

IL FOLLOW-UP DOPO TRATTAMENTO PER CIN: CERTEZZE E DUBBI

T.MAGGINO

con il contributo di

P.CATTANI

S.CIATTO

G.MONTANARI

POSSIBILI OBIETTIVI DEL FOLLOW-UP

MEDICI

NON MEDICI

SCIENTIFICI

MEDICAL

- DETECTING PRECLINICAL RELAPSE
- SCREENING OF THERAPY-RELATED COMPLICATIONS
- SEARCHING FOR SECOND (NEW) TUMOR
- TREATING PATIENTS (COUNSELLING AND INFORMATION)

NON MEDICAL

- MAINTENANCE OF RAPPORTS WITH REFERRING DOCTORS
- PSYCHOLOGICAL SUPPORT FOR PATIENTS
- AVOIDANCE OF LAWSUITS

SCIENTIFIC

- DATA BASE OF TRETAMENT OUTCOME
- IMPACT AND COSTS OF DIFFERENT FOLLOW-UP STRATEGIES

Follow up post trattamento per CIN: CERTEZZE

- Necessità del follow-up
- Il periodo di maggior rischio di persistenza/recidiva sono i primi 24 mesi

NECESSITA' DEL FOLLOW UP

Rischio di persistenza/recidiva della CIN dopo trattamento

Le pazienti trattate per CIN hanno un rischio aumentato (fino a 55%) di ripresentare una CIN

Petterson F. Radiotherapy and oncology 1989

Anderson MC. Gynecol Oncol 1990

Levi F. Br. J. Cancer 1996

Nagai Y. Gynec Onc. 2000

Vikki M. Acta Obst Gynecol Scand 2000

Soutter W.P. Br. J. Obstet Gynec 2001

Mitchell M.F. Int J Gynec Cancer 2002

Australian NHMRC : guidelines for the management of women with screen detected abnormalities 2005

NHSCSP: colposcopy and programme management 2004

SICPCV: linee guida per la gestione della paziente con PAP test anormale 1997-2002

TASSI DI RECIDIVE/PERSISTENZE DOPO TRATTAMENTO PER CIN

AUTORE	CASI	CRIO	LASER	LEEP
Wright '81	334	14%	3%	
Townsend '83	200	7%	11%	
Ferenczy '85	294	9%	4%	-
Ferenczy '96	883	-	-	8%
Luesley '90	557	-	-	4%
Gunasekera '90	199	-	8%	5%
Whiteley '90	79	-	-	5%
Cecchini '94	325	-	-	7%
Bigrigg '94	1000	-	-	5%
Flannelly '97	977	-	-	10%

NECESSITA' DEL FOLLOW UP

Rischio di Carcinoma in pazienti trattate per CIN

Le pazienti trattate per CIN presentano un
aumentato rischio (fino all' 8‰) di cancro
della cervice

Pearson J. Br J Obstet Gyn 1989

Cullmore J I Gynec Surg 1990

Mojane Onc Prevent in Gin 2002

Soutter WP Lancet 1997

McInobe WA Obstet Gynecol 1984

Mitchell MF. Int J Gynec Cancer 2002

NCSP: New Zeland guidelines for the management of women with abnormal cervical smears 1999

NHSCSP: colposcopy and programme management 2004

SICPCV: linee guida per la gestione della paziente con PAP test anormale 1997-2002

RISCHIO DI RECIDIVA/PERSISTENZA DELLA CIN DOPO TRATTAMENTO

È massima nei primi 24 mesi

Flanelly G Br J Obstet Gyn 2001

Chew GK Int J Gynec Cancer 1999

Petterson F. Radiotherapy and oncology 1989

Soutter WP Lancet 1997

Mitchell M.F. Int J Gynec Cancer 2002

European CCSN: European guidelines for quality assurance in cervical screening 2003

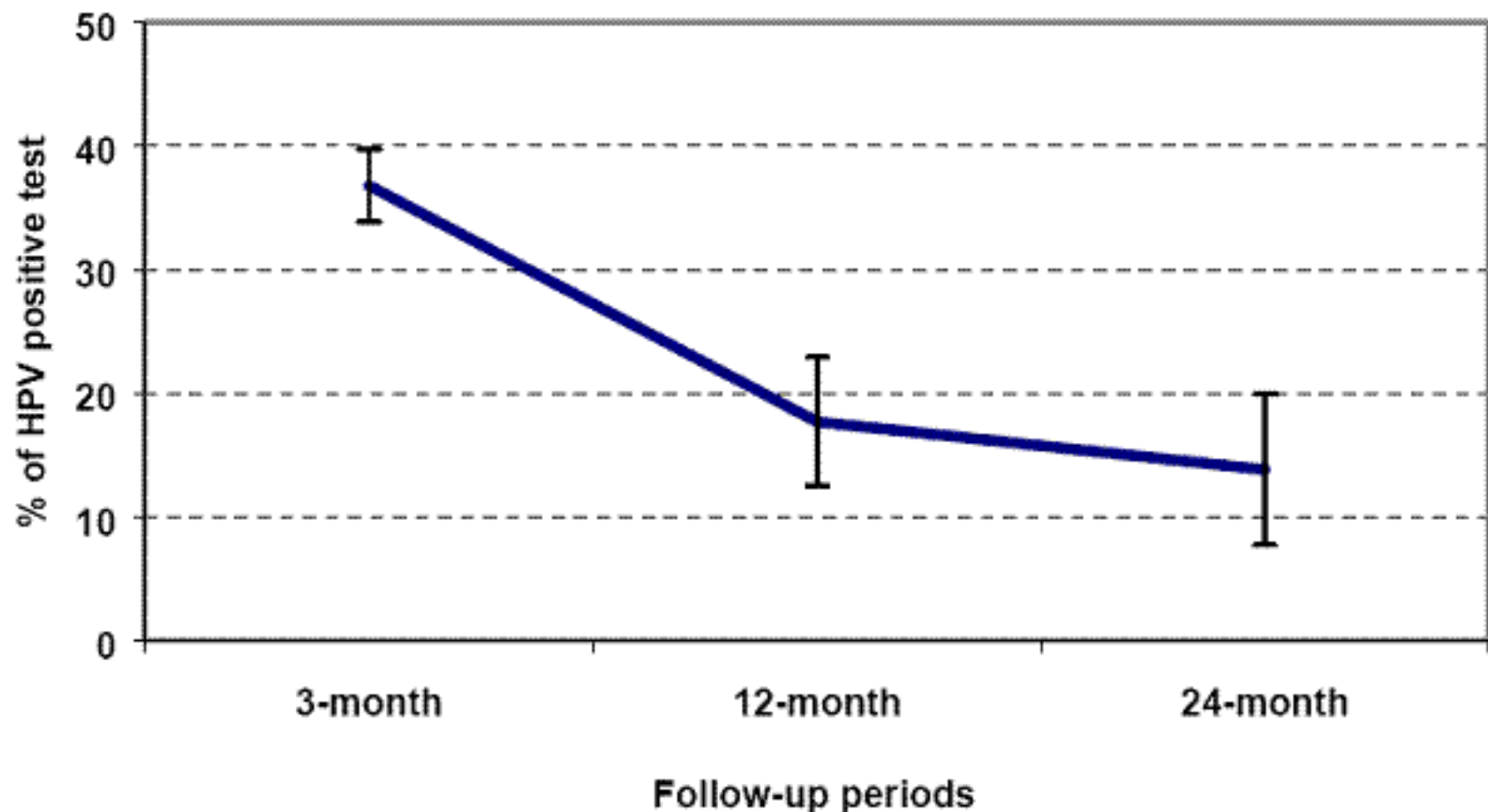
Australian NHMRC 2005 : guidelines for the management of women with screen detected abnormalities

NHSCSP: colposcopy and programme management 2004

TASSO E ANDAMENTO NEL TEMPO DELLE RECIDIVE DOPO TRATTAMENTO CONSERVATIVO DI CIN2-3

STUDIO	REC/CASI	FUP	REC %	MESI					
				6	12	18	24	36	60
Costa 2002	28/699	24 m	4.0	2.4	2.2	1.5	0	0	-
Flannelly 1997	80/975	60 m	8.2	3.7	1.1	2.2	0.9	0	0
Paraskevaidis 2000	31/635	24 m	4.8	-	4.7	-	0.1	-	-
Cecchini 2002	52/622	60 m	9.1		8.6		0.9	0.8	0

RISCHIO DI RECIDIVA/PERSISTENZA DELLA CIN DOPO TRATTAMENTO



Source: Nagai et al 2000, Kucera et al 2001, Nobbenhuis et al 2001b, Paraskevaidis et al 2001, Bar-Am et al 2003, Debarge et al 2003, Zielinski et al 2003, Chao et al 2004.

Follow up post trattamento per CIN:

DUBBI

- Modalità dei controlli
- Frequenza dei controlli
- Durata dei controlli

CRITICAL POINTS ON FOLLOW-UP AFTER CIN TREATMENT

- POOR DATA FROM THE LITTERATURE
- MANY CLINICAL TRIALS ON CIN TREATMENT IGNORE TO DESCRIBE THE FOLLOW-UP METHODOLOGY AND/OR THE RATE OF PATIENTS LOST TO FOLLOW-UP
- FREQUENCY AND CAUSE OF FOLLOW-UP FAILURES ARE INSUFFICIENTLY ADDRESSED
- RATE OF 25% OR OVER HAS OCCASIONALLY BEEN OBSERVED
- PARTIAL NON ADHERENCE TO FOLLOW-UP PROGRAMME HAS GENERALLY BEEN IGNORED

FOLLOW-UP AFTER CIN TREATMENT AN OVERVIEW

- FOLLOW-UP HAS SO FAR CONSISTED OF REPEAT CYTOLOGY AND POSSIBILITY COLPOSCOPY
- A DRAWBACK WITH REPEAT CYTOLOGY IS THE RELATIVELY HIGH RATE OF FALSE POSITIVE RESULTS
- A HISTOLOGICALLY PROVEN CIN LESION HAS BEEN FOUND IN ONLY 40 TO 60% POSITIVE PAP SMEAR AFTER CONIZATION (BOLLEN LJ 1999)
- COLPOSCOPY AFTER TREATMENT COULD BE UNSATISFACTORY FOR CERVICAL ANATOMICAL DISTORSIONS

FOLLOW-UP DOPO TRATTAMENTO CONSERVATIVO PER CIN

	RECIDIVE	CONTROLLI
LSIL	7	24
HSIL	9	3
HPV-	0	12
HPV+	16	15

Bollen et al, Gynecol Oncol 1999

HPV TESTING AFTER CIN TREATMENT

- A SUCCESSFUL CIN TREATMENT USUALLY RESULTS IN HPV CLEARANCE
- HPV NEGATIVITY AFTER SUCCESSFUL TREATMENT WITHOUT RECURRENCE/PERSISTANCE
 - AT 3 MONTHS: 86% OF CASES
 - AT 24 MONTHS: 99% OF CASES
- AVERAGE HPV NEGATIVITY IN PATIENTS WITHOUT RECURRENCE IS: 8 MONTHS (RANGE 4-18 MONTHS)
- CLEARANCE RATES OF HR-HPV DNA DECREASED WITH INCREASED SEVERITY OF THE LESION (P=0.02)
- HPV CLEARANCE OCCURED, ON AVERAGE, 3 MONTHS BEFORE CYTOLOGICAL REGRESSION

HPV TESTING AFTER CIN TREATMENT

- A NEGATIVE HPV TESTING AFTER TREATMENT HAS A VERY HIGH NEGATIVE PREDICTIVE VALUE (92% TO 100%)
- THIS ALSO HOLDS TRUE FOR CONIZATIONS OF CIN 3 WITH POSITIVE RESECTION MARGINS (Jain 2001)
- NPV OF HPV TEST AFTER CONIZATION IS SUPERIOR TO CYTOLOGY (98% vs 93% AT 6 MONTHS) – (Nobbenhuis 2001)
- 3 MONTHS INTERVAL FOR HPV TEST STILL HAS A HIGH PERCENTAGE OF HPV-POS. PATIENTS (Costa S.)

HPV TEST E RECIDIVE DOPO TRATTAMENTO CONSERVATIVO DI CIN2-3

STUDIO	CASI	HPV+	HPV-	SENS	SPEC	VPP	VPN
Cecchini 2004	10 (/84)	9	1	90.0	63.5	25.5	97.9
Nobbenhuis 2001	29 (/184)	27	2	93.1	98.7	93.1	98.7
Costa 2004	18 (/252)	14	4	77.7	90.1	37.8	98.1
Zielinski 2003	5 (/108)	4	1	80.0	81.5	17.3	98.8
Paraskevaidis 2002		38	3	92.6	86.3		
Paraskevaidis 2004				82.8	84.2		
Chao 2004	32 (/279)	28	4	87.5			
Guijon 1993	23 (/297)	23	0	100			100

FOLLOW-UP* OF SCREENING PATIENTS CONSERVATIVELY TREATED FOR CIN 2-3 (PERIOD 1996-2000)

STUDY PATIENTS	1560	
LOST TO FOLLOW-UP	326	(21%)
INCOMPLETE ADHERENCE	678	(43%)
FOUR NEGATIVE TESTS	353	(23%)
PERSISTENT DISEASE	204	(13%)

*EARLY CECK AND 6-12-18-24 MONTHS WITH CYTOLOGY AND COLPOSCOPY

FOLLOW-UP AFTER CIN TREATMENT

- AT THE MOMENT, POST TREATMENT CYTOLOGY CANNOT BE OMITTED IN THE FOLLOW-UP
- DESPITE THE GROWING NUMBER OF PUBLISHED STUDIES, RACCOMANDATIONS CONCERNING THE ACCURACY OF HPV TESTING IN THE FOLLOW-UP AFTER CIN ARE LIMITED BECAUSE OF MISSING PROSPECTIVE RANDOMIZED STUDY WITH LONG PERIOD OF OBSERVATION
- HOWEVER, BASED ON CURRENT EVIDENCE, A SUCCESSFUL CIN TREATMENT USUALLY LEADS TO A HPV CLEARANCE

FACTORS INFLUENCING FREQUENCY AND DURATION OF FOLLOW-UP AFTER CIN TREATMENT

- PATIENT'S AGE: INCREASE RISK FOR >40 AGE
- TYPE OF LESION: GLANDULAR DISEASE NEEDS
SPECIAL ASSESSMENT
- GRADE OF LESION: INCREASE RISK FOR HIGH
GRADE LESIONS
- HISTOLOGY: MARGINS STATUS (AFFECTED OR NOT)

CONVENTIONAL STRATEGY FOR FOLLOW-UP AFTER CIN TREATMENT

HIGH RISK: CYTOLOGY ± COLPOSCOPY AT 6-12-18-24
MONTHS ANNUAL CYTOLOGY FOR 5-9
YEARS BEFORE RETURNING TO GENERAL
SCREENING

LOW RISK: CYTOLOGY ± COLPOSCOPY AT 6-12-24
MONTHS, IF NEGATIVE RETURN TO
GENERAL SCREENING

FOLLOW-UP POLICY WITH HPV TEST

CLINICAL-COLPOSCOPIC POST-TREATMENT EVALUATION AT 3 MONTHS (?)

