

**RADIOCHEMIOTERAPIA NEOADIUVANTE  
SEGUITA DA CHIRURGIA RADICALE  
NEL CANCRO CERVICALE LOCALMENTE AVANZATO:  
ANALISI DEFINITIVA DEL PATTERN DI  
COMPLICANZE POSTOPERATORIE**

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## CH dopo RT/CT: Ruolo clinico dibattuto

Studi retrospettivi o fase II

Eterogeneità del campione esaminato



Bassi livelli di evidenza su reale  
efficacia/necessità

Presunta maggiore tossicità  
(trattamento trimodale)

Interdisciplinarietà





Studio randomizzato

## Cetina L. Annals of Oncology 2013

211 IB2-IIB

CRT 50 Gy  
CDDP+Gem

- BRT (100)

- CH (isterectomia radicale-PIVER III) (111)

FUP mediano 36 mesi (3-80)

Fallimenti

- BRT 15%

- CH 11.7%

- 10% locali
- 5% sistemici



- 7% locali
- 5.4% sistemici

P=0.918



Tossicità tardiva

Event	BCT arm (100)		RH arm (111)		<i>p-value</i>
	G1	G2	G1	G2	
Proctitis	22	36	2	8	0.0750
Cystitis	11	36	3	2	
Hydronephrosis	4	32	2	5	
Grade	G3	G4	G3	G4	<i>p-value</i>
Proctitis	2	2	2	0	0.5303
Cystitis	1	2	0	0	
Hydronephrosis	0	0	0	0	

BRT

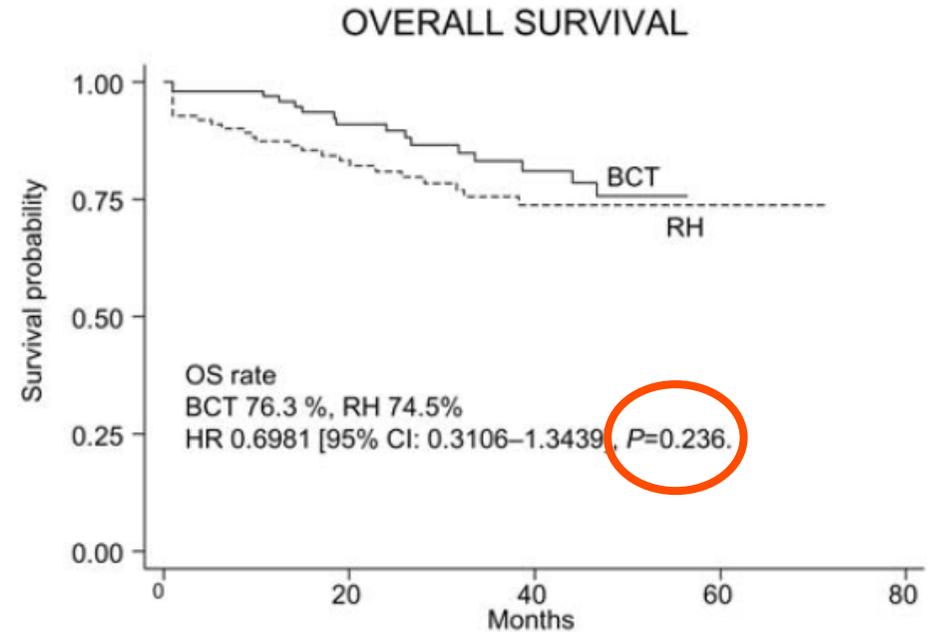
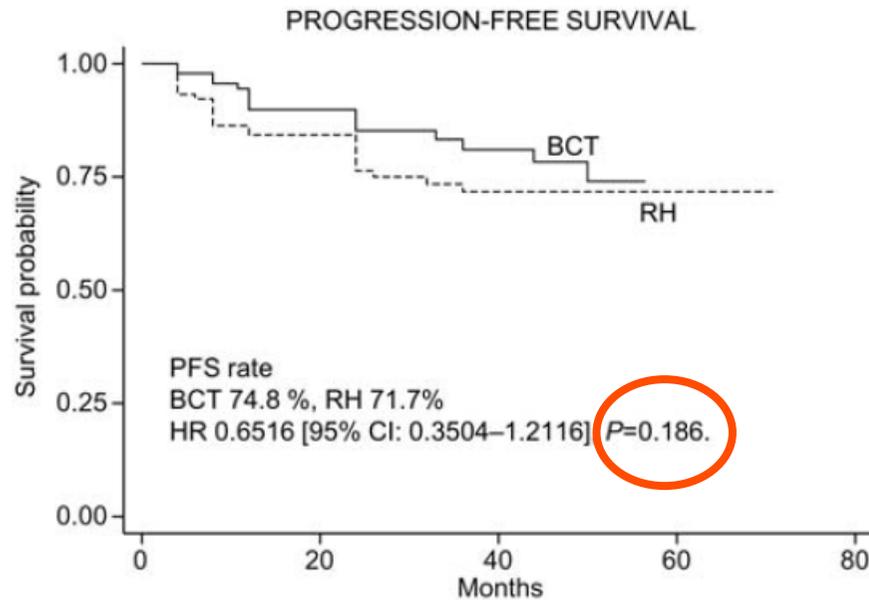
- 50% pz G1-2 proctite e cistite
- 2% pz G3
- 2% pz G4

CH

- 3.4% chirurgia per linfoceli
- 2.3% chirurgia fistole ureterocut.



Studi randomizzati



CH dopo RT/CT **NON** è superiore allo standard (BRT)  
**MA**

- isterectomia radicale dopo RT/CT: fattibile e sicura
- CH invece di BRT dopo RT/CT **NON** compromette OS
- particolare rilevanza in contesti con risorse BRT limitate o assenti

## CH dopo RT/CT

Rischio aumentato di complicanze

Complicanze (urinarie e linfatiche) > Grade 2: 9%-26%

numerosità della casistica

tipo di CH su T e N



Limite per l'affidabilità dei risultati e la generalizzazione delle conclusioni

## Scopo

### Analisi



dell'incidenza,  
della tipologia  
della gravità

delle  
**complicanze**  
postoperatorie  
**precoci e tardive**



**362** pazienti consecutive

**IB2-IVA** FIGO LACC trattate con RT/CT neoadiuvante + CH

**Singola Istituzione**

RTCT neoadiuvante in stadi avanzati del cervicocarcinoma

Staging

Response

RADIOCHEMOTHERAPY

CDDP 20 mg/mq/day iv

5-FU 1 g/mq/day iv  
for 96 hrs

ERT  
40-45 Gy

S  
U  
R  
G  
E  
R  
Y

Weeks

I

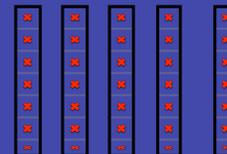
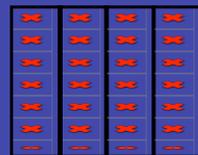
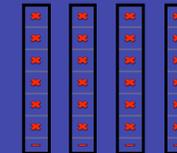
II

III

IV

V

XI-XII



### COMPLETION SURGERY AFTER CONCOMITANT CHEMORADIATION IN LOCALLY ADVANCED CERVICAL CANCER: A COMPREHENSIVE ANALYSIS OF PATTERN OF POSTOPERATIVE COMPLICATIONS

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313 pazienti (86,5%): isterectomia radicale tipo III-IV

362 pazienti (100%): linfadenectomia pelvica

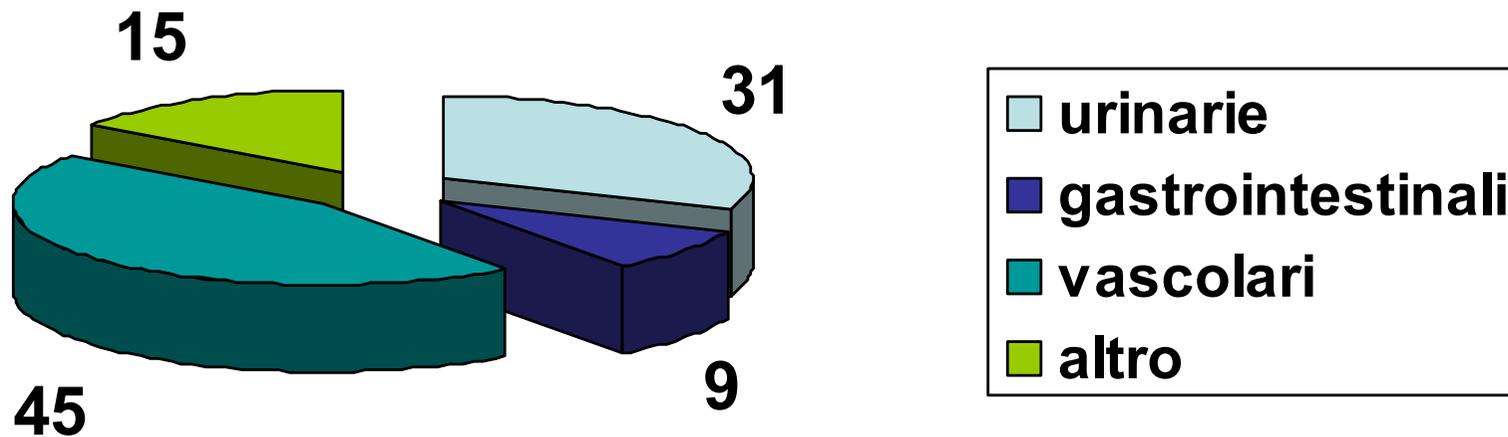
116 pazienti (32,1%) linfadenectomia aortica.

93 pazienti (25,7%): complicanze postoperatorie

60 pazienti (16,6%): complicanze  $\geq$  Grado 2

21 pazienti (5,8%): complicanze Grado 3-4

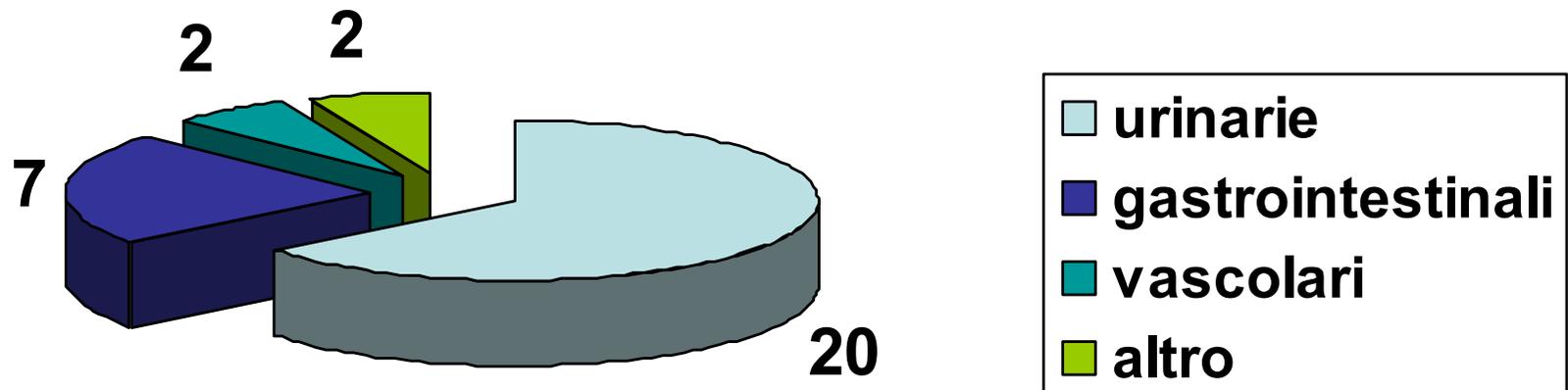
## Complicanze postoperatorie precoci: 100



**Table 2. Type of early postoperative complications according to organ system and grade**

ORGAN SYSTEM	N.	TYPE
<b>ALL</b>	<b>100</b>	
<b>Urinary</b>	<b>31</b>	
G1	5	Ureteral dilatation without hydronephrosis (N=2) Occasional incontinence (N=2) Urinary retention <6 months (N=1)
G2	16	Ureteral stenosis requiring surgery with subsequent normal renal function (N=9) Abnormal bladder function >6 months (N=3) Urinary retention requiring temporary catheterization (N=1) Uretero-vaginal fistula requiring surgery with subsequent normal renal function (N=1) Urinary incontinence (N=2)
G3	9	Urinary retention with long term catheterization (N=3) Vesico-vaginal fistula with subsequent inadequate renal function (N=3) Ureteral stenosis with permanent nephrostomy (N=3)
G4	1	Acute renal failure
<b>Gastrointestinal</b>	<b>9</b>	
G2	5	Chronic obstruction not requiring surgery
G3	3	Colonic obstruction requiring surgery (N=1). Fistula (N=2)
G4	1	Bowel perforation with septicaemia
<b>Vascular</b>	<b>45</b>	
G1	36	Lymphocele (N=27) Thrombophlebitis (N=4) Leg edema not interfering with normal activity (N=5)
G2	8	Lymphocele requiring drainage (N=5) Leg edema interfering with normal activity (N=3)
G3	1	Bleeding requiring major surgery
<b>Other</b>	<b>15</b>	
G1	9	Wound dehiscence not requiring surgery (N=4) Neurological sensory symptom with mild functional impairment (N=3) Pulmonary edema (N=2)
G2	5	Pelvic abscess requiring surgical drainage (N=2) Abdominal wound dehiscence requiring surgery (N=3)
G3	1	Pelvic abscess requiring laparotomy

## Complicanze postoperatorie tardive: 31



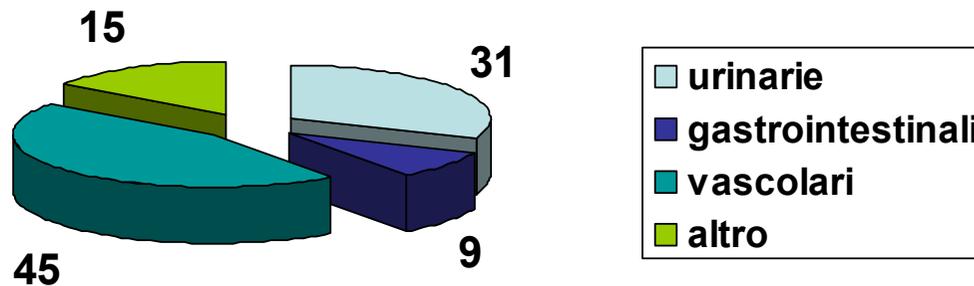
## RTCT neoadiuvante in stadi avanzati del cervicocarcinoma

**Table 3. Type of late postoperative complications according to organ system and grade**

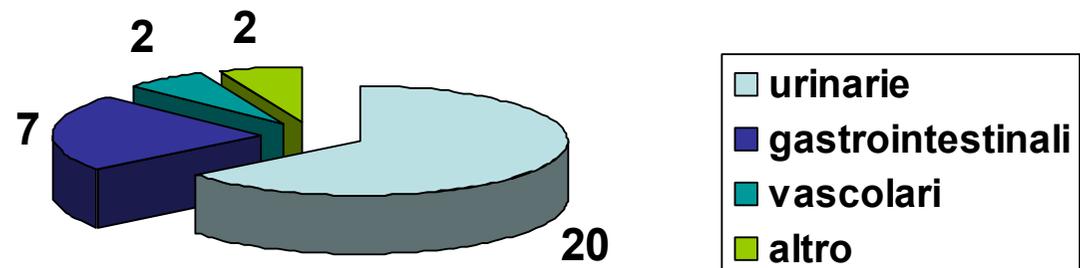
ORGAN SYSTEM	N	TYPE
<b>ALL</b>	<b>31</b>	
<b>Urinary</b>	<b>20</b>	
G2	14	Ureteral stenosis requiring surgery with subsequent normal renal function (N=5) Hematuria requiring hospitalization and/or vesical therapy (N=4) Urinary retention requiring self-catheterization (N=2) Urinary incontinence (N=3)
G3	5	Ureteral stenosis with subsequent inadequate renal function (n=3) Urinary retention with long term catheterization (N=1) Total incontinence (N=1)
G4	1	Septicaemia <sup>a</sup>
<b>Gastro-intestinal</b>	<b>7</b>	
G1	1	Post-operative obstruction settling on conservative treatment (N=1)
G2	5	Persistent symptoms or sign of rectal origin requiring medical and/or dietary treatment (N=3) Chronic obstruction not requiring surgery (N=2)
G3	1	Any signs or symptoms requiring surgery not resulting in normal activity
<b>Vascular</b>	<b>2</b>	
G1	2	Lymphocele (N=1) Thrombophlebitis (N=1)
<b>Other</b>	<b>2</b>	
G1	1	Wound dehiscence not requiring surgery
G3	1	Severe dyspareunia

<sup>a</sup> Early G3 urinary complication

## Complicanze postoperatorie precoci: 100



## Complicanze postoperatorie tardive: 31



## RTCT neoadiuvante in stadi avanzati del cervicocarcinoma

**Table 4. Univariate analysis of clinical, and surgical variables associated with number of patients developing postoperative complications (N=362)**

Variable	N.	Patients with any complications N. (%)	p value <sup>a</sup>	Patients with $\geq$ G2 complications No. (%)	p value <sup>a</sup>
<b>All cases</b>	362	93		60	
<b>Age, yrs</b>					
<55	216	52 (24.1)	0.46	32 (14.8)	0.34
>55	146	41 (28.1)		28 (19.2)	
<b>FIGO Stage</b>					
IB2-IIIB	299	72 (24.1)	0.17	42 (14.0)	0.0085
III-IVA	63	21 (33.3)		18 (28.6)	
<b>Pelvic LFN status at imaging</b>					
Negative	208	50 (24.0)	0.47	31 (14.9)	0.39
Positive	154	43 (27.9)		29 (18.8)	
<b>Aortic LFN status at imaging</b>					
Negative	348	91 (26.1)	0.37 <sup>b</sup>	58 (16.7)	0.89
Positive	14	2 (14.3)		2 (14.3)	
<b>Dose of External Beam Radiation (EBRT) (Gy)</b>					
39.6	121	33 (27.3)	0.71	19 (15.7)	0.67
39.7-50.4	241	60 (24.9)		41 (17.0)	
<b>Level of EBRT field</b>					
L4-L5	205	52 (25.4)	0.96	31 (15.1)	0.47
L3	157	41 (26.1)		29 (18.5)	
<b>Interval to Radical surgery</b>					
$\leq$ 6 weeks	129	33 (25.6)	0.96	17 (13.2)	0.34
>6 weeks	233	60 (25.7)		43 (18.3)	
<b>Clinical Response</b>					
Complete	139	28 (20.1)	0.06 <sup>c</sup>	14 (10.1)	0.013 <sup>c</sup>
Partial	215	59 (27.4)		40 (18.6)	
SD	8	6 (75.0)		6 (75.0)	
<b>Radical Hysterectomy</b>					
Piver II	49	10 (20.4)	0.65	7 (14.3)	0.54
Piver III	278	74 (26.7)		45 (16.2)	
Piver IV	35	9 (25.7)		8 (22.8)	
<b>Lymphadenectomy</b>					
Pelvic and aortic	116	36 (31.0)	0.14	25 (21.5)	0.11
Only pelvic	246	57 (23.2)		35 (14.2)	



Table 5. Multivariate analysis of clinical, and surgical variables associated with patient risk of developing  $\geq$ G2 postoperative complications

Variable	Patients with $\geq$ G2 complications		
	<u>Multivariate<sup>a</sup></u>		
	$\beta$	$\chi^2$	p value
<b>Clinical response to treatment</b>			
Complete			
Partial	+0.9675	9.90	0.0017
Stable disease			
<b>Stage</b>			
IB2-IIIB	+0.5958	3.07	0.0802
III-IVA			
<b>Lymphadenectomy</b>			
Only pelvic	+0.5101	2.54	0.1009
Pelvic and aortic			

<sup>a</sup>only variables with p value < 0.20 in the univariate analysis were included in the multivariate analysis

## Conclusioni

Mancata risposta clinica completa al trattamento,  
lo stadio avanzato,  
l'esecuzione della linfadenectomia aortica,

rischio più elevato di sviluppare complicanze  
sia di qualsiasi grado che di Grado > 2

