?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Leukemia?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Malignant lymphoma?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Myocardial infarction?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Peripheral vascular disease?	<input type="radio"/>	<input type="radio"/>	
Ulcér disease?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Diabetes mellitus	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Liver disease	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Renal disease	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Malignant solid tumor	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Calculate **Reset**

Evaluate	Result
Weighted index of comorbidity	2
Combined condition and age-related score	5
Estimated 10 year survival	21%

Survival may be underestimated for higher combined scores

<http://www.medal.org/OnlineCalculators/ch1/ch1.13/ch1.13.01.php#result>

1. Guía Clínica ASTRO/AUA. Directrices (7)

EFICACIA: Predictores (1):

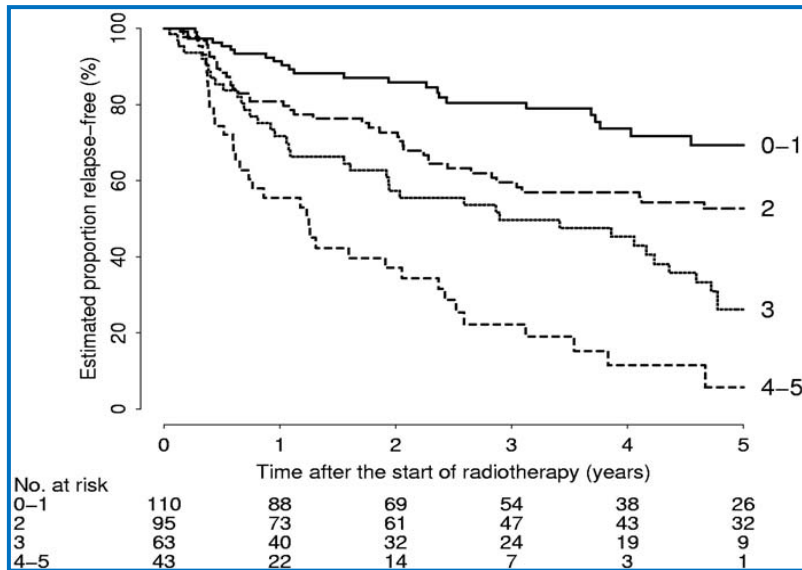


TABLE 4. *Score algorithm*

	Score
Pathological tumor stage:	
T2 Or T3a	0
T3b	1
Gleason score:	
1-6	0
7	1
8-10	2
Pre-RT PSA:	
Less than 0.5	0
0.5-1.0	1
Greater than 1.0	2

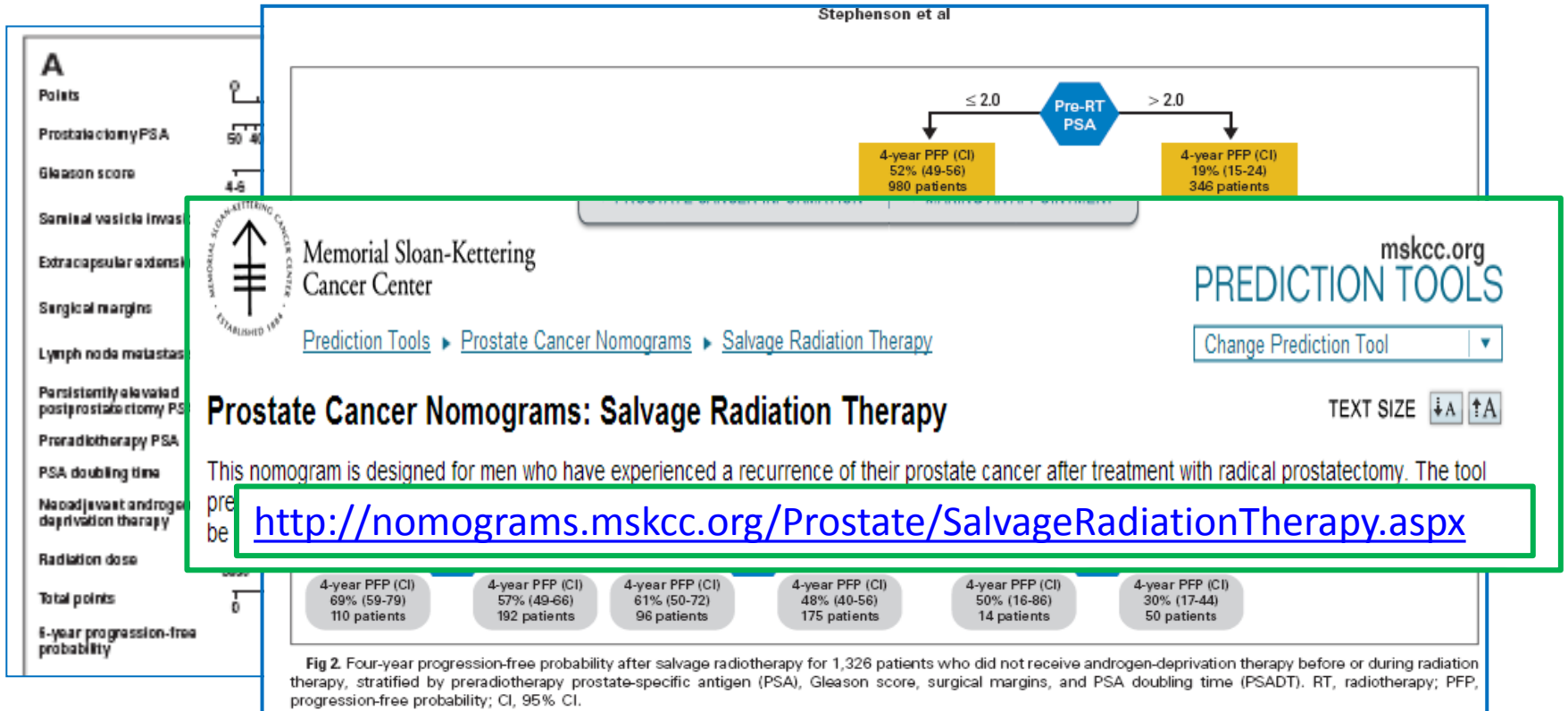
These scores are added together to obtain a total score from 0 to 5.

SLFBq a los 5 a: **0-1: 69%; 2: 53%; 3: 26%; 4-5: 6%**

J Urol 2006; 176: 985-990. Buskirk SJ *et al*

1. Guía Clínica ASTRO/AUA. Directrices (7)

EFICACIA: Predictores (2):



J Clin Oncol 2007; 25: 2035-2041. Stephenson A *et al*

1. Guía Clínica ASTRO/AUA. Directrices (7)

¿Por qué no “Vigilancia Cuidadosa” en este caso?:

Prostate-Specific Antigen Doubling Time, mo	Risk Estimate, % (95% Confidence Interval)			
	Recurrence >3 y After Surgery		Recurrence ≤3 y After Surgery	
	Gleason Score <8	Gleason Score ≥8	Gleason Score <8	Gleason Score ≥8
5-y Estimate				
≥15.0	100 (98 to 100)	99 (98 to 99)	99 (96 to 100)	98 (90 to 100)
9.0-14.9	99 (70 to 100)	98 (75 to 100)	97 (76 to 100)	94 (63 to 99)
3.0-8.9	97 (81 to 100)	94 (74 to 99)	91 (67 to 98)	81 (46 to 95)
<3.0	92 (70 to 98)	83 (52 to 96)	74 (37 to 93)	51 (19 to 82)
10-y Estimate				
≥15.0	98 (96 to 100)	96 (93 to 98)	93 (80 to 98)	86 (61 to 96)
9.0-14.9	95 (75 to 99)	90 (58 to 98)	85 (49 to 97)	69 (30 to 92)
3.0-8.9	84 (62 to 94)	68 (37 to 89)	55 (25 to 82)	26 (7 to 62)
<3.0	59 (29 to 83)	30 (10 to 63)	15 (3 to 53)	1 (<1 to 55)
15-y Estimate				
≥15.0	94 (87 to 100)	87 (79 to 92)	81 (57 to 93)	62 (32 to 85)
9.0-14.9	86 (57 to 97)	72 (35 to 92)	59 (24 to 87)	31 (7 to 72)
3.0-8.9	59 (32 to 81)	30 (10 to 63)	16 (4 to 49)	1 (<1 to 51)
<3.0	19 (5 to 51)	2 (<1 to 38)	<1 (<1 to 26)	<1 (<1 to 2)

Freedland JAMA 2005

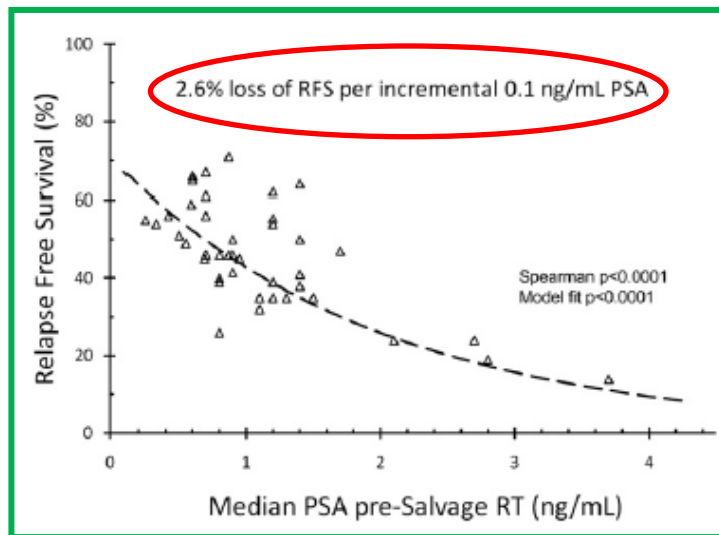
Supervivencia CE >15 a: **94%**, si:

- FBq >3 a
- GS <8
- PSADT >15 meses

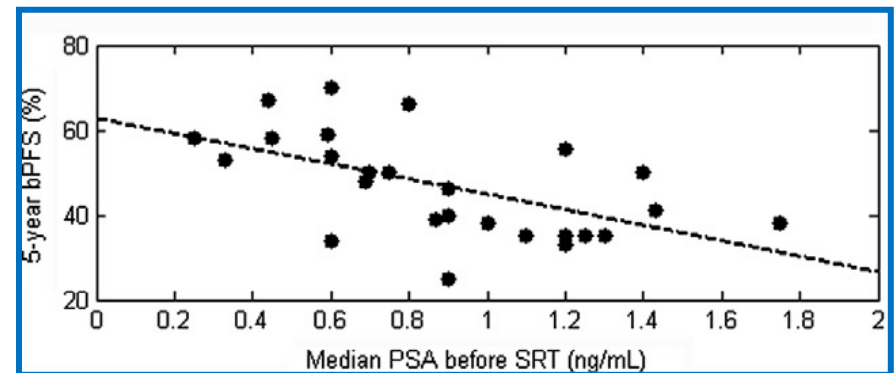
1. Guía Clínica ASTRO/AUA. Directrices (8)

8. **CLINICAL PRINCIPLE.** Patients should be informed that the effectiveness of radiotherapy for PSA recurrence is greatest when given at lower levels of PSA.

47 estudios observacionales se revisaron: 41 distinguían entre grupos de alto y bajo riesgo con el valor de 1 ng/mL o menos. 46 a menor PSA pre-RT mayor b-RFS



Int J Radiat Oncol Biol Phys 2012; 84:104-111. King CR.
-41 estudios y 5600 pts-

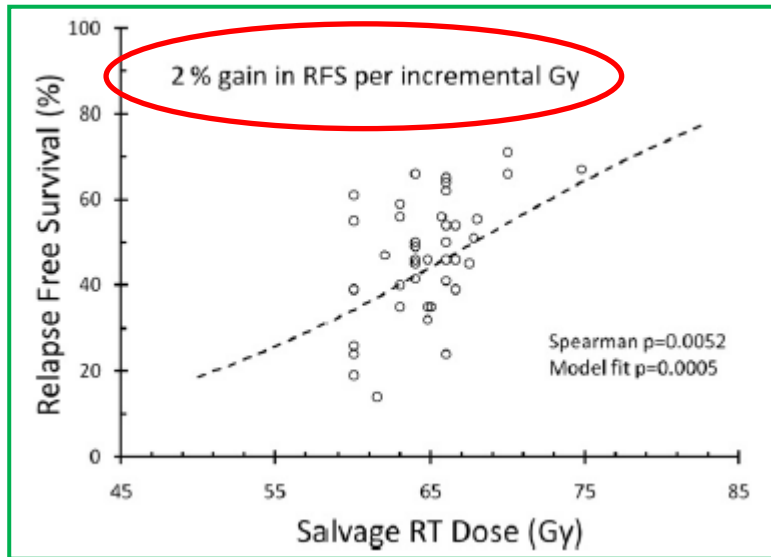


Eur J Cancer 2012; 48: 837-844. Ohri N
-25 estudios y 3800 pts-

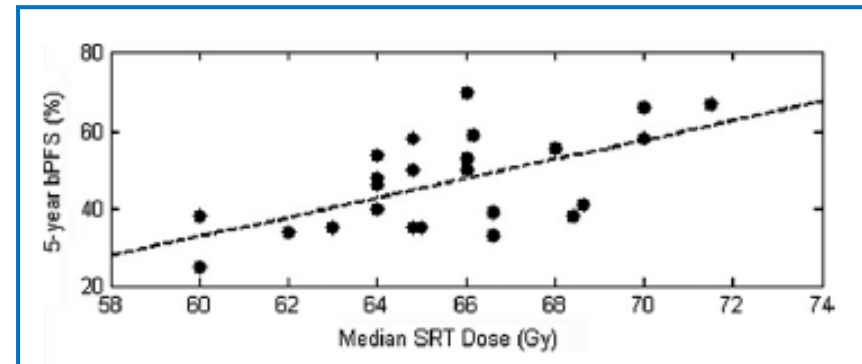
Pérdida del 18% por cada 1 ng/mL de aumento

1. Guía Clínica ASTRO/AUA. Directrices (8)

Dosis de RT:



Int J Radiat Oncol Biol Phys 2012; 84:104-111. King CR.



Eur J Cancer 2012; 48: 837-844. Ohri N

Aumento de 2.5% de control por cada Gy

Recomendar RT de rescate tras el más precoz signo de aumento de PSA e, idealmente, <1 ng/mL.

1. Guía Clínica ASTRO/AUA. Directrices (8)

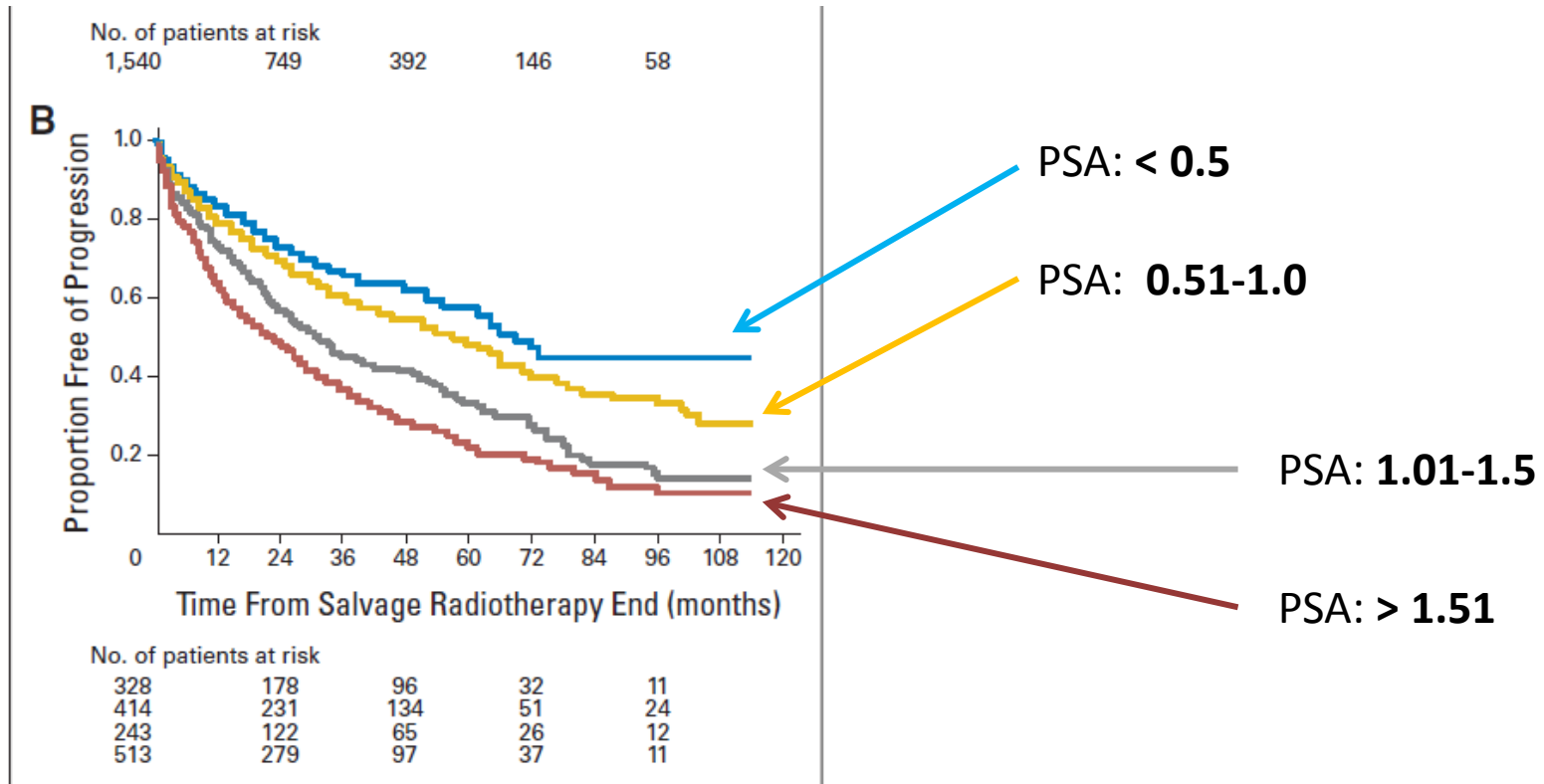


Fig 1. (A) Kaplan-Meier estimate of the overall progression-free probability after salvage radiotherapy. (B) Progression-free probability after salvage radiotherapy stratified by preradiotherapy prostate-specific antigen 0.50 or less (blue), 0.51 to 1.00 (yellow), 1.01 to 1.50 (gray), and more than 1.50 ng/mL (red).

J Clin Onc 2007; 25:2035-2041. Stephenson AJ et al

1. Guía Clínica ASTRO/AUA. Directrices (9)

9. **CLINICAL PRINCIPLE.** Patients should be informed of the possible short-term and long-term urinary, bowel, and sexual side effects of radiotherapy as well as of the potential benefits of controlling disease recurrence.

Toxicidad Aguda (hasta 90 días).

- RTOG
- CTCAE

Toxicidad crónica (>90 días; h. a los 4-5 a):

- RTOG/EORTC
- CTCAE

0: asintomático / **5:** muerte.

1: Cambio funcional menor

2: Cambio moderado que requiere F.

3: Cambios mayores con F agresivos o proc amb

4: Cambios severos con Hospitalización/Cirugías.

1. Guía Clínica ASTRO/AUA. Directrices (9)

Globalmente:

Table 1 Acute toxicity effects of RT after prostatectomy (ranges based on RTOG or CTCAE grading system)

Study arm type	Genitourinary		Gastrointestinal	
	Grades 1-2	Grades 3-4	Grades 1-2	Grades 3-4
Adjuvant	10.5%-26%	2.0%-8.0%	22.0%-25.0%	0.0%-2.0%
Salvage	3.0%-82.0%	0.0%-6.0%	2.9%-96.0%	0.0%-2.2%
Mixed	5.0%-92.0%	0.0%-3.0%	4.3%-87.0%	0.0%-1.3%

Técnicas no conformadas la gran mayoría...

G1-2: h. 80-90%

G3-4: <5%

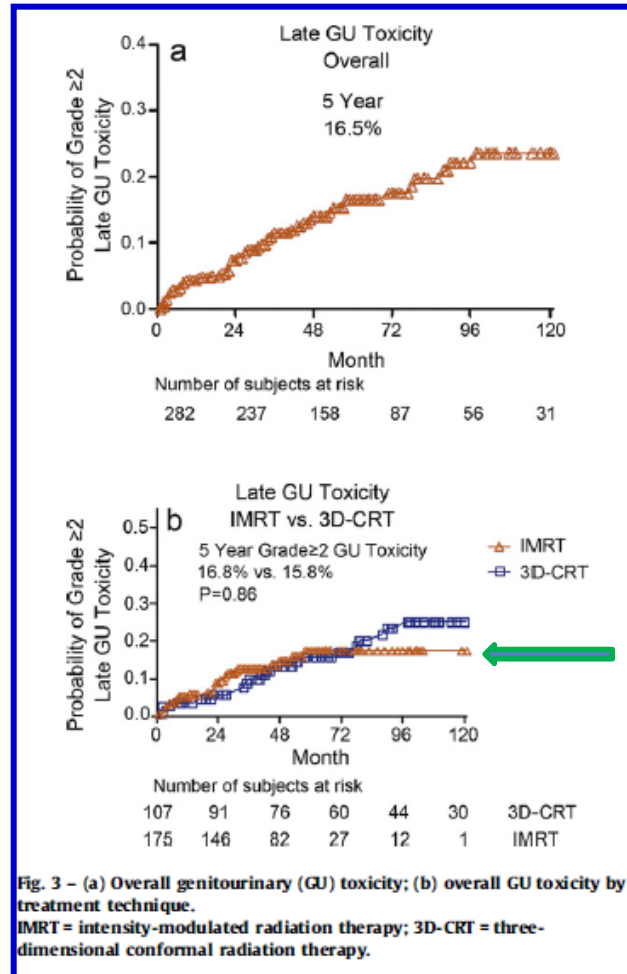
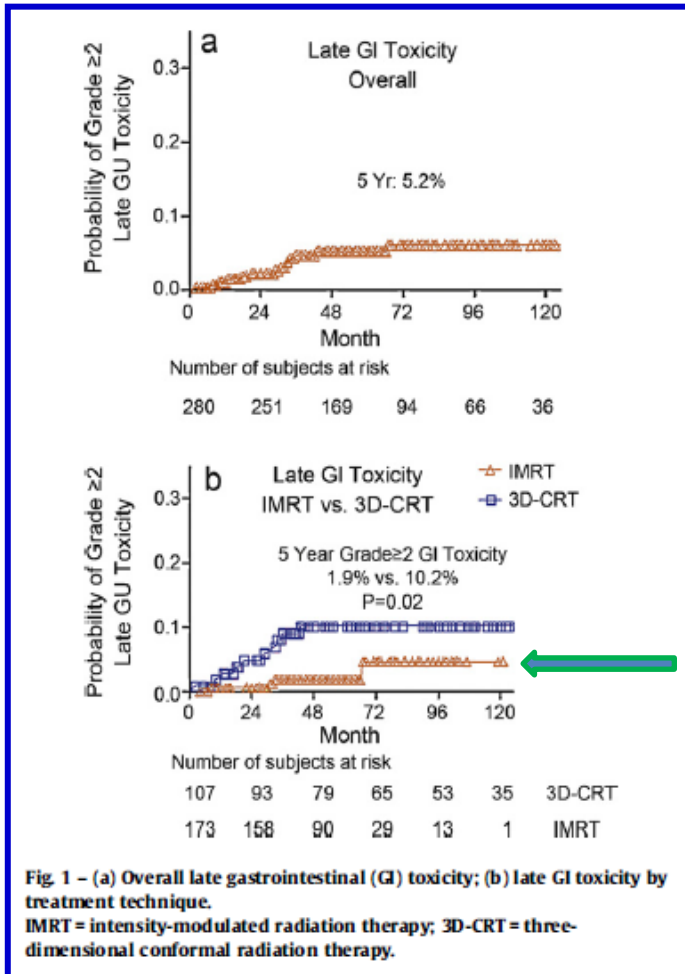
G1-2: 30-50 %

G3-4: <10 %

Table 2 Late toxicity effects of RT after prostatectomy (ranges based on RTOG/EORTC or CTCAE grading system)

Study arm type	Genitourinary		Gastrointestinal	
	Grades 1-2	Grades 3-4	Grades 1-2	Grades 3-4
Adjuvant	2.0%-22.0%	0.0%-10.6%	1.0%-12.7%	0.0%-6.7%
Salvage	1.0%-49.0%	0.0%-6.0%	0.0%-66.0%	0.0%-18.0%
Mixed	1.3%-79.0%	0.0%-17.0%	2.0%-59.0%	0.0%-4.3%

1. Guía Clínica ASTRO/AUA. Directrices (9)

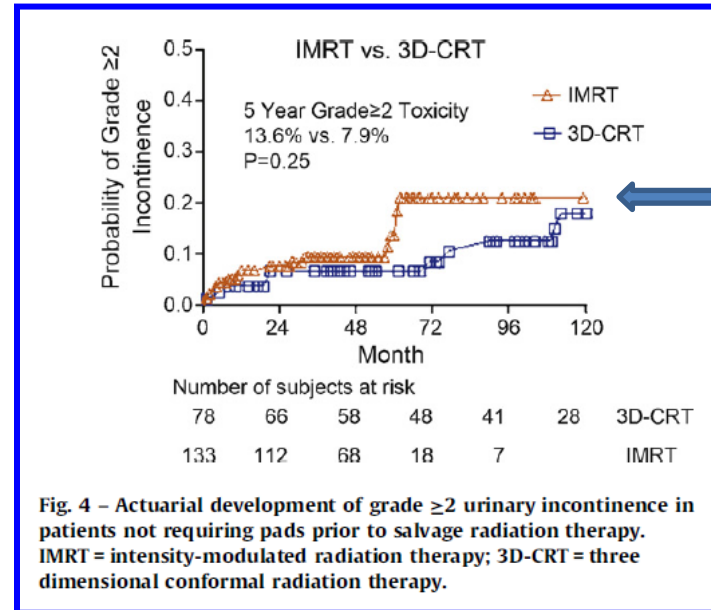
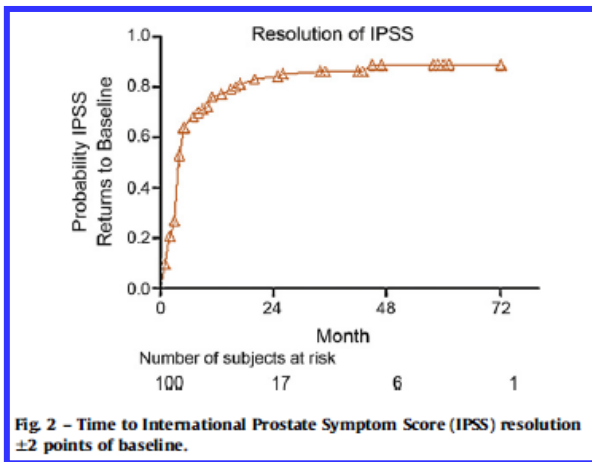


- Toxicidad ≥ 2
Con 3D-IMRT:
- GI: 11-4%
 - GU: 25-16.8 %

Eur Urol 2011; 60: 1142-48.
 Goenka A et al

1. Guía Clínica ASTRO/AUA. Directrices (9)

Toxicidad GU con 3D-IMRT:

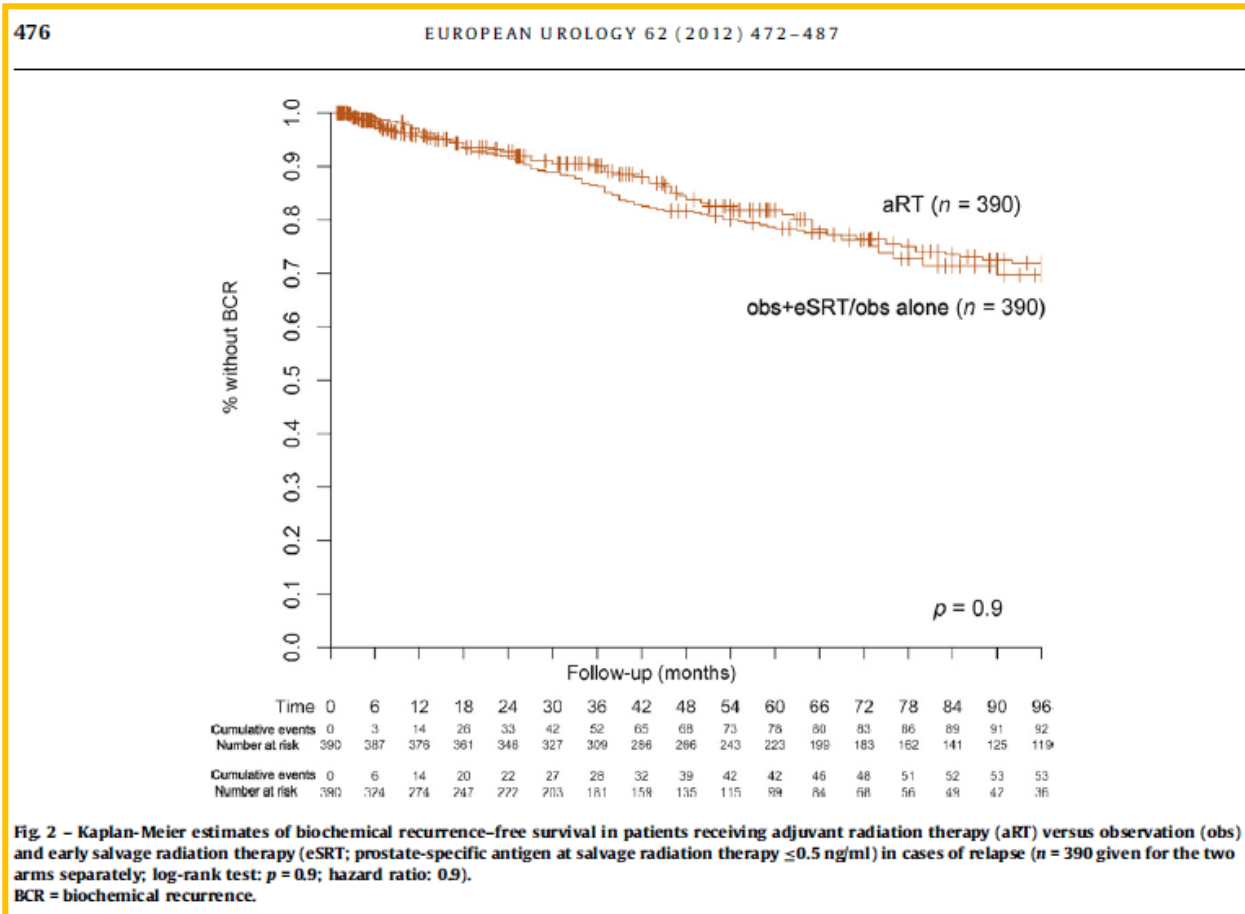


Estenosis uretral ≥ 2 fue 1.4% y 3.7% a 2 y 5 a.; mediana: 2.5 a y 1/3 >5a y no dif. entre 3D/MIRT.

Un 35% de las incontinencias fueron por el tratamiento de las estenosis uretrales

Eur Urol 2011; 60: 1142-48. Goenka A et al

2. Radiación de Rescate Precoz



Cohortes:

- ART vs
- Obs/RT precoz < 0.5

MedSeg: 47 meses

SLFb : **78%** vs **82%**
5a

**Sin
sobretreatmento**

Eur Urol 2012; 62: 472-87. Briganti A et al

2. Radiación de Rescate Precoz

Table 4 – Oncologic outcome

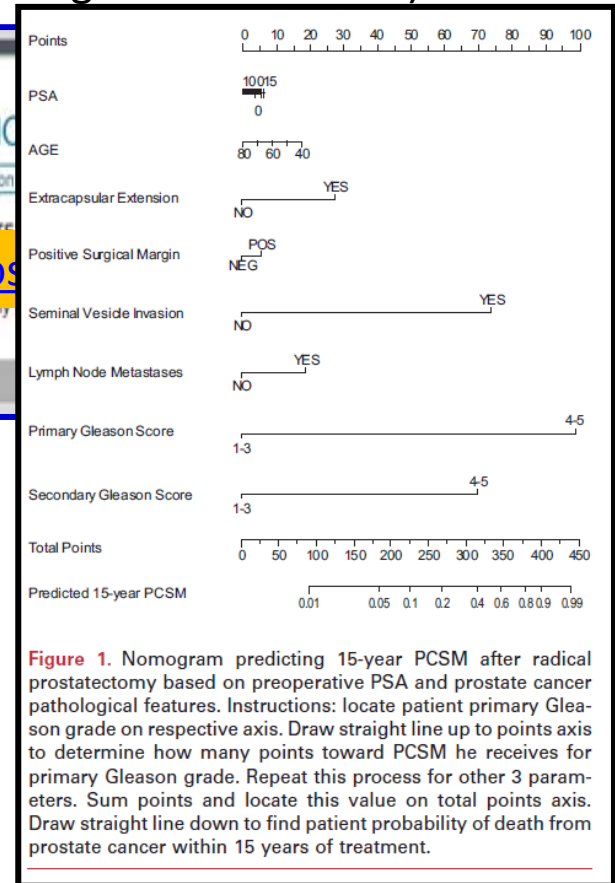
First author	No. of patients	PSA pre-RT, ng/ml, (range)	Follow-up (range)	Fraction bRFS at specific time points	Nodal involvement
Bernard [23]	69	0.32 (0.1–0.49)	8 yr (0.6–15)	5 yr: 79.8%	pN0
Terai [29]	21 of 37	<0.15	31.9 mo (34.3–69.8)	5 yr: 80%	N0
Liauw [24]	34	0.27 (0.05–0.5)	72.4 mo (5.2–136.3)	5 yr: 71%	pN0
Goenka [25]	143	<0.5	60 mo (4–221)	5 yr: 48%	pN0
Briganti [4]	390	<0.5 <0.3	40.6 mo	2 yr: 92.8% 5 yr: 81.8%	pN0
Stephenson [26]	181	0.4 (0.3–0.4)	33 mo (15–56)	6 yr: 48% 5 yr: 61% 3 yr: 69%	pN0
Ost [11]	48	0.3 (0.1–0.5)	53 mo (18–132)	5 yr: 77.1%	pN0/cN0

PSA = prostate-specific antigen; RT = radiation therapy; bRFS = biochemical recurrence-free survival.

Article in Press: Early Salvage Radiotherapy Following Radical Prostatectomy. Eur Urol (2013), <http://dx.doi.org/10.1016/j.eururo.2013.08.013>

3. ¿Qué hacer hoy, ante un pte. recién operado?

1. Establecer el riesgo de fallo/muerte específica (nomogramas validados).



- J Clin Onc 2005; 23: 7000-7012. Stephenson *et al*
- J Urol 2011; 185: 869-75. Eggener *et al*

3. ¿Qué hacer hoy, ante un pte. recién operado?

2. Si pT3 y/o Mg+:

1. Considerar **RT adyuvante inmediata** (tras 1er PSA_t postop, 6 sem):

2. Considerar **RT de rescate precoz** (PSAs c/3meses):

y como **posible fallo: PSA+ (>0.02/0.05 ng/mL) y ascenso.**

1. **Sobretratados hasta un 40%** (41%EORTC-35%ARO-25%SWOG)

2. **No parece existir pérdida de oportunidad** ¿idóneo PSA?: 0.1-0.2
¿Aceptable?: <0.5. No >1

3. RT: IMRT con dosis **66-70 Gy** (adyuvancia) **70 Gy** (PSA+) [y >70 Gy, si macro]

4. Si pT2R0: esperar hasta >0.2 ng/mL (x2) y, siempre, <0.5 ng/mL. H^aN/Exp-Vida

4. Ensayos Clínicos

Sobre RT de rescate o adyuvante con/sin Hn:

RTOG 0534, RTOG 9601, RADICALS, RAVES.

Sobre RT de rescate precoz o adyuvante con/sin Hn:

GETUC-17, EORTC 22043-30041, RADICALS, RAVES.

Sobre dosis de RT:

SAKK 9/10

FIN

GRACIAS

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