Il team multidisciplinare nel carcinoma della prostata

Negrar - 24 Novembre, 2016

La scelta del trattamento :
la malattia organo confinata e localmente avanzata

La chirurgia

Salvatore Siracusano

Antonio Benito Porcaro

Walter Artibani

Key points

- **Malattia organo confinata: classi di rischio**
  - **Linfadenectomia**
  - **Nerve sparing**
- **Malattia localmente avanzata**
- **Progressione linfonodale di malattia**
- **Malattia oligometastatica**

Malattia organo confinata: classi di rischio

	Low-risk	Intermediate-risk	High-risk	
Definition	PSA < 10 ng / mL and GS < 7 and cT1-2a	PSA 10-20 ng /mL or GS 7 or cT2b	PSA > 20 ng / mL or GS > 7 or cT2c	any PSA any GS cT3-4 or cN+
	Localised			**Locally advanced**

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PCa Low risk: strategie di trattamento

OSSERVAZIONALI

Watchful Waiting (WW)

Sorveglianza Attiva (AS)

To delay or to avoid active treatments
(related toxicity)

TERAPEUTICHE

Chirurgia

Radioterapia

Focal treatment:
HIFU vs
cryotherapy (?)

RP in low risk

Radical prostatectomy	Offer RP to patients with a life expectancy > 10 years.	A
	Offer a nerve-sparing surgery in pre-operatively potent patients with low risk of extracapsular disease (T1c, GS < 7 and PSA < 10 ng/mL, or refer to Partin tables/ nomograms).	B
	Do not perform LND in low-risk PCa	A

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RP in low and very – low risk

Low

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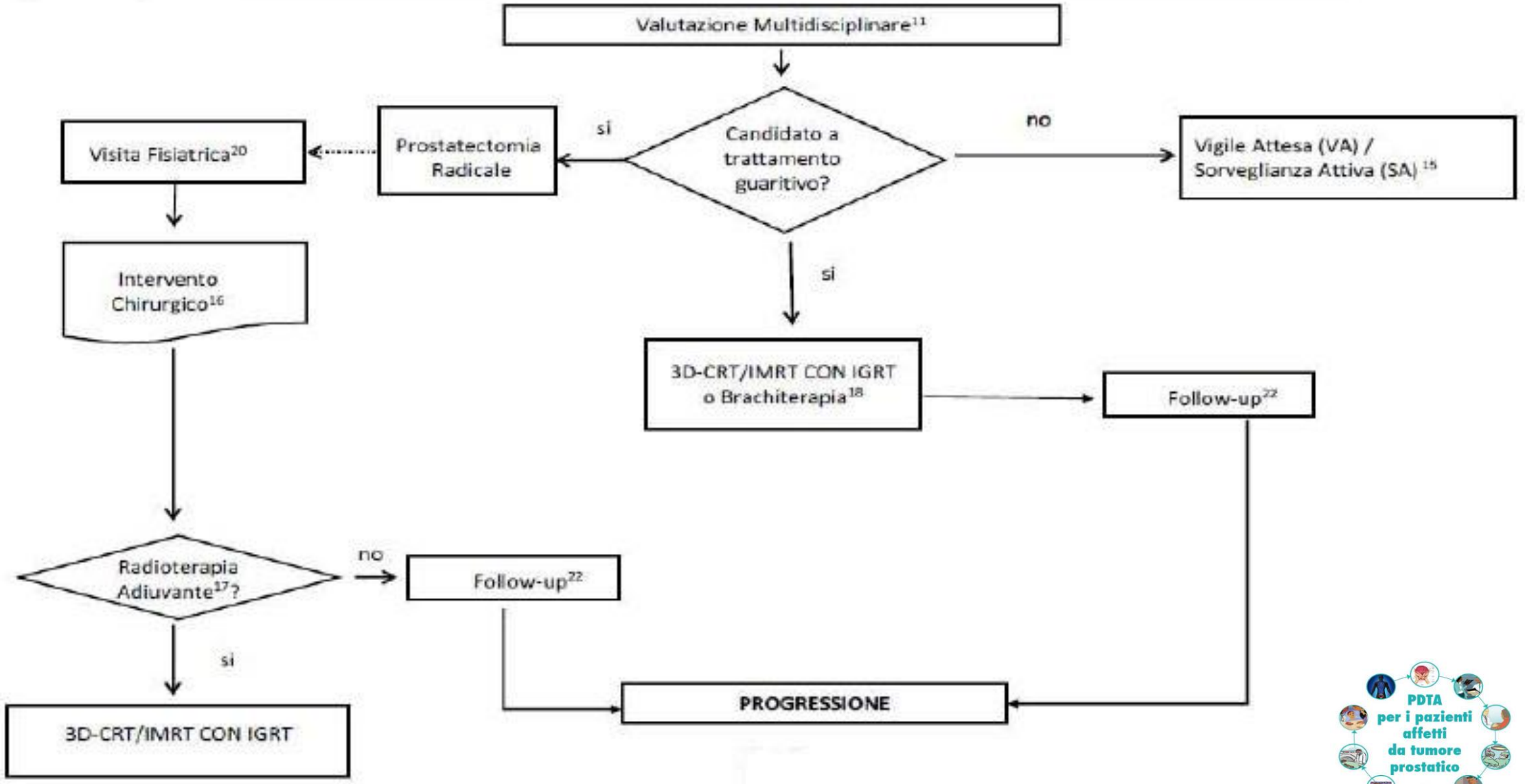
Risk group	Expected patient survival	Initial Therapy
T1-T2a GS <=6 PSA < 10 ng/ml	> 20 y	RP +/- PLND if predicted probability of lymph nodes metastasis >2%

Very low

Risk group	Expected patient survival	Initial Therapy
T1c GS<=6 PSA < 10ng/ml fewer than 3 prostate biopsy cores positive PSA density < 0.15 ng/ml/g	> 20 y	RP +/- pelvic lymph node dissection (PLND) if predicted probability of lympo nodes metastasis >2%

RP in low risk (PDTA)

Classe di rischio basso



RP in Intermediate-risk

Radical prostatectomy	Offer RP to patients with a life expectancy > 10 years.	A
	Offer a nerve-sparing surgery in pre-operatively potent patients with low risk of extracapsular disease (T1c, GS < 7 and PSA < 10 ng/mL, or refer to Partin tables/ nomograms).	B
	In intermediate- risk, extracapsular disease, use mpMRI as a decision tool to select patients for nerve-sparing procedures.	B
	Perform an eLND if the estimated risk for positive lymph nodes exceeds 5%.	B
	Do not perform a limited LND.	A

Ln (+) between 3,9-20% in IR
se rischio > 5% ---> eLND

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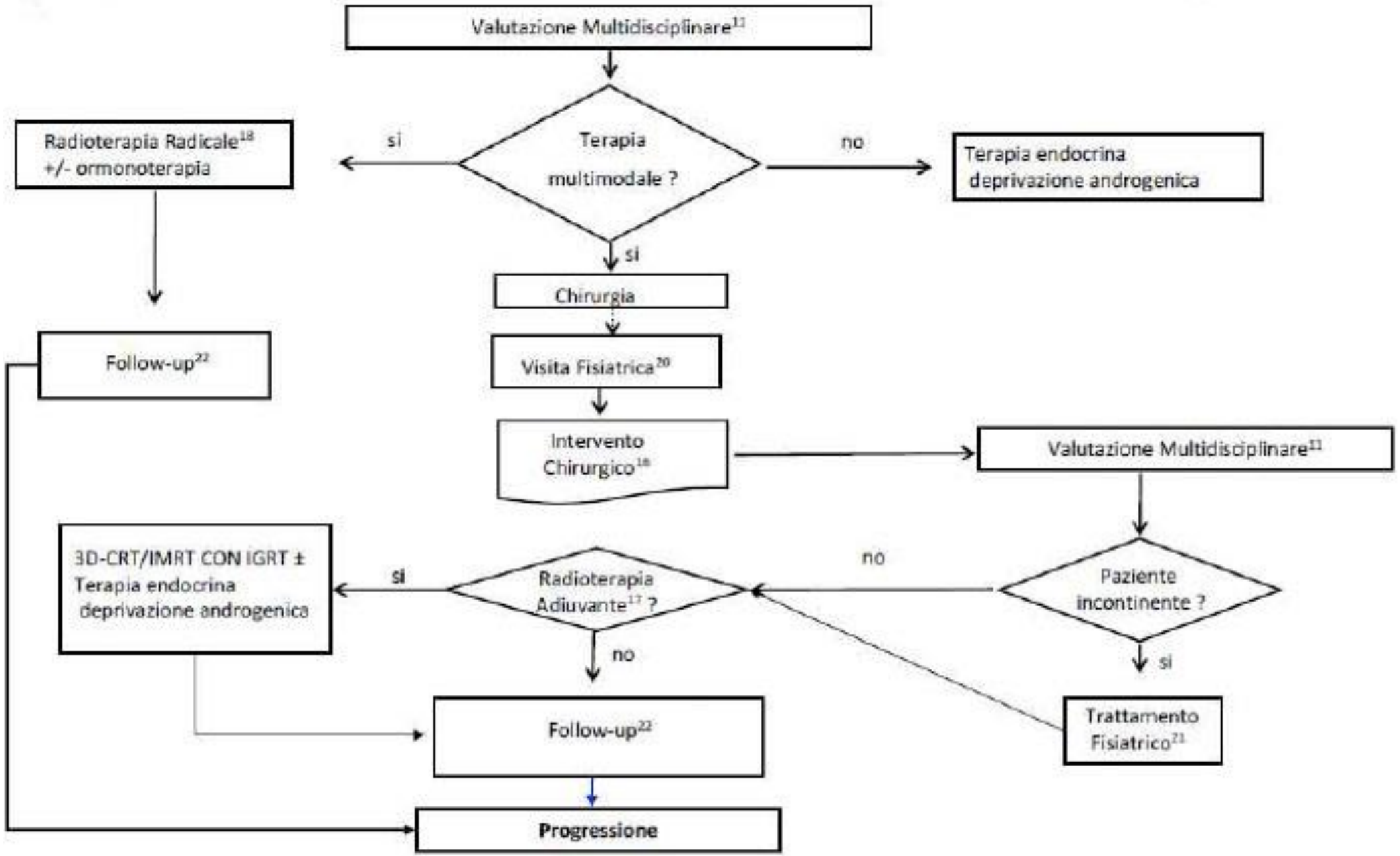
RP in Intermediate-risk

National Comprehensive Cancer Network

NCCN guidelines 2016

Risk group	Expected patient survival	Initial Therapy
T2b-T2c or GS > 7 or PSA 10- 20ng/ml	> 10 y	RP + PLND if predicted probability of lymph nodes metastasis >2%

Classe di rischio intermedio



RP in Intermediate-risk (PDTA)

RP in High risk

Do not offer NHT before RP.	A
Perform an eLND in high-risk PCa.	A
Do not perform a limited LND.	A
High risk localised: Offer RP in a multimodality setting to patients with high-risk localised PCa and a life expectancy of > 10 years.	B

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RP in High-risk

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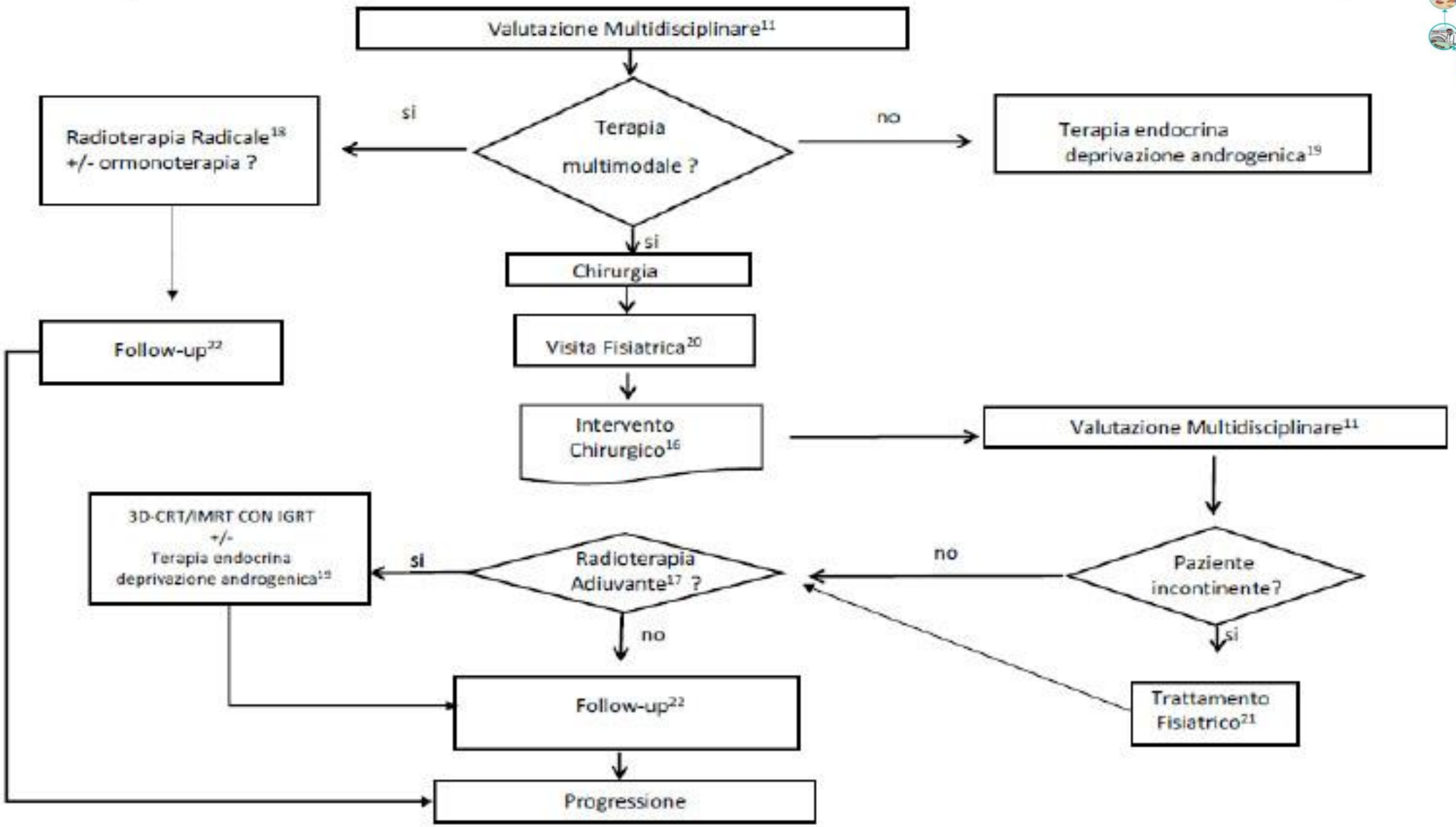
NCCN guidelines 2016

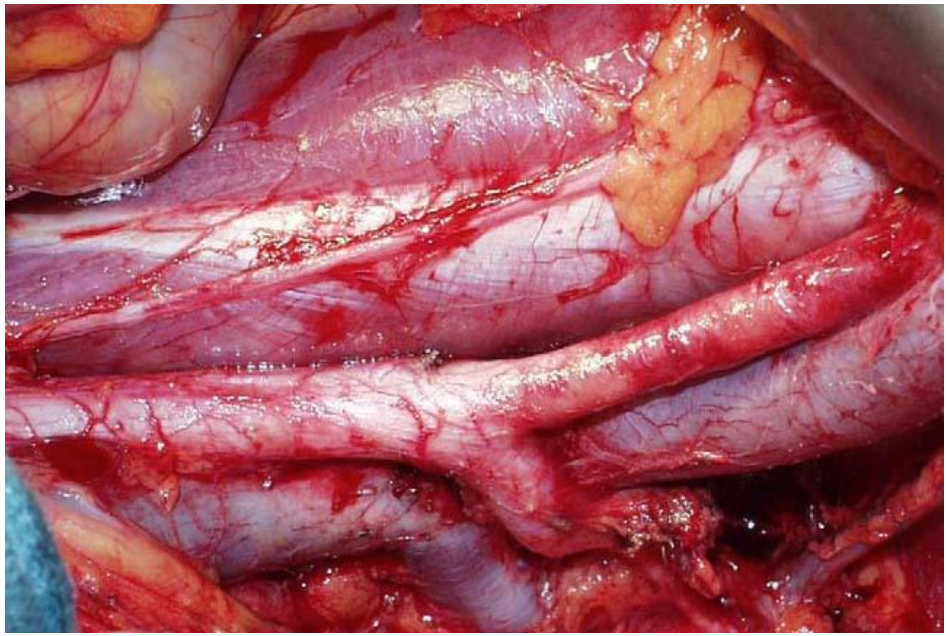
RISK GROUP	INITIAL THERAPY
High:[e] • T3a or • Gleason score 8–10 or • PSA >20 ng/mL	EBRT[h] + ADT[l] (2–3 y) (category 1) or EBRT[h] + brachytherapy ± ADT[l] (2–3 y) or EBRT[h] + ADT[l] (2–3 y) + docetaxel[p] or RP[i] + PLND
Very High: • T3b-T4 • Primary Gleason pattern 5 or • >4 cores with Gleason score 8–10	EBRT[h] + ADT[l] (2–3 y) (category 1) or EBRT[h] + brachytherapy ± ADT[l] (2–3 y) or EBRT[h] + ADT[l] (2–3 y)+ docetaxel[p] or RP[i] + PLND (in select pat or ADT[l] in select patients[q]

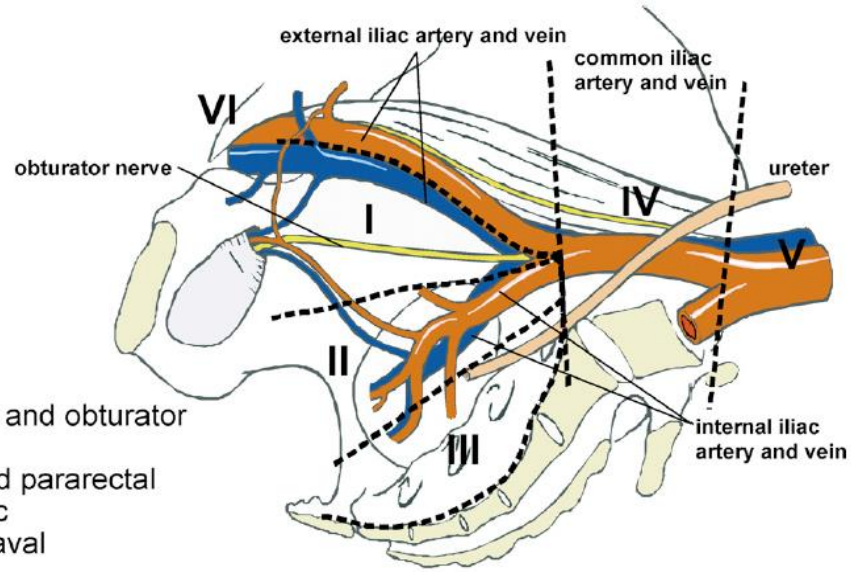
In selected patient: with no involvement of surrounding organs

Classe di Rischio Alto



RP in High-risk (PDTA)





I = external iliac and obturator
II = internal iliac
III = presacral and pararectal
IV = common iliac
V = paraaortic/caval
VI = inguinal

EUROPEAN UROLOGY 63 (2013) 450–458

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

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Platinum Priority – Prostate Cancer

Editorial by Alberto Briganti, Nazareno Suardi, Andrea Gallina, Firas Abdollah and Francesco Montorsi on pp. 459–461 of this issue

Mapping of Pelvic Lymph Node Metastases in Prostate Cancer

Steven Joniau [a,†,], Laura Van den Bergh [b,†], Evelyne Lerut [c], Christophe M. Deroose [d], Karin Haustermans [b], Raymond Oyen [e], Tom Budiharto [b], Filip Ameye [a], Kris Bogaerts [f], Hein Van Poppel [a]*

Template della linfadenectomia estesa

EAU 2015

6.2.7 *Guidelines for eLND in prostate cancer*

	LE	GR
LND is not indicated in low-risk PCa.	2b	A
eLND should be performed in intermediate-risk PCa if the estimated risk for positive lymph nodes exceeds 5%.	2b	B
eLND should be performed in high-risk PCa.	2a	A
Limited LND should not be performed.	2a	A

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Recommendation	LE	GR
Do not perform LND in low-risk PCa.	2b	A
Perform an eLND in intermediate-risk PCa if the estimated risk for positive lymph nodes exceeds 5%.	2b	B
Perform an eLND in high-risk PCa.	2a	A
Do not perform a limited LND.	2a	A

Nerve sparing

Controindicazioni

- **Malattia extracapsulare (cT2c/cT3)**
- **GS >7**

Offer nerve-sparing surgery in pre-operatively potent patients with low risk of extracapsular disease (refer to Partin tables/nomograms).	B
In high-risk disease, use multiparametric MRI as a decision-making tool to select patients for nerve-sparing procedures.	B

Malattia localmente avanzata

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any PSA any GS cT3-4 or cN+
Locally advanced

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Any T, N1, M0

Malattia localmente avanzata

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Il trattamento chirurgico dei cT3 è stato tradizionalmente sconsigliato, principalmente per l'aumentato rischio dei margini positivi e per la comparsa di metastasi linfonodali e/o a distanza

Chirurgia e PCa localmente avanzato

Radical prostatectomy for clinically advanced (cT3) prostate cancer since the advent of prostate–specific ar

Outcome of Surgery for Clinical Unilateral T3a Prostate Cancer: A Single-Institution Experience

JOH
and
Divis
+Dep

Chao-Yu Hsu[a], *Steven Joniau*[a], *Raymond Oyen*[b], *Tania Roskams*[c], *Hein Van Poppel*[a,*]

[a] *Department of Urology, University Hospitals KULeuven, Leuven, Belgium*
[b] *Department of Radiology, University Hospitals KULeuven, Leuven, Belgium*
[c] *Department of Histopathology, University Hospitals KULeuven, Leuven, Belgium*

PROCESSO MULTIDISCIPLINARE

Malattia localmente avanzata : CN0

Outcomes for Patients with Clinical Lymphadenopathy Treated with Radical Prostatectomy

Marco Moschini [a,b], Alberto Briganti [b], Christopher R. Murphy [a], Marco Bianchi [b], Giorgio Gandaglia [b], Francesco Montorsi [b], J. Fernando Quevedo [c], Rachel Carlson [d], Eugene Kwon [a], R. Jeffrey Karnes [a,]*

[a] *Department of Urology, Mayo Clinic, Rochester, MN, USA;* [b] *Unit of Urology/Division of Oncology; IRCCS Ospedale San Raffaele; URI Milan, Italy;* [c] *Division of Medical Oncology, Mayo Clinic, Rochester, MN, USA;* [d] *Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN, USA*

Outcomes: 50 cN+ vs 252 pN1 cN0

cN+ non è fattore predittivo per la CSM ***(p=0,6)***

Malattia localmente avanzata

European Association of Urology

Offer RP in a multimodality setting to patients with high-risk localised PCa and a life expectancy of > 10 years.	2a	A
Offer RP in a multimodality setting to selected patients with locally advanced (cT3a) PCa, and a life expectancy > 10 years.	2b	B
Offer RP in a multimodality setting to highly selected patients with locally advanced PCa (cT3b-T4 N0 or any T N1).	3	C

National Comprehensive Cancer Network

Regional:

Any T, N1, M0 → **EBRT^{h} + ADT^{l} (2–3 y)** or **ADT^{l}**

?

Progressione linfonodale di malattia : linfadenectomia di salvataggio

EUROPEAN UROLOGY 67 (2015) 852–863

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Review – Prostate Cancer

Editorial by Eric A. Klein on pp. 864–865 of this issue

Metastasis-directed Therapy of Regional and Distant Recurrences After Curative Treatment of Prostate Cancer: A Systematic Review of the Literature

Piet Ost[a,], Alberto Bossi[b], Karel Decaestecker[c], Gert De Meerleer[a], Gianluca Giannarini[d], R. Jeffrey Karnes[e], Mack Roach III[f], Alberto Briganti[g]*

Progressione linfonodale di malattia : linfadenectomia di salvataggio

6.10.11 ***Salvage lymph node dissection***

Novel imaging modalities improve the early detection of nodal metastases [815]. The surgical management of (recurrent) nodal metastases has been the topic of several retrospective analyses [815, 816, 817]. The majority of treated patients showed biochemical recurrence but clinical recurrence-free and cancer specific 10-year survival over 70% has been reported [818]. Biochemical recurrence rates were found to be dependent on PSA at surgery and location and number of positive nodes [577]. Addition of RT to the lymphatic template after salvage LND may improve BCR rate [819]. No level 1 evidence is available on the effects of salvage nodal dissection on survival [820].

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Progressione linfonodale di malattia linfadenectomia di salvataggio

TEAM MULTIDISCIPLINARE

Recommendation	GR
Discuss salvage lymph node dissection with men experiencing nodal recurrence after local treatment but it should be considered experimental and biochemical recurrence after salvage LND occurs in the majority of cases.	C

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Cytoreductive Radical Prostatectomy in Patients with Prostate Cancer and Low Volume Skeletal Metastases: Results of a Feasibility and Case-Control Study

Axel Heidenreich,* David Pfister and Daniel Porres

From the Department of Urology, Uniklinik RWTH Aachen, Aachen, Germany

J Urol 193 : 832, 2015

Gruppo 1 (n=23)

- PCa resecabile
- M+ ossee minime (<3)
- Assenza N+ retroperitoneali
- Assenza LMN pelviche > 3cm
- Assenza M+ viscerali
- PSA <1ng/ml dopo BAT neoadiuvante
- Firmato consenso

Gruppo 2 (n=38)

- ADT only

Malattia oligometastatica

Table 1. *Patient characteristics*

	CRP (group 1)		Control (group 2)		p Value
Mean age (range)	61	(42–69)	63.9	(47–83)	
No. age (%):					Not significant
Less than 60	7	(30.4)	9	(23.7)	
61–70	10	(43.5)	18	(47.4)	
Greater than 70	6	(26.1)	11	(28.9)	
Mean Eastern Cooperative Oncology Group performance status (range)	0.6	(0–2)	0.71	(0–2)	Not significant
Mean Charlson comorbidity score (range)	6.6	(6–9)	7.1	(6–11)	Not significant
Mean ng/ml PSA (range)	135.2	(3.5–150.4)	105.9	(45–195)	0.049
Median ng/ml 6-mo PSA (range)	0.42	(less than 0.01–2.2)	1.25	(less than 0.01–9.8)	0.052
Mean U/l baseline lactate dehydrogenase (range)	194	(165–294)	201	(153–286)	Not significant
Mean U/l baseline alkaline phosphatase (range)	105	(67–145)	108	(71–155)	Not significant
Mean mg/l baseline CRP (range)	3.6	(0.5–7.8)	3.8	(0.5–8.1)	Not significant
No. clinical stage (%):					Not significant
cT2c	7	(30.4)	10	(26.3)	
cT3a/b	16	(69.6)	24	(63.1)	
cT4	0		4	(10.5)	
Mean biopsy Gleason score	7.6		7.9		Not significant
No. biopsy Gleason score (%):					
6	0		4	(10.5)	
7 (3+4, 4+3)	5	(21.7)	11	(28.9)	
8	7	(30.4)	11	(28.9)	
9	7	(30.4)	8	(21.1)	
10	4	(17.4)	4	(10.5)	
No. skeletal metastases (%)	23	(100)	38	(100)	Not significant
Mean bone metastases (range)	2.1	(1–3)	2.5	(1–5)	Not significant
No. pelvic lymph nodes (%):	4	(17.4)*	8	(21.1)*	Not significant
Less than 2 cm	3	(13.1)	6	(15.8)	
2–3 cm	1	(4.3)	2	(5.3)	
No. suspicious retroperitoneal lymph nodes (%)	3	(13.1)	4	(10.5)	Not significant

Outcomes

- Time to biochemical progression
- Time to clinical progression
- Time to castration resistance
- OS and CSS
- Surgery related complication

Follow Up

- Ogni 3 mesi per i primi due anni
- Ogni 6 mesi per il terzo e quarto anno
- Oltre annualmente

Table 2. *Oncologic outcomes*

	Group 1	Group 2 (all)	Group 2 (adapted)*	p Value
No. pts	23	38	26	
Median mos followup (range)	40.6 (3–71)	44.0 (24–96)	42.3 (27–89)	Not significant
Median mos to castration resistant PCA (range)	40 (9–65)	29 (16–54)	35.4 (22–47)	0.014
Median mos CSS (range)	47 (9–71)	40.5 (19–75)	44.3 (21–75)	Not significant
Median mos clinical PFS (range)	38.6 (42–52)	26.5 (12–48)	32.4 (19–48)	0.032
Surgery-free survival rate (%)	100	71.1		<0.01
Overall survival rate (%)	91.3	78.9		0.048
CSS rate (%)	95.6	84.2		0.043

* Only patients with PSA less than 1.0 ng/ml after 6 months of ADT.

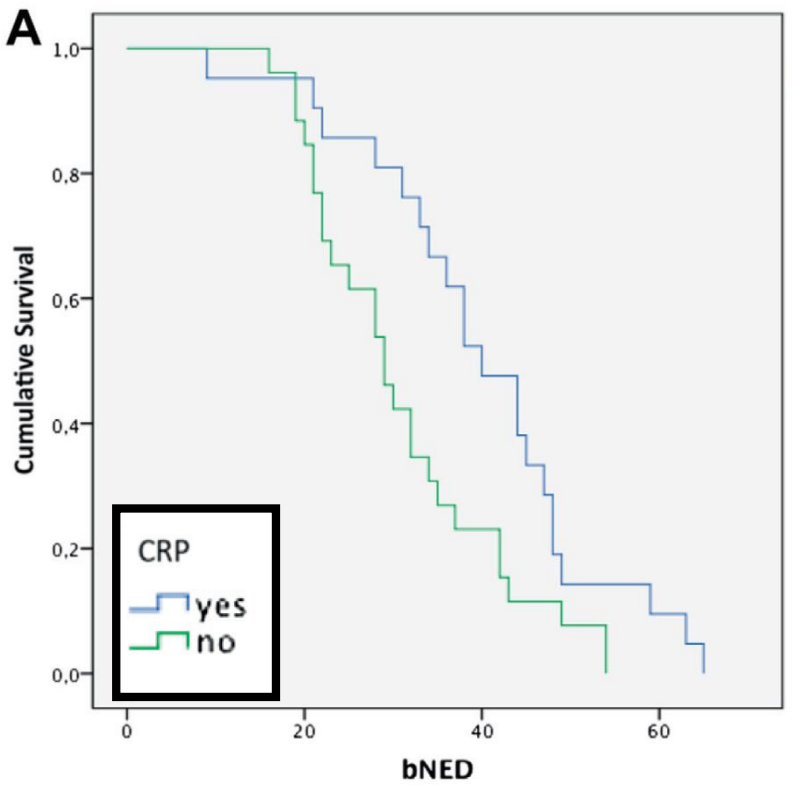

Table 3. *Complications according to Clavien-Dindo classification*

Complication Grade	No. Group 1 (%)	No. Group 2 (%)	p Value
I	4 (17.4)*	7 (18.4)	Not significant
II	2 (8.7)	4 (10.4)	Not significant
IIIa	2 (8.7)	2 (5.2)	Not significant
IIIb	1 (4.3)	9 (23.7)	0.04
IVa	0	0	
IVb	0	0	
V	0	0	Not significant

* Includes 2 patients with an anastomotic leak and prolonged catheterization times, and 2 patients with a urinary tract infection.

Malattia oligometastatica

- **CRP nei Pazienti mPCA è possibile e non incrementa le complicanze correlate alla chirurgia**

- **CRP può migliorare OS e CSS nei pazienti selezionati sulla responsività al BAT neoadiuvante**

- **Uno studio prospettico randomizzato di confronto tra BAT e CRP è in corso**

PDTA