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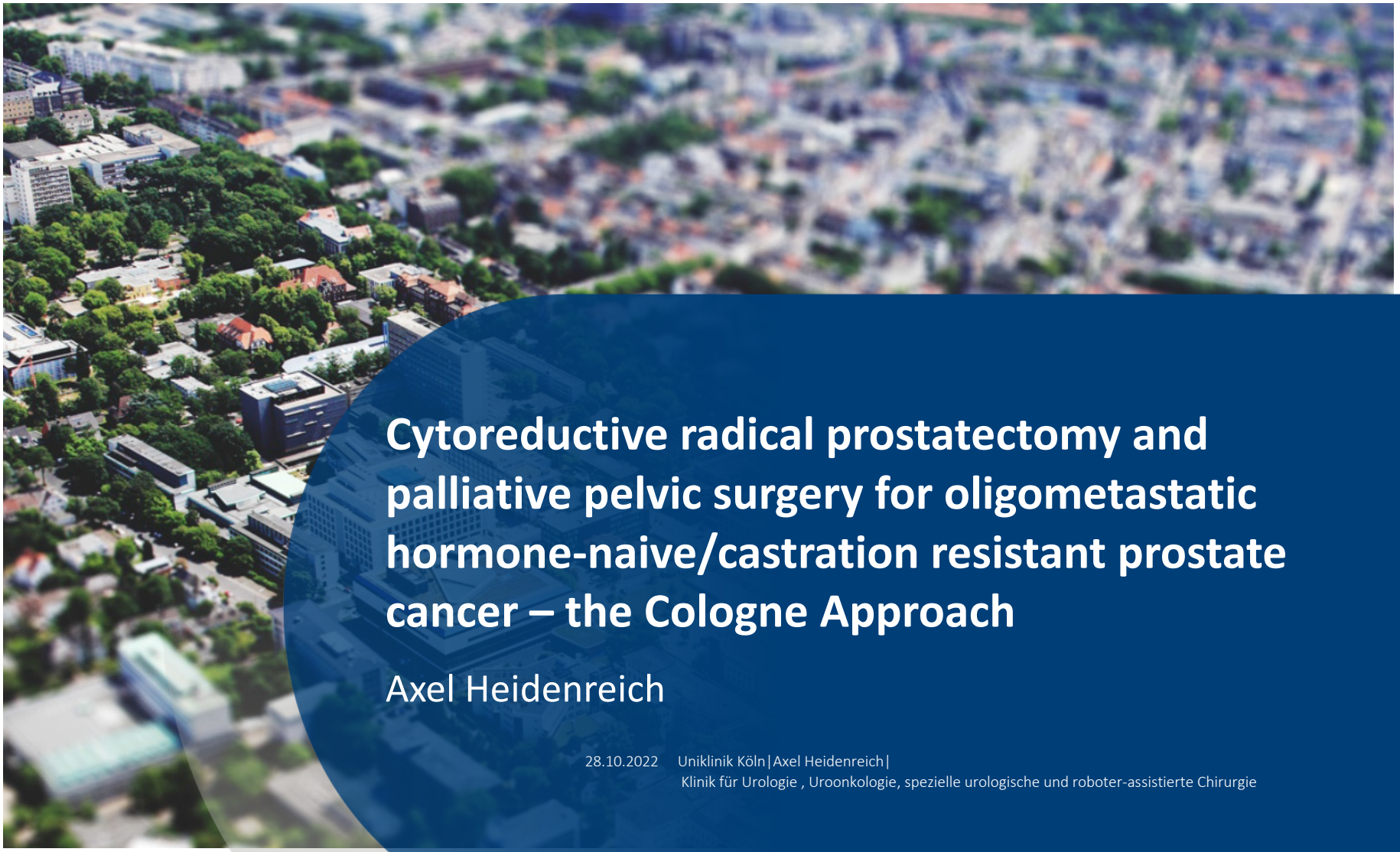

Cytoreductive radical prostatectomy and palliative pelvic surgery for oligometastatic hormone-naive/castration resistant prostate cancer – the Cologne Approach

Axel Heidenreich

Rationale of cytoreductive Prostatectomy

- first step of multimodality therapy
- elimation of intraprostatic, castration-resistant, potentially lethal prostate cancer cell clones

with the purpose

- to improve progression-free and overall survival
- to prevent local progression and associated morbidities

Persistent, biologically meaningful prostate cancer after 1 year of androgen ablation and docetaxel

Vassiliki Tzelepi et al., J Clin Oncol 2011; 29: 2574-2581

„Molecular features associated with potentially lethal prostate cancer remain in tumour cells within the microenvironment of prostate cancer„

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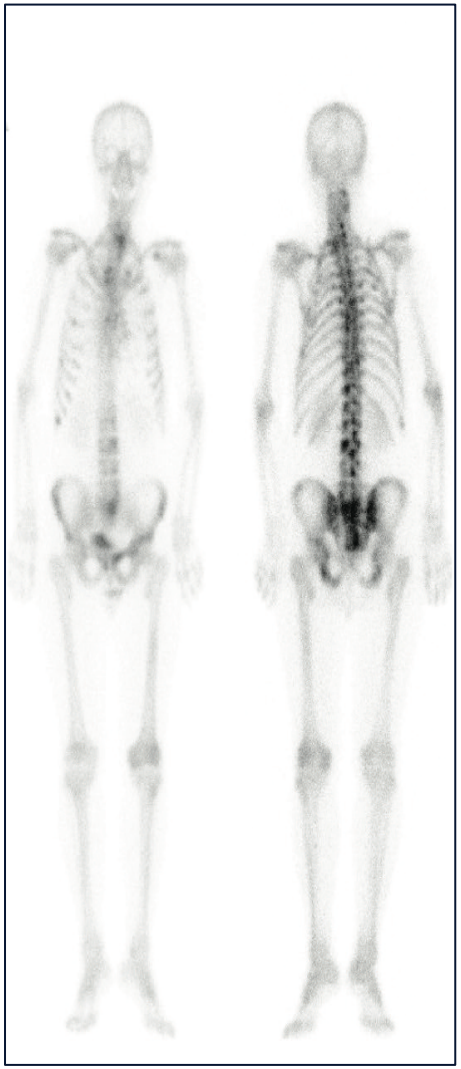
Clinical Scenario: Skeletal Metastases



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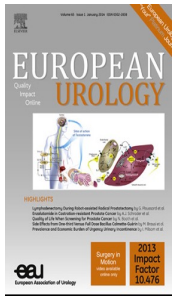
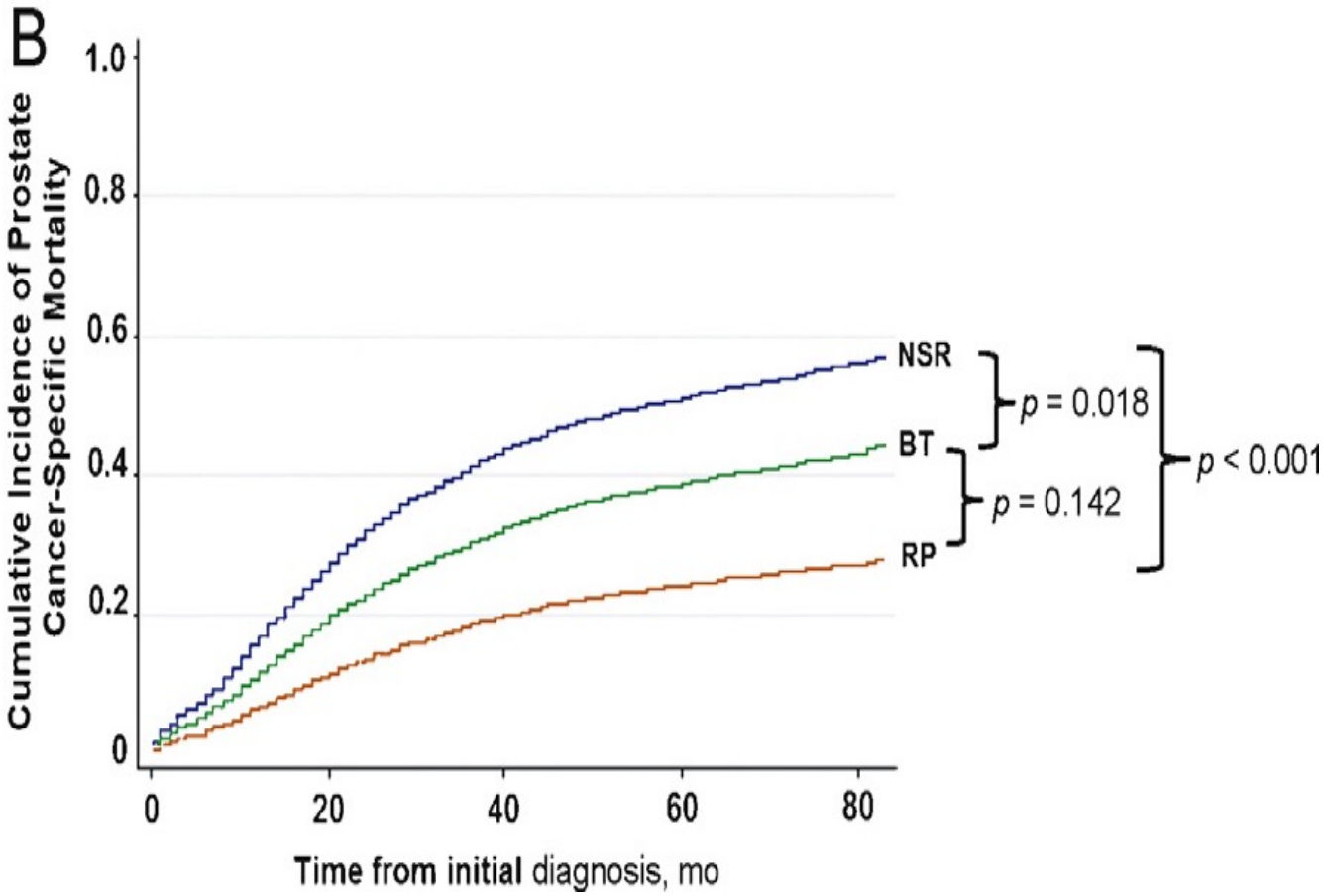


Might Men Diagnosed with Metastatic Prostate Cancer Benefit from Definitive Treatment of the Primary Tumor? A SEER-Based Study.

Culp Sh et al., Eur Urol 2014; 65: 1058 - 1066



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Cytoreductive radical prostatectomy in men with prostate cancer and low volume skeletal metastases.

Heidenreich A et al., J Urol 2015; 193: 832 - 838

Highly selected patient cohort

- Locally resectable PCA (mpMRI)
- ≤ 3 hot spots on bone scan
- pelvic lymph node metastases allowed except bulky disease
- no retroperitoneal lymph node metastases
- no visceral metastases

Therapeutic strategy

- neoadjuvant androgen deprivation (LHRH) for 6 months
- PSA⇓ < 0.4 ng/ml ➔ extended RP and extended pelvic LAD
- adjuvant ADT for 2 years

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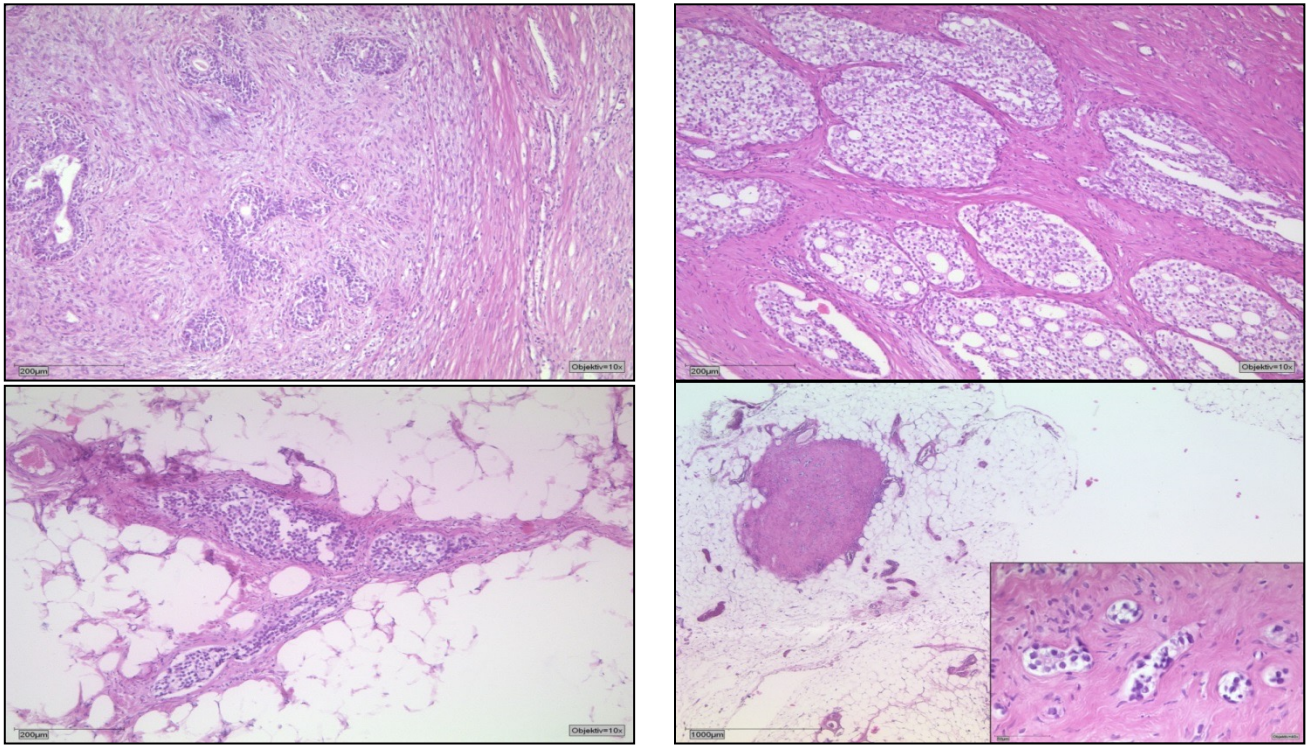
Cytoreductive radical prostatectomy in men with prostate cancer and low volume skeletal metastases.

Heidenreich A et al., J Urol 2015; 193: 832 - 838

Pathohistologic Findings	
pT2c, n (%)	5 (13.1)
pT3a, n (%)	10 (30.4)
pT3b, n (%)	17 (52.2)
pT4, n (%)	1 (4.3)
Vital PCa	**32 (100)**
Prostate volume, ml (range)	46.95 (28–85)
PCa – Volume, ml (range)	17.88 (1–64.5)
Positive surgical margins, n (%)	4 (14.3)
Positive lymph nodes, n (%)	13 (56.5)

Cytoreductive radical prostatectomy in men with prostate cancer and low volume skeletal metastases.

Heidenreich A et al., J Urol 2015; 193: 832 - 838



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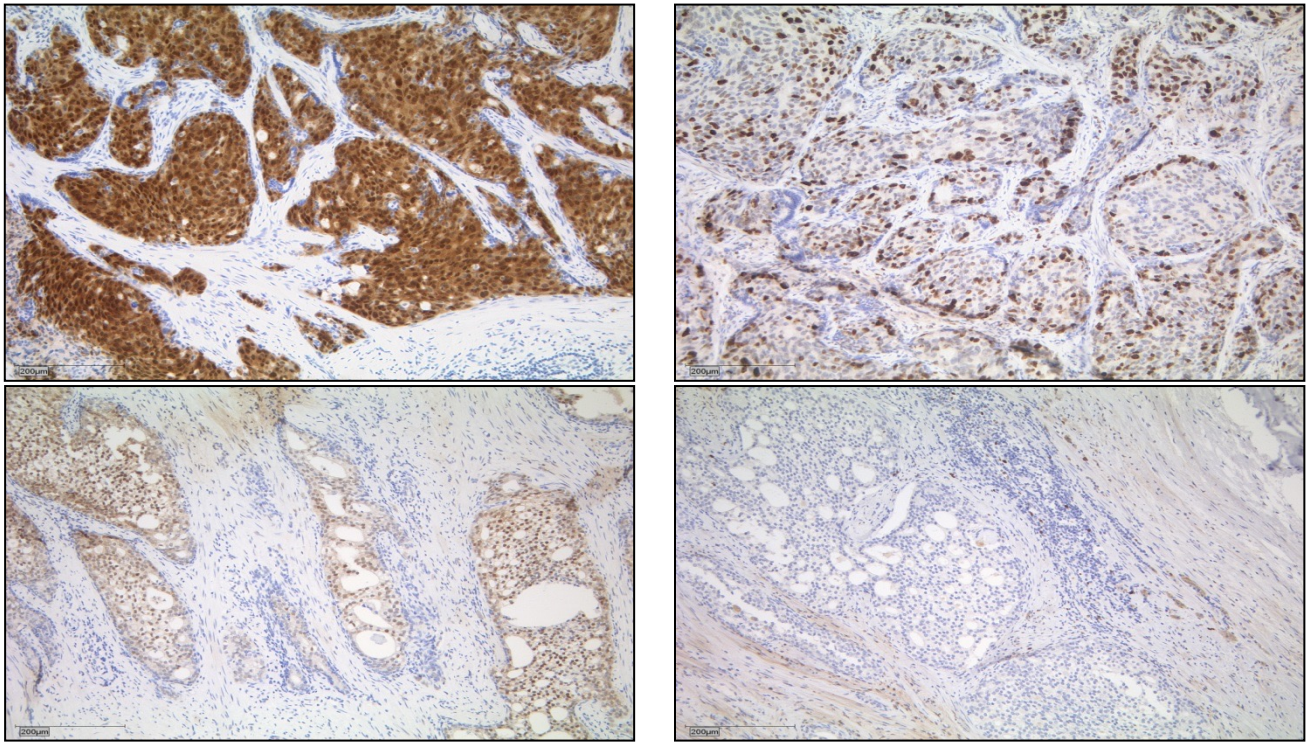

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Cytoreductive radical prostatectomy in men with prostate cancer and low volume skeletal metastases.

Heidenreich A et al., J Urol 2015; 193: 832 - 838

*Gleason 8-10 only

	cRPE	control	adapted control	P value
Patients	32	38	26	
Mean Follow-up, months	40.6 (3–71)	44 (24–96)	42.3 (27–89)	NS
Median time, months				
Clinical PFS	38.6 (22–52)	26.5 (12–48)	32.4 (19–48)	0.032
CRPC- free survival	40 (9–65)	29 (16–54)	35.4 (22–47)	0.014
CCS	47 (9–71)	40.5 (19–75)	44.3 (21–75)	NS
Freedom from surgery, %	100	71.1		0.01
Overall survival, %	91.3	78.9		0.048
CCS, %	95.6	84.2		0.043

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Cytoreductive Prostatectomy

- 113 men with biopsy-proven low volume mPCA were included in this retrospective, multi-institutional analysis
- All men underwent radical prostatectomy and pelvic lymphadenectomy, see table 1 for patient characteristics

Mean age	61 (42-69) years
Mean follow-up	53.0 (13-96) months
Median follow-up	45.7 (13-96) months
Lymph node metastases	10/113 (8.8%)
Low volume skeletal metastases	85/113 (75.2%)
High volume skeletlal metastases	25/113 (22.1%)
Visceral metastases	4/113 (3.5%)
RPE/RALP	104/9 (92%/8%)
No/limited/extended pLAD	1.8%/8.8%/89.4%
Neoadjuvant ADT	80/113 (70.8%)

Heidenreich A et al., Eur Urol Oncol 2018; 1: 43 - 48

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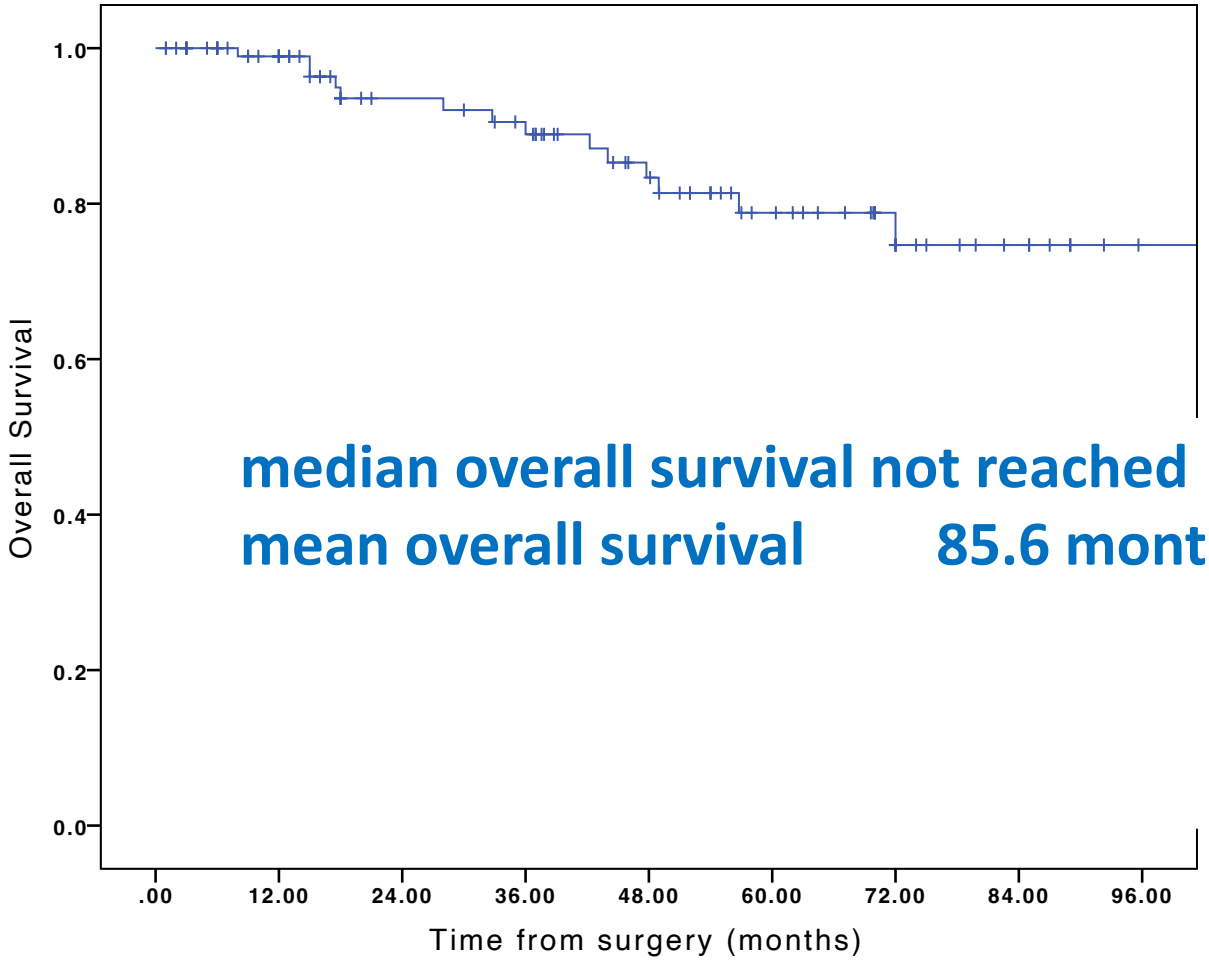
The role of cytoreductive radical prostatectomy (cRP) in men with hormone-sensitive, metastatic prostate cancer (mPCA)



median overall survival not reached

mean overall survival 85.6 months

Heidenreich A et al., Eur Urol Oncol 2018; 1: 43 - 48

UNIKLINIK KÖLN

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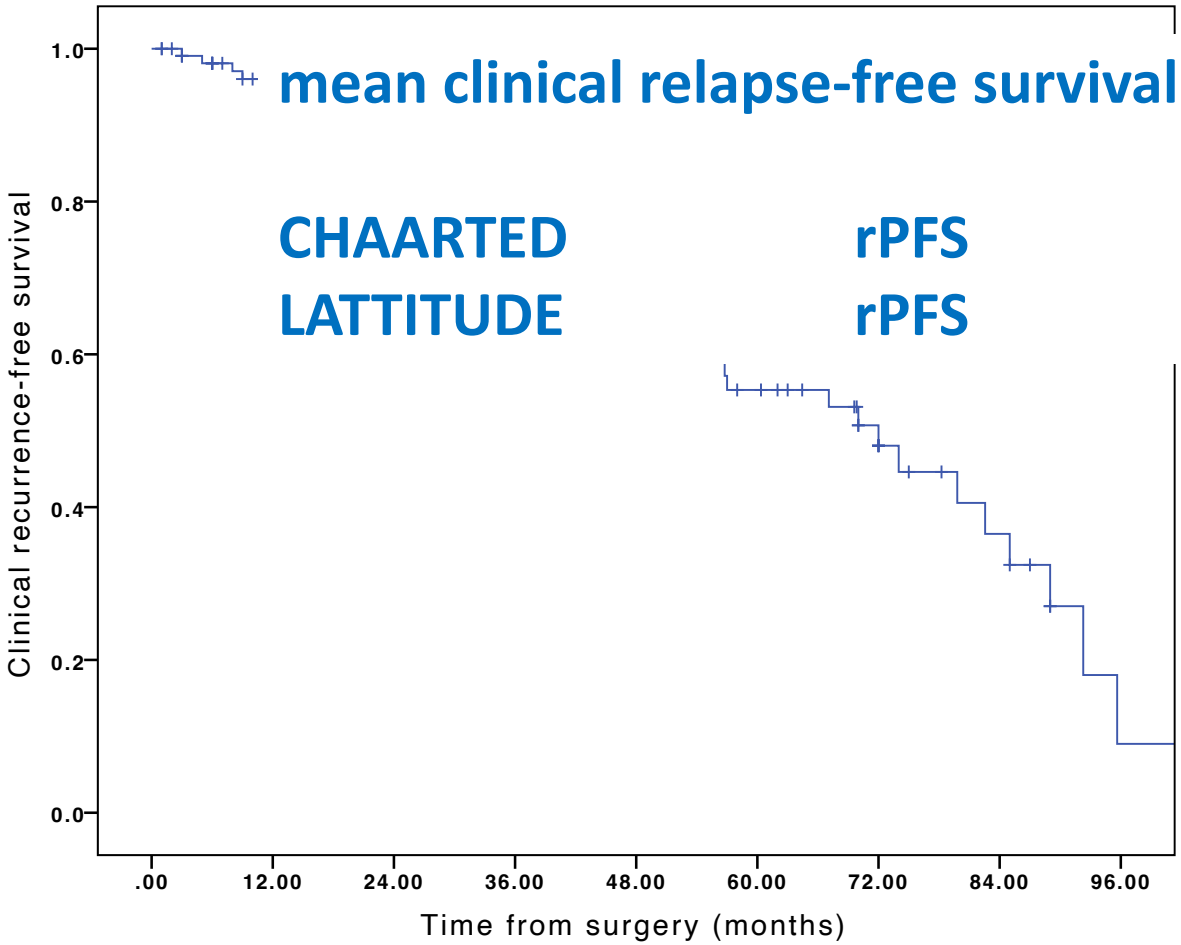

Heidenreich A et al., Eur Urol Oncol 2018; 1: 43 - 48

UNIKLINIK KÖLN

The role of cytoreductive radical prostatectomy (cRP) in men with hormone-sensitive, metastatic prostate cancer (mPCA)

- single-center experience:
- n = 134 patients with mHSPC
- neoadjuvant ADT for 6 months
  - n = 34 (25.4%) ADT
  - n = 15 (11.2%) ADT + DOC
  - n = 85 (63.4%) ADT + Abi/Apa/Enza

Patient characteristics

- n = 115 (85.6%) low risk, n = 19 (13.4%) high risk
- M1a 28 (20.9%)
- M1b 98 (73.1%)
- M1c 8 (6.0%)

- median Follow-up: 53.7 (4-168) months

Heidenreich A et al., 2022, submitted

UNIKLINIK KÖLN

The role of cytoreductive radical prostatectomy (cRP) in men with hormone-sensitive, metastatic prostate cancer (mPCA)

Results

• pT0	3	2.2%
• pT2a-c	21	15.7%
• pT3a-b	105	78.3%
• pT4	5	3.7%
• pN+	96	71.7%

No difference with regard to type of ADT

Complications

• Clavien-Dindo 3a-b	13 (9.7%)
• Clavien-Dindo 4	2 (1.5%)

Oncological Outcome

• CSS	88.1%
• cPFS	53%
• local relapse	00%

Predictors of Outcome

CSS

• high risk	HR = 1.49, p=0.03
• PSA decrease ≤ 60%	HR = 1.37, p=0.03

OS

• high risk	61.9% vs 92.8%, p=0.002)

Heidenreich A et al., 2022, submitted

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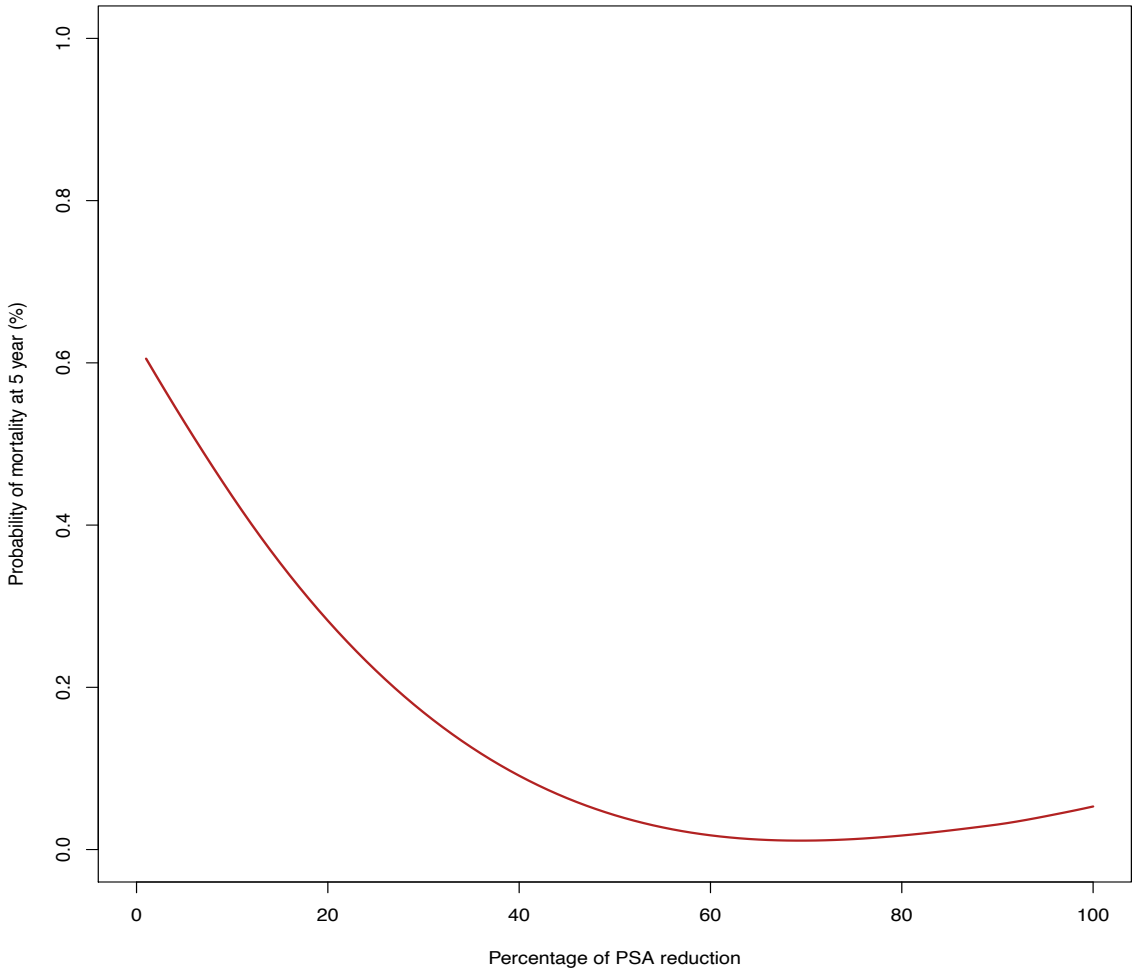
External Validation of the Cologne Criteria to select the best candidates for cytoreductive radical prostatectomy

Axel Heidenreich, Giorgio Gandaglia, David Pfister, Shahrokh Shariat, Bernhard Grubmuller, Nicola Fossati, Giuseppe Fallara, Antony Pellegrino, R. Jeffrey Karnes, Francesco Montorsi, Alberto Briganti

EAU, 2020



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Radical cytoreductive prostatectomy in men with prostate cancer and oligometastatic disease. Heidenreich A, Pfister D, Curr Opinion Urol 2020; 30: 90-97

Author	Type of study	cRP	Control group	Complications	Follow-up (months)	PFS (months)	OS	CSS
Heidenreich	Case–control	23	23	13%	34.5 vs. 47.1	38.6 vs. 26.5, $P=0.032$	95.6 vs. 84.2%, $P=0.043$	
Culp	SEER data, retrospective	245	7811	No data	16.0	No data	67.4 vs. 22.5%, $P<0.001$	75.8% vs. 48.7%, $P<0.001$
Sooriakumaran	Retrospective, multiinstitutional	106	None	20.8%	22.8	No data	88.7%	88.7%
Gratzke	Cancer registry	74	None	No data	No data	No data	55 vs. 21% at 5 years, $P<0.01$	
Steuber	Case–control	43	40	7 vs. 35%	32.7 vs. 82.2			
Leyh-Bannurah	SEER data, retrospective		None	No data	43.5 vs. 31.0	No data	–	65 vs. 52%, $P<0.001$
Heidenreich	Retrospective, multiinstitutional	113	None	9.7%	53.6	72.3	85.6	

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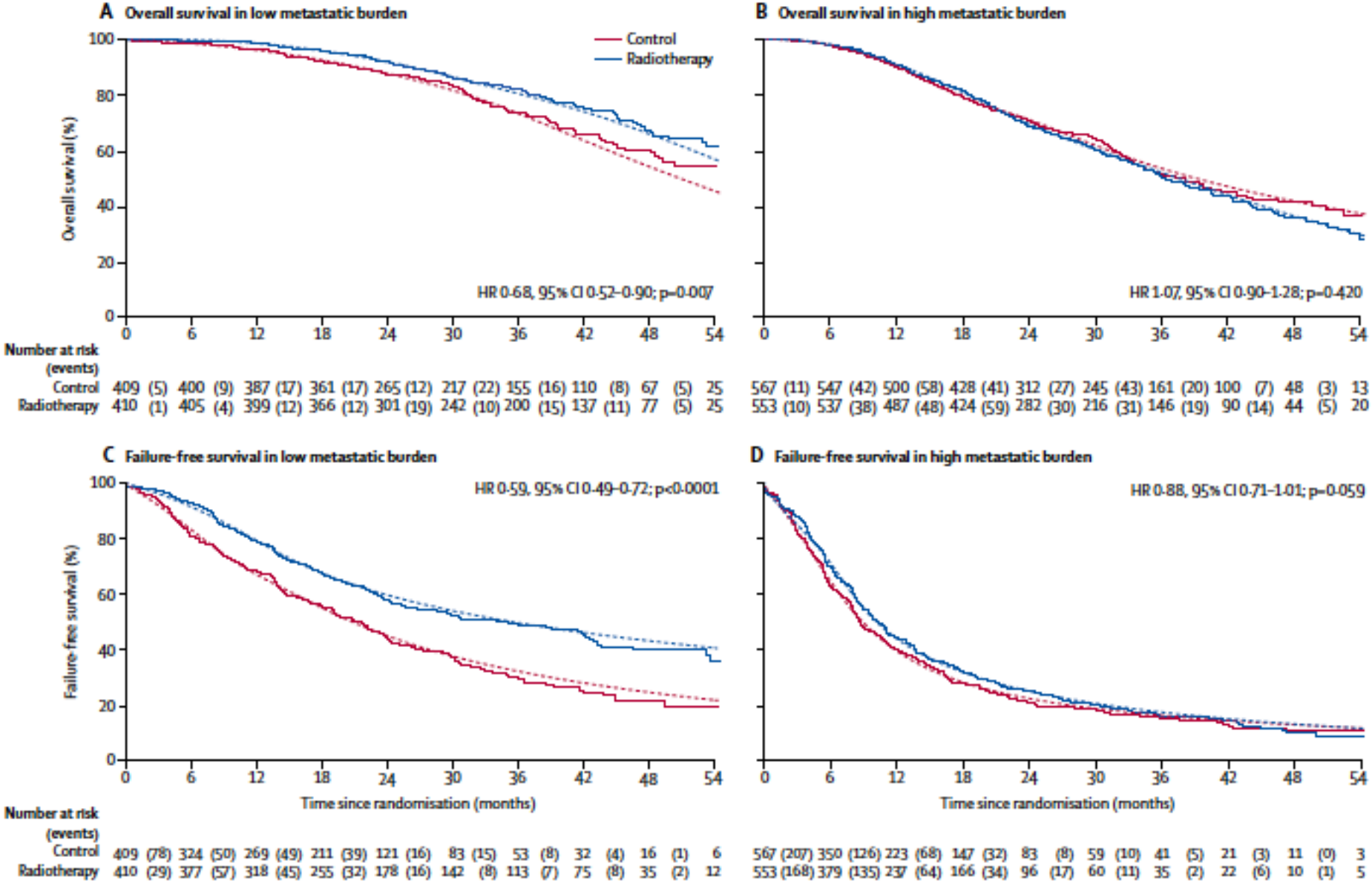
Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial.

Parker C et al., Lancet Oncol 2018; 392: 2353



Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. Parker CC et al., Lancet 2018; 392: 2353-66

	Adjusted hazard ratio (95% CI)	Survival at 3 years*		Restricted mean survival time (months)*		
		Control	Radiotherapy	Control	Radiotherapy	Difference (95% CI)
Symptomatic local event-free survival						
All patients	1·07 (0·93–1·22)	57%	55%	38·2	37·2	–1·1 (–3·1 to 0·9)
Low metastatic burden	0·82 (0·64–1·05)	65%	72%	41·6	44·0	2·4 (–0·7 to 5·4)
High metastatic burden	1·23 (1·05–1·46)	50%	43%	35·8	32·2	–3·6 (–6·2 to –1·0)

28% der low volume und **57%** der high volume Patienten mit symptomatischer lokaler Progression

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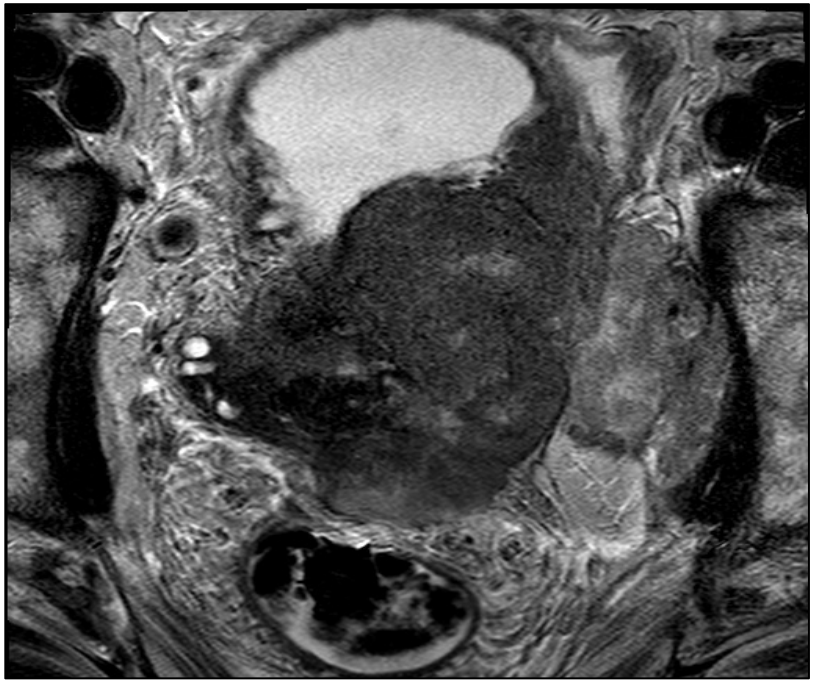
Palliative pelvic surgery in prostate cancer

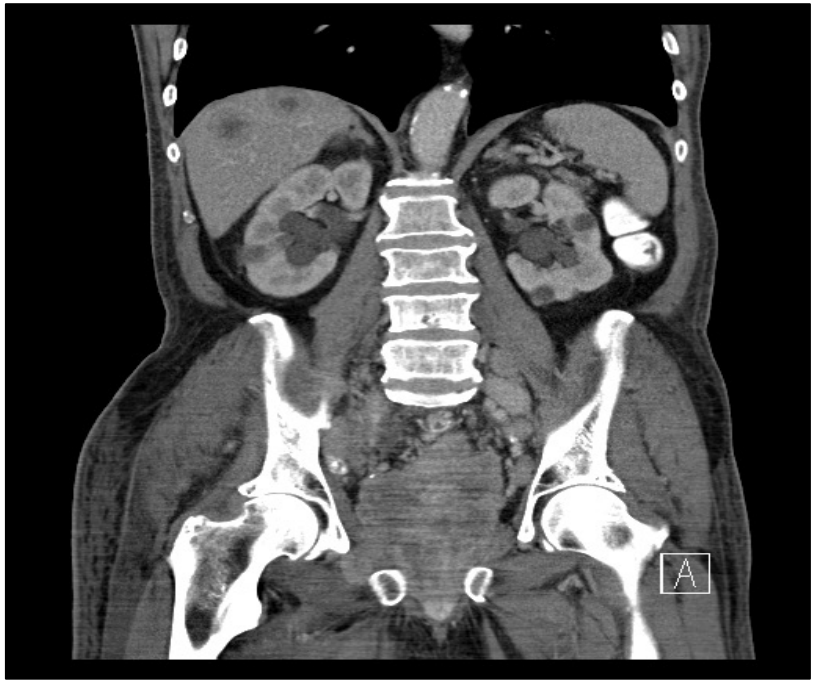
28.10.2022 Uniklinik Köln|Axel Heidenreich|
Klinik für Urologie , Uroonkologie, spezielle urologische und roboter-assistierte Chirurgie

The problem

- Development of new drugs (i.e. Abirateron, Enzalutamide) improved life expectancy from 20 months to about 80 months in patients with CRPC
- Higher frequency of complications of the lower and upper urinary tract system due progression of the prostate itself
- ADT exerts a fundamental impact on metastases, effects on local tumor growth are less prominent
- One third of CRPC patients will develop significant local complications as a result of local progression

Locally advanced, progressive castration-resistant prostate cancer (mCRPC)





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Which way to go?

or find an individual solution

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Patients and Methods I
N = 103 (current status n = 136)

Patients (n = 103)	
Mean age (years)	64.6 (42-85)
Mean follow-up (months)	36.5 (2-104)
Treatment at initial diagnoses	
Radical prostatectomy	19 (18.4%)
Radiation therapy	35 (34.0%)
Androgen deprivation therapy	49 (46.7%)
Treatment sequenzing following therapy	
Salvage RT + ADT + ARI	42 (40.8%)
ADT + ARI + docetaxel	32 (34.9%)
ADT + ARI + docetaxel + 2nd ARI	25 (24.3%)
Multivisceral surgery	
Mean PSA – level (ng/ml)	13.4 (3.4 – 135.7)
ECOC 0 - 1	101 (98.1%)

Heidenreich A et al., BJU Int 2020; 126: 342 - 349

Patients and Methods II
N = 103

Preoperative symptoms (multiple options possible):	
Lower urinary tract obstruction:	64 (62.1%)
Upper urinary tract obstruction:	57 (55.3%)
Gross hematuria +/- blood transfusion:	37 (35.9%)
Refractory pelvic pain:	18 (17.5%)
Obstructive ileus:	13 (12.6%)
Rectal infiltration:	11 (10.7%)

Heidenreich A et al., BJU Int 2020; 126: 342 - 349

Preoperative Evaluation

- MRI of the small pelvis for assessment of local extension of disease
- urethrocystoscopy +/- bladder neck biopsy to assess infiltration of the bladder
- Rectoscopy to assess intraluminal or submucosal rectal infiltration
- serum albumine as an indicator for potential malnutrition & serum CRP as an indicator for activation of immune cascade

Heidenreich A et al., BJU Int 2020; 126: 342 - 349

Surgical Strategy

Surgical intervention	
Radical prostatectomy, bladder neck closure, continent vesicostomy	9 (8.7%)
Radical cystoprostatectomy, urinary diversion Ileum conduit Ureterocutaneostomy	81 (78.6%)
Anterior and posterior Exenteration	23 (22.3%)

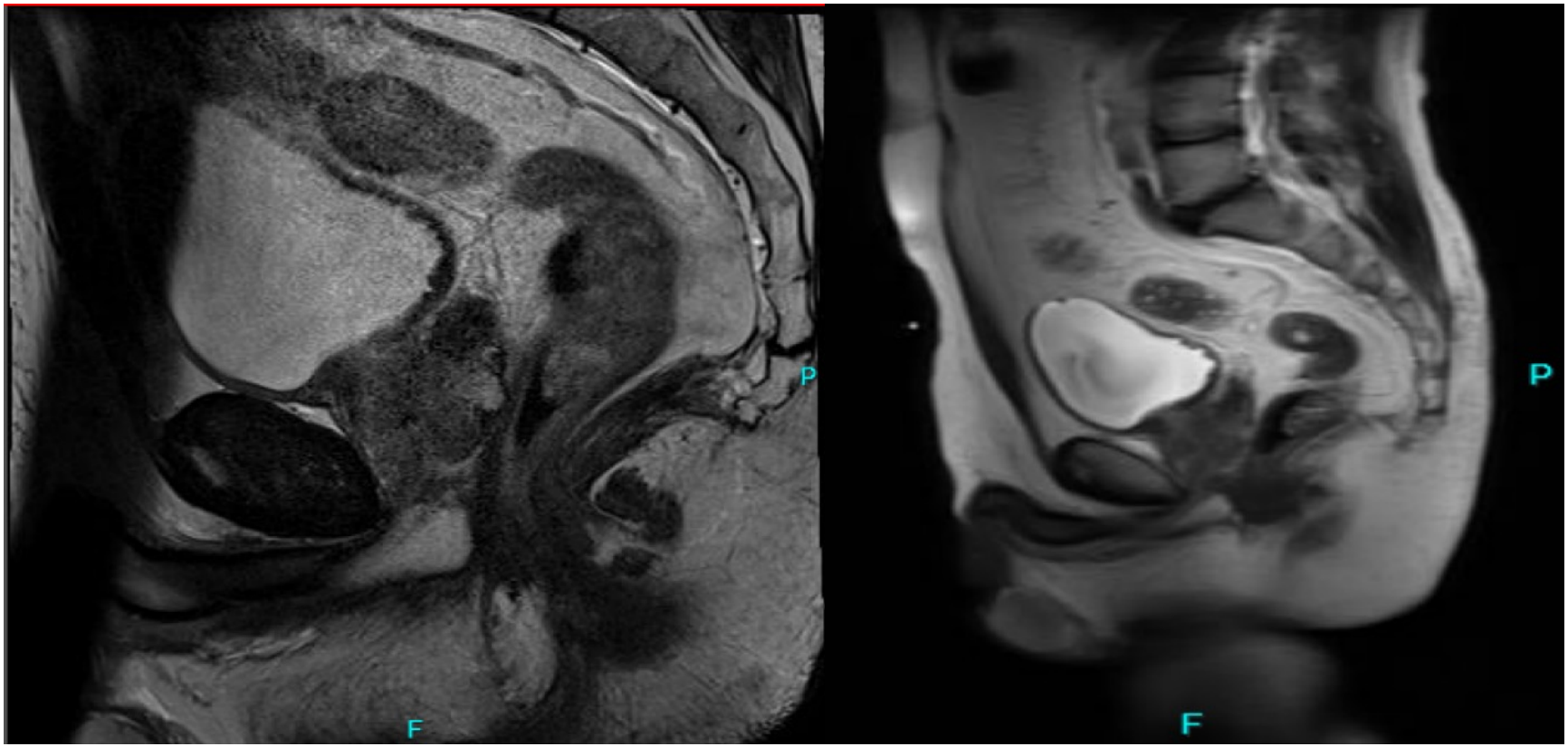
perioperative Characteristics	
Mean OR time	271 (210-371) Min
Mean blood loss	450 (300 – 780) ml
HB preoperative/HB postoperative	12.2/10.1 g/dl
Transfusion rate	15 (14.6%)
Mean time of hospitalisation	14.8 (10-41) Tage

Heidenreich A et al., BJU Int 2020; 126: 342 - 349

Operationsstrategie

Surgery: Radical prostatectomy, bladder neck closure, continent vesicostomy

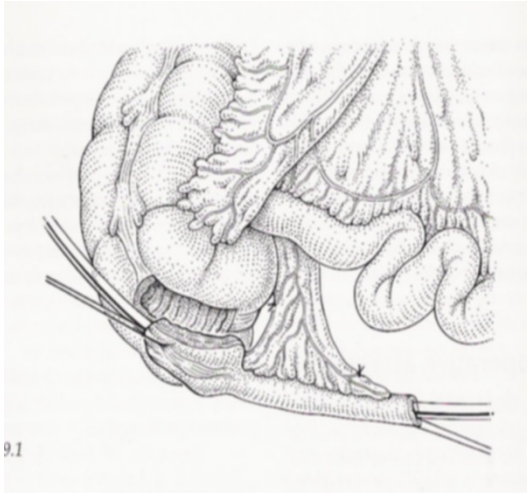
Indication: locally advanced PCA with infiltration of prostate apex and external urinary sphincter

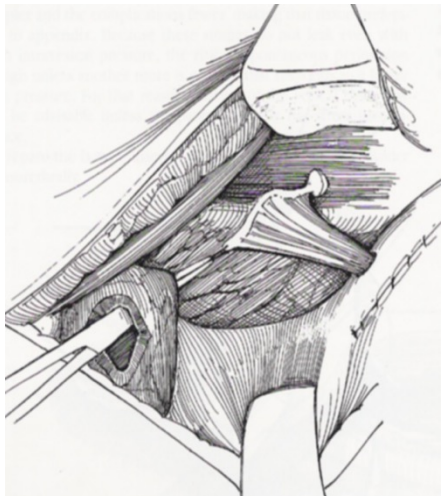


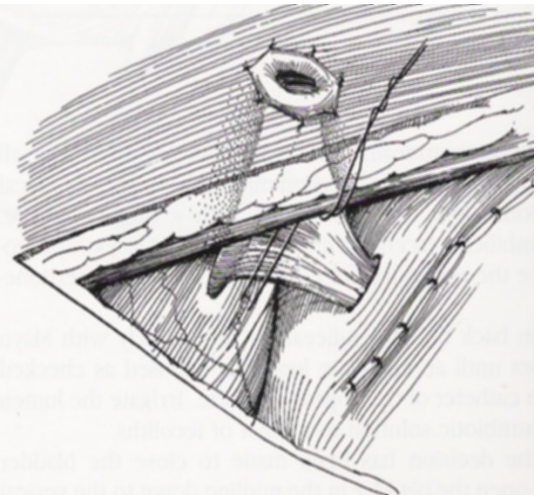
Heidenreich A et al., BJU Int 2020; 126: 342 - 349

Surgical Strategy

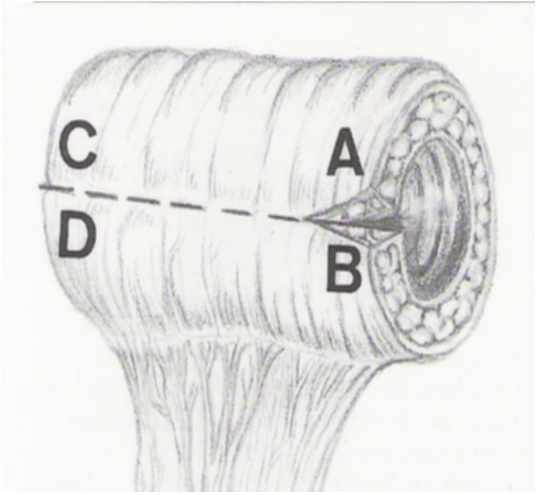
Appendicovesicostomy

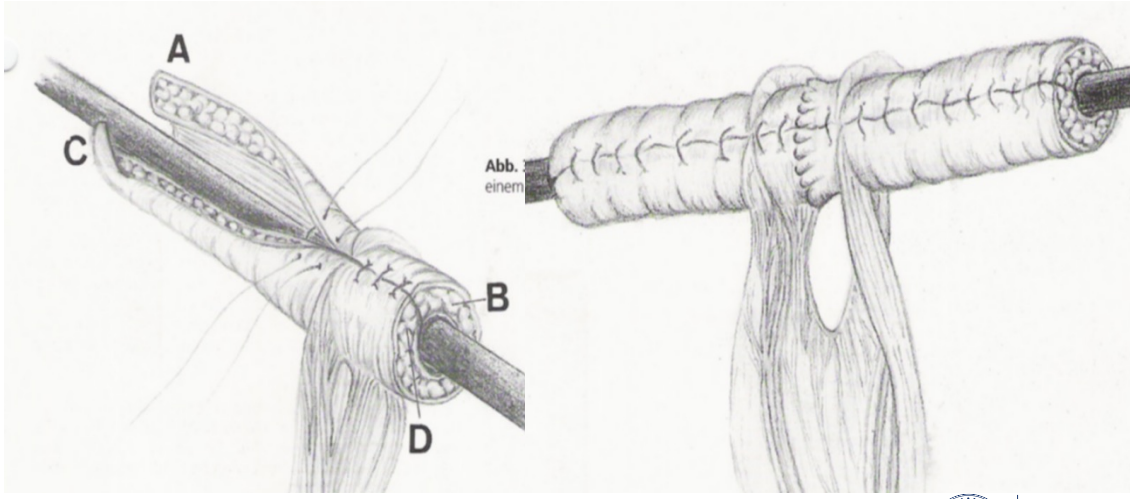






Montie - Stoma





Albers P, Heidenreich A (Hrsg), Standardoperationen in der Urologie, Thieme Verlag, 2022

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Surgical Strategy

surgery: radical cystoprostatectomy and urinary diversion (n = 81)

indication: locally advanced PCA with infiltration of bladder neck and/or infiltration of dorsal bladder

Heidenreich A et al., BJU Int 2020; 126: 342 - 349

Surgical Strategy

surgery: radical cystoprostatectomy and urinary diversion (n = 81)

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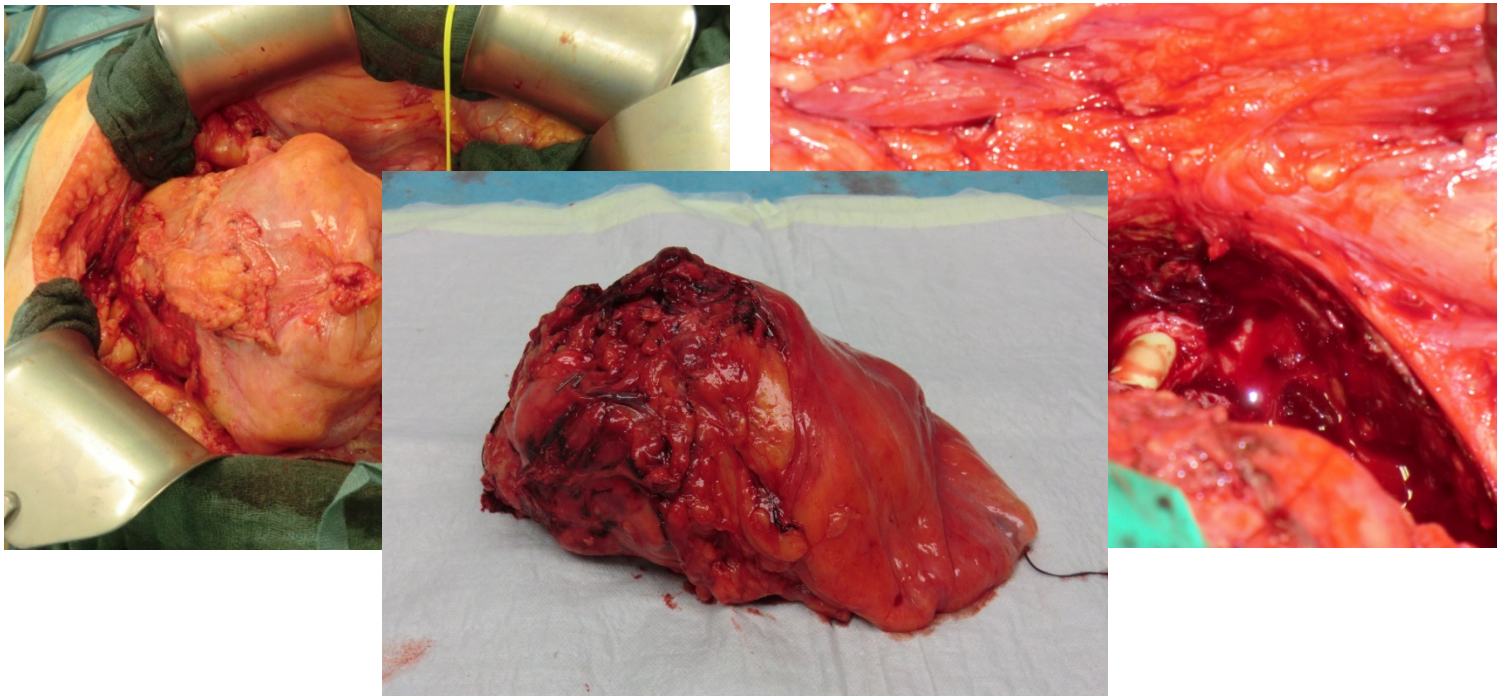

pT4 pN0 (0/26) L0, V1 R0, Gleason Score 10

Heidenreich A et al., BJU Int 2020; 126: 342 - 349

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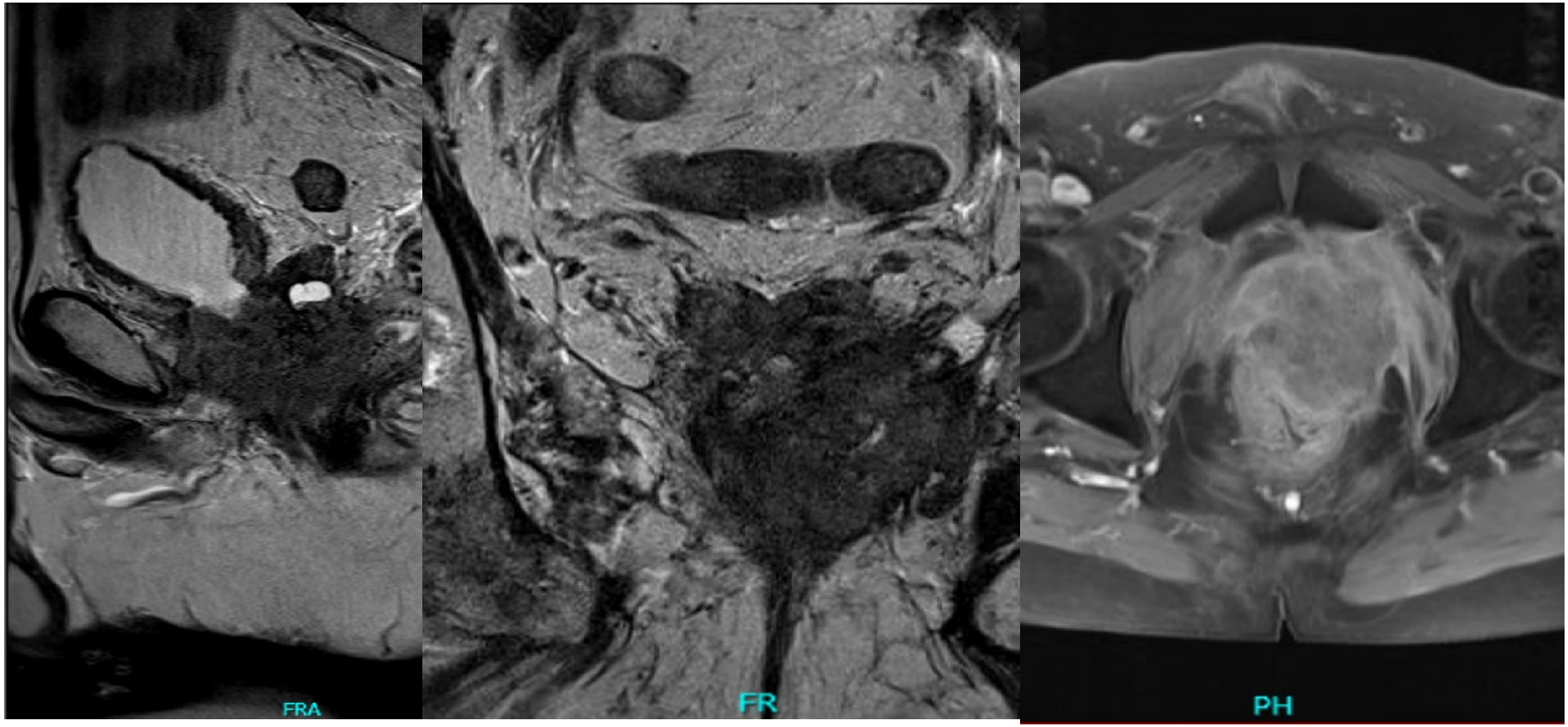
Surgical Strategy

surgery: anterior and posterior exenteration (n = 23)
indication: locally advanced PCA with infiltration of urinary bladder and rectum or sigma



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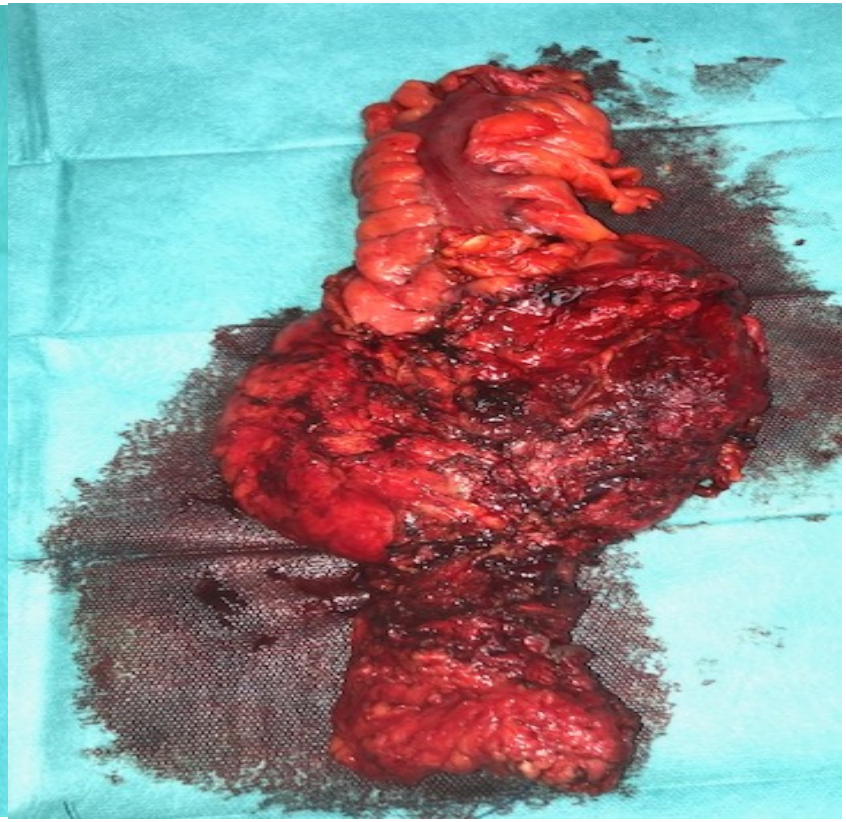


Heidenreich A et al., BJU Int 2020; 126: 342 - 349

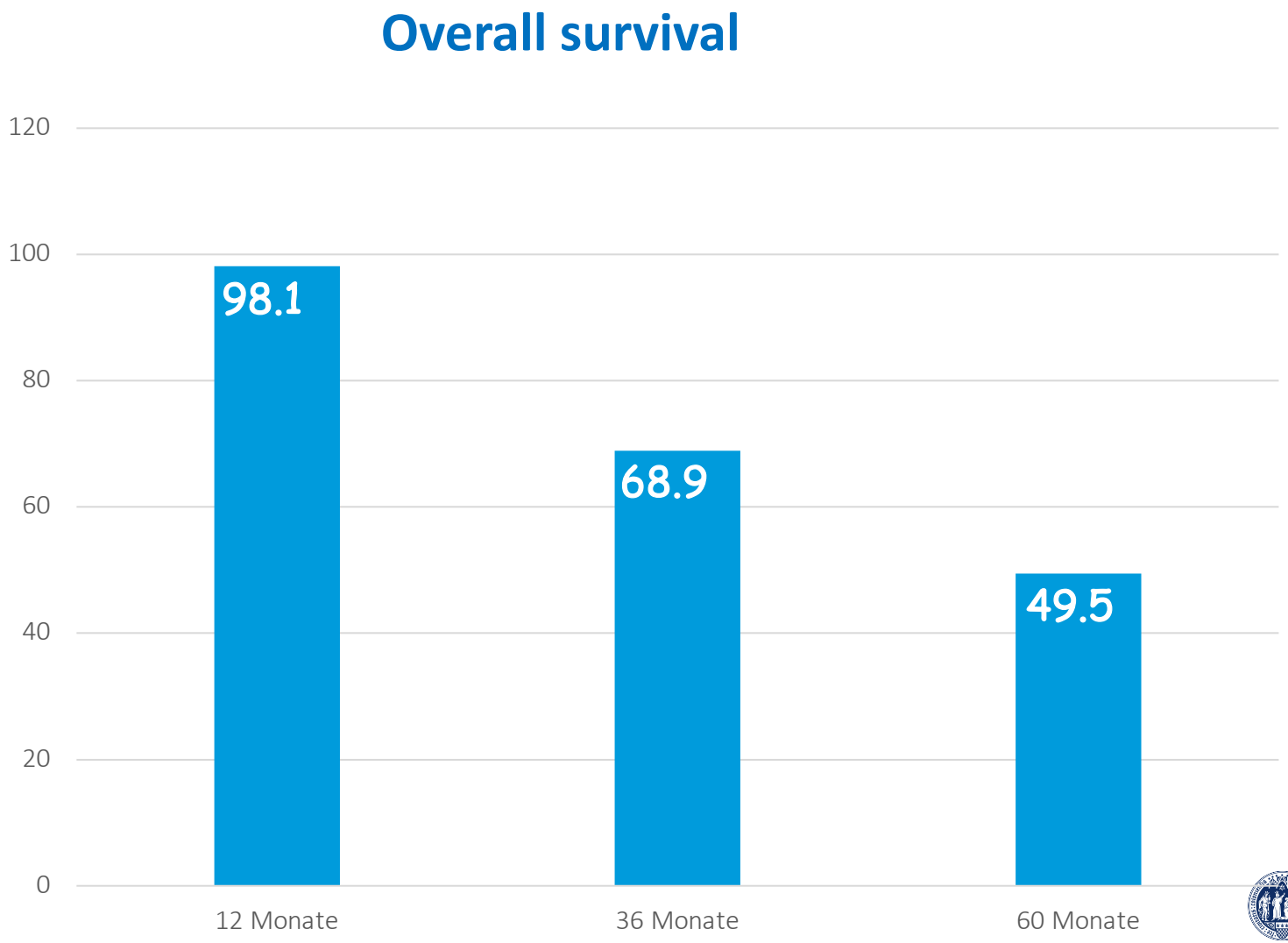
Complications

Classification	
Clavien - Dindo 2	29 (28.2%)
Clavien – Dindo 3 3 wound revision 2 symptomatic lymphocele 1 ureteroileal anastomotic insufficiency 1 stenosis of efferent limb of continent pouch	13 (12.8%)
Clavien – Dindo 4 5 pulmonary emboli 2 obstructive Ileus due to scar/volvulus	6 (5.8%)
Clavien – Dindo 5 aspiration pneumonia	1 (0.9%)

Heidenreich A et al., BJU Int 2020; 126: 342 - 349

Oncological results

mean Follow-up: 36 (2 – 104) months



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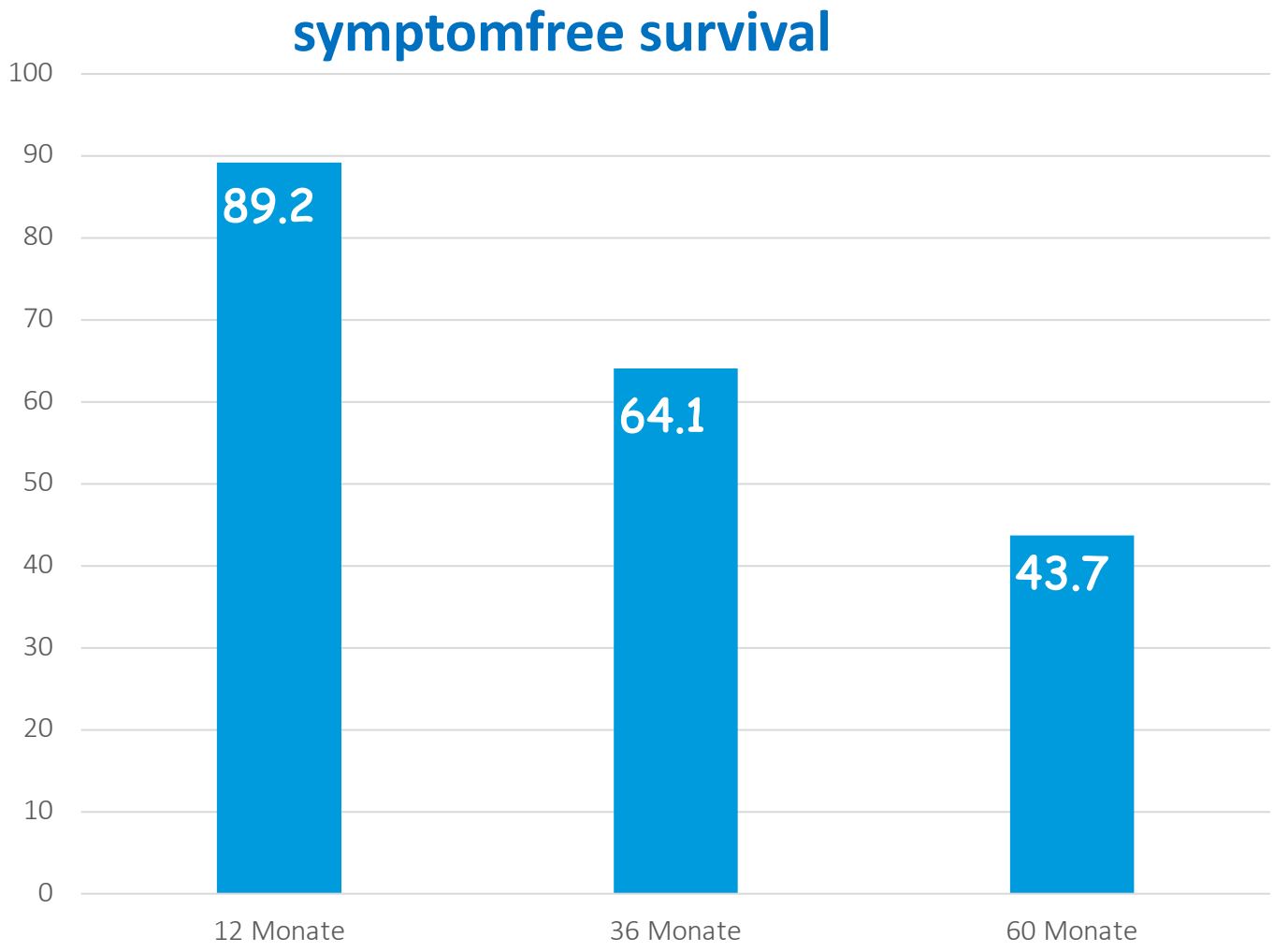
Oncological Outcome

mean Follow-up: 36 (2 – 104) months



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TOTAL PELVIC EXENTERATION: EFFECTIVE PALLIATION OF PERINEAL PAIN IN PATIENTS WITH LOCALLY RECURRENT PROSTATE CANCER

ASHISH M. KAMAT, SAMUEL F. HUANG, CARLOS E. BERMEJO, CHARLES J. ROSSER, CURTIS A. PETTAWAY, PETER W. T. PISTERS, DARRIN P. GUITREAU AND LOUIS L. PISTERS*,†

From the Departments of Urology (AMK, SFH, CEB, CJR, CAP, DPG, LLP) and Surgical Oncology (PWTP), The University of Texas M. D. Anderson Cancer Center, Houston, Texas

- palliative effect of anterior exenteration for locally advanced and symptomatic prostate cancer
- n = 14 with locally advanced and locally recurrent prostate cancer => radical cystoprostatectomy, ileum conduit
- n = 7 with significant complications (pulmonary emboli, ileus, wound infection, stomal stenosis, intrapelvic abscess)
- n = 11 (78.6%) with complete eradication of symptoms
- Mean symptom-free survival: 14.1 months

Safety, Efficacy and Impact on Quality of Life of palliative Cystoprostatectomy for advanced Prostate Cancer

Bhanvadia RR et al., 2019, J Urol submitted

- palliative effect of anterior exenteration for locally advanced and symptomatic prostate cancer
- n = 17 with locally advanced and locally recurrent prostate cancer => radical cystoprostatectomy, ileum conduit
- mean Follow-up: 1.7 years
- n = 14 (82%) with complete eradication of symptoms
- Mean symptom-free survival: 18.2 months

Thank you for your attention

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