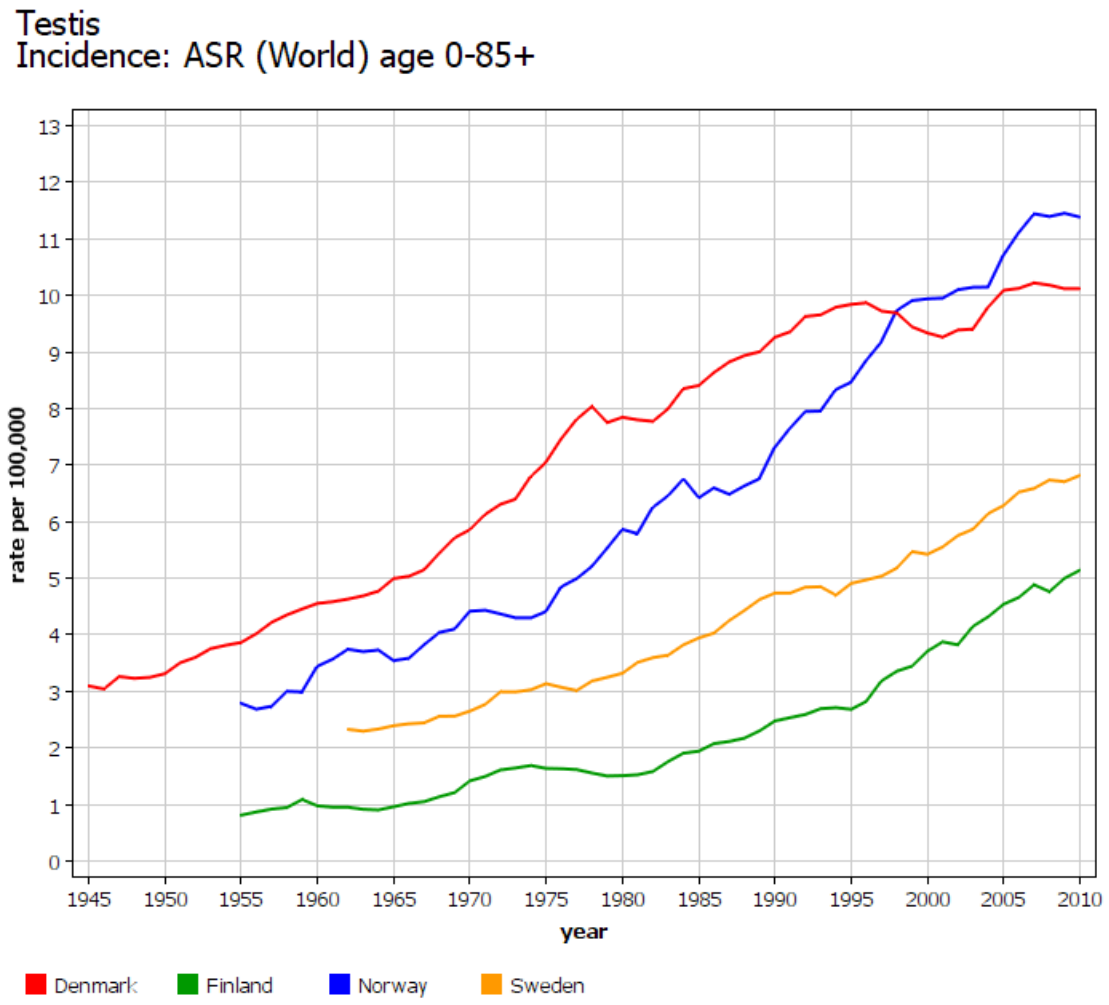
Seminoman hoito ja seuranta

S. Jyrkkiö

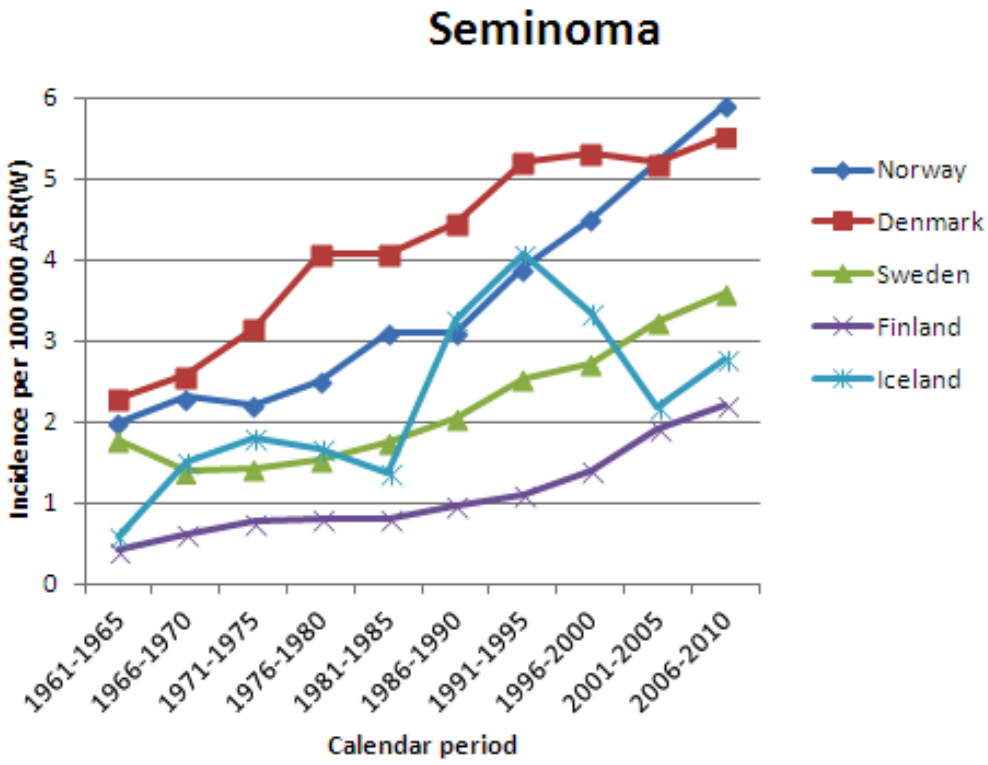
17.4.2015

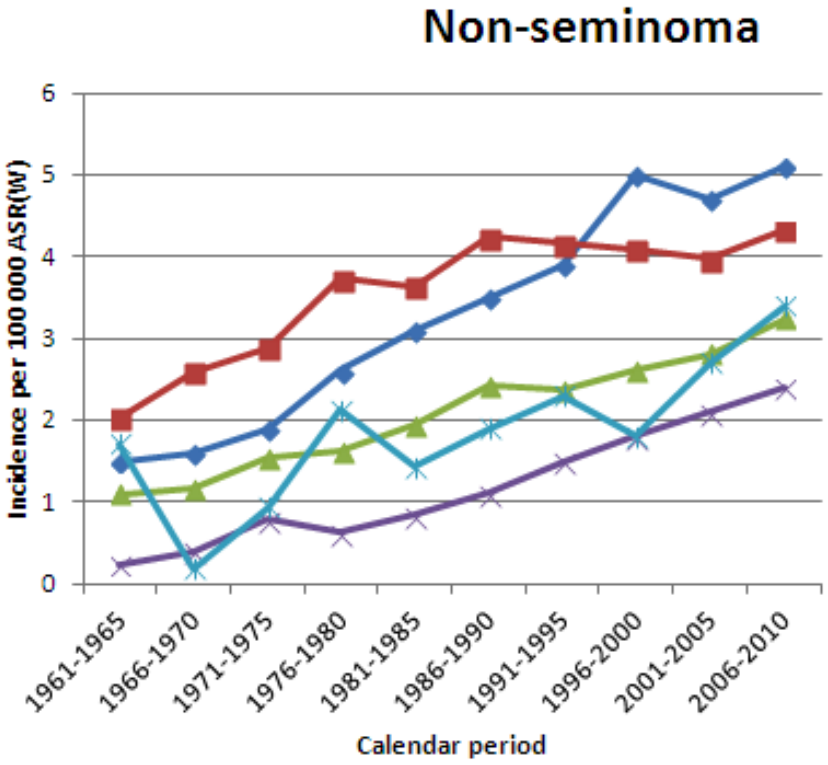
Kivessyöpä yleistyy Pohjoismaissa



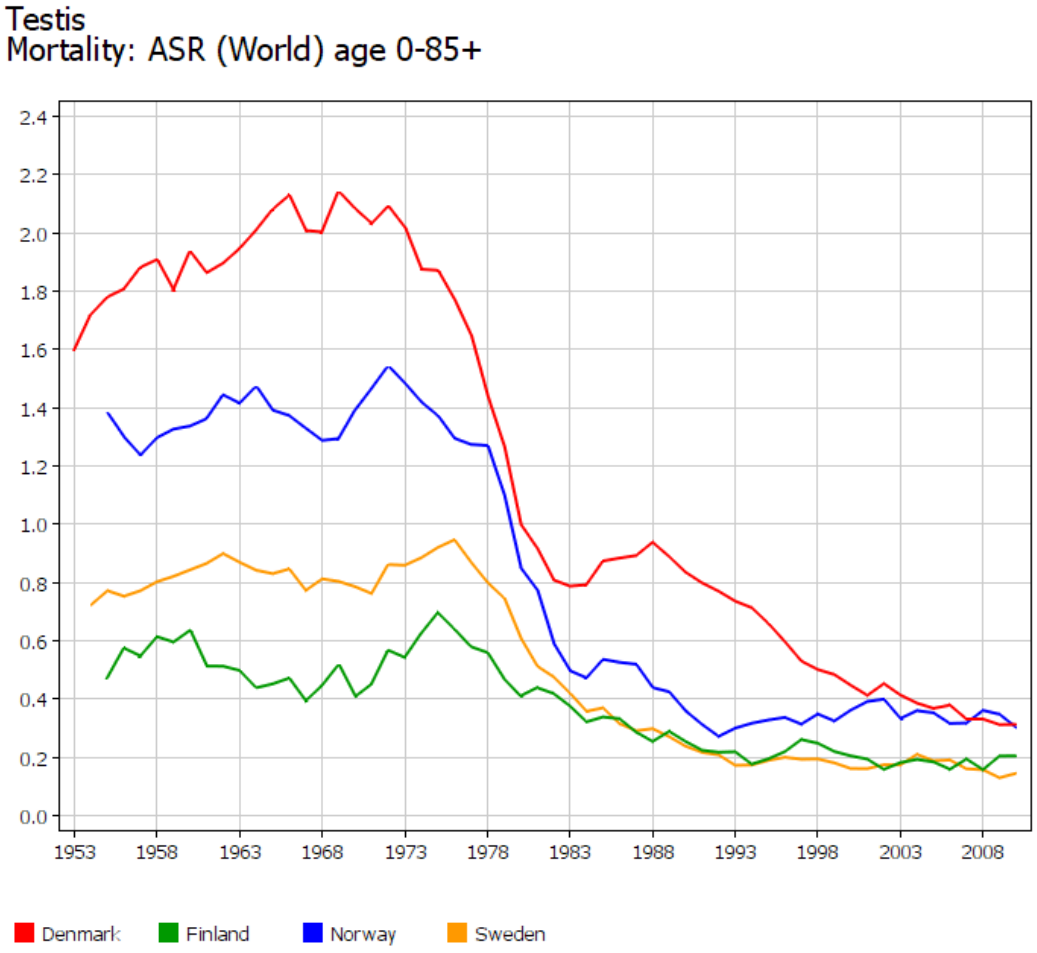
NORDCAN © Association of the Nordic Cancer Registries (6.4.2015)

Seminoman ja non-seminoomien yleisyys Pohjoismaissa





Kuolleisuus kivessyöpään Pohjoismaissa



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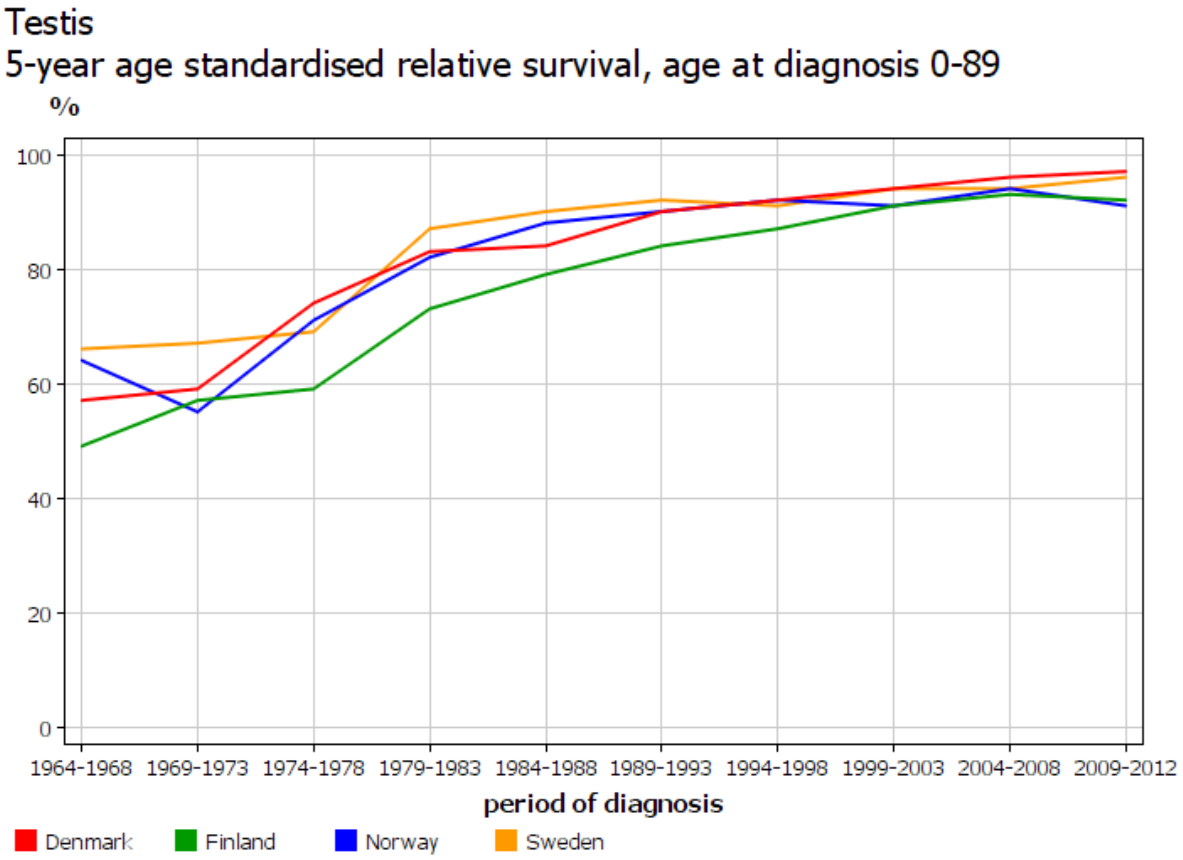
Kivessyöpä 5 v OSS



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Kivestuumoreiden luokittelu

Clin Oncol 2012;24:30-38

Table 1
Testicular tumour classification

2004 WHO classification
Tumours of one histological type
Seminoma with syncytiotrophoblastic giant cells
Spermatocytic seminoma with sarcomatous change
Embryonal carcinoma
Yolk sac tumour
Choriocarcinoma
Other trophoblastic tumours
Monophasic choriocarcinoma
Placental site trophoblastic tumour
Teratoma*
Dermoid cyst (a benign entity)
Monodermal teratoma
Teratoma with somatic transformation
Tumours of more than one histological type
Embryonal carcinoma/yolk sac and teratoma
Choriocarcinoma and other non-seminoma
Seminoma and non-seminoma

Spermatosyyttinen seminoma

- Harvinainen, < 1 % kaikista kivestuumoreista
- Yleensä > 60v miehillä
- Hidas taudinkulku
- Adjuvanttihoitoa ei tarvita (ST I)
- Sarkomatoidi variantti on huonoennusteinen

Jeetle ym. Clin Oncol 2012;24:30-38

ST I Seminoma

- Kakista kivessyövistä tavallisin (40-45 %)
- Hyväennusteinen

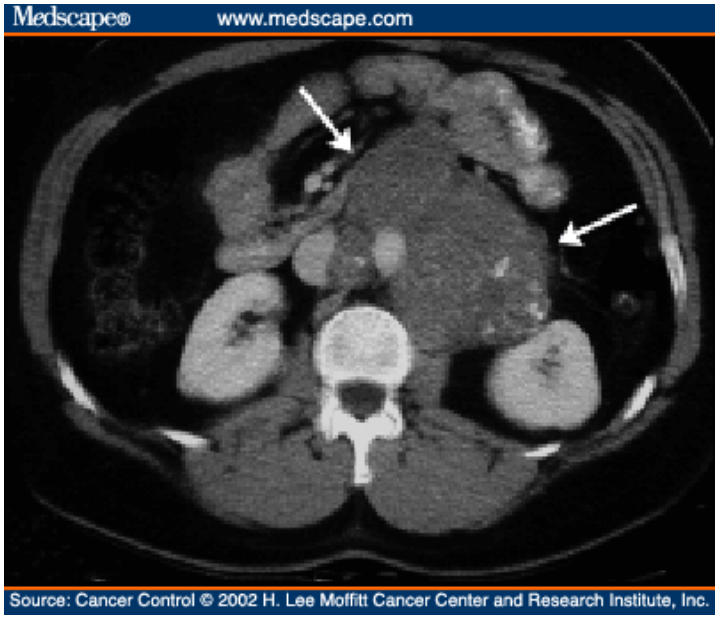
Tarvitaanko liitännäishoitoa?

- Vaihtoehdot:
  1. Aktiivi seuranta
  2. Single karboplatiini (tai kaksi)
  3. Sädehoito

ST II-III Seminoma

- < 5 cm imusolmukkeet => sädehoito
- > 5 cm imusolmukkeet tai ST III => BEP x 3

- Jos > 3cm residuaalituumori, suos FDG PET
- ➢ PET neg => seurantaan
- ➢ PET pos => voi merkitä akt tautia, harkitse residuaali-tuumorin resektiota
- PET ajoitus (4-) 12 vk hoidosta



Residual retroperitoneal tumor

International Prognostic System for advanced germ cell cancer

	Good	Intermediate	Poor
Seminona	Ei NPVM	NPVM	N/A
Nonseminoma	Testis tai RP ja Ei NPVM ja S0 tai S1	Testis tai RP ja Ei NPVM ja S2	Prim. Mediastinum tai NPVM tai S3
5 v PFS	88 %	75 %	41 %
5 v OS	91 %	**79 %**	**48 %**

NPVM = nonpulmonary visceral metastases
RP = retroperitoneal
S1 LD < 1,5 x N ja HCG < 5000 ja AFP < 1000
S2 LD 1,5-10 x N tai HCG 5000-50000 tai AFP 1000-10000
S3 LD > 10xN tai HCG>50000 tai AFP >10000

JCO 1997;15:594

ST I Seminoma: onkologisen hoidon haasteet

- Hoitotulokset erinomaisia
- Hoidoista pitkäaikaishaittoja
- Liitännäishoitona sädehoito vs karboplatiini, satunnaistetusta tutkimuksesta on näyttöä
- Aktiiviseuranta vs karboplatiini tai sädehoito, ei näyttöä satunnaistetusta tutkimuksesta
- SWENOTECA: *”We recommend patient autonomy”*

Onkologisten hoitojen myöhäishaitat

- Fertiliteetti säilynyt n 70 %:lla
- Jälkeläiset terveitä
- 11-35 % hypogonadismi (S-testo < 8 nmol/l)
- 2-3 x riski kardiovaskulaarisairauksiin, kumulatiivinen riski 20 v 18 %
- Raynaudin oire voi olla merkki lis riskistä
- Metabolinen syndrooma 25 %:lla 5 v kuluttua
- Keuhko-, munuais ja ototoksisuus
- Sekundaarimaligniteettien riski x 2
- Psykososiaaliset oireet

ST I Seminoma, aktiivi seuranta

Table 3. Summary of surveillance studies in stage I seminoma

Author	Year	Median follow-up (mo)	No. patients	No. patients relapse	Relapse, %	Cause-specific survival, %
Daugaard[13]	2003	60	394	69	17.5	100
Germa Lluch[14]	2002	33	233	38	16	100
Horwich[15]	1992	62	103	17	16.5	100
Oliver[16]	2001	98	110	21	19	100
Ramakrishnan[17]	1992	44	72	13	18	100
Von der Maase[18]	1993	48	261	49	18.8	98.9
Warde[19]	2005	98	421	64	15.2	99.7
Tyldesley[20]	2006	33	93	16	17.2	97.8

CUAJ 2010

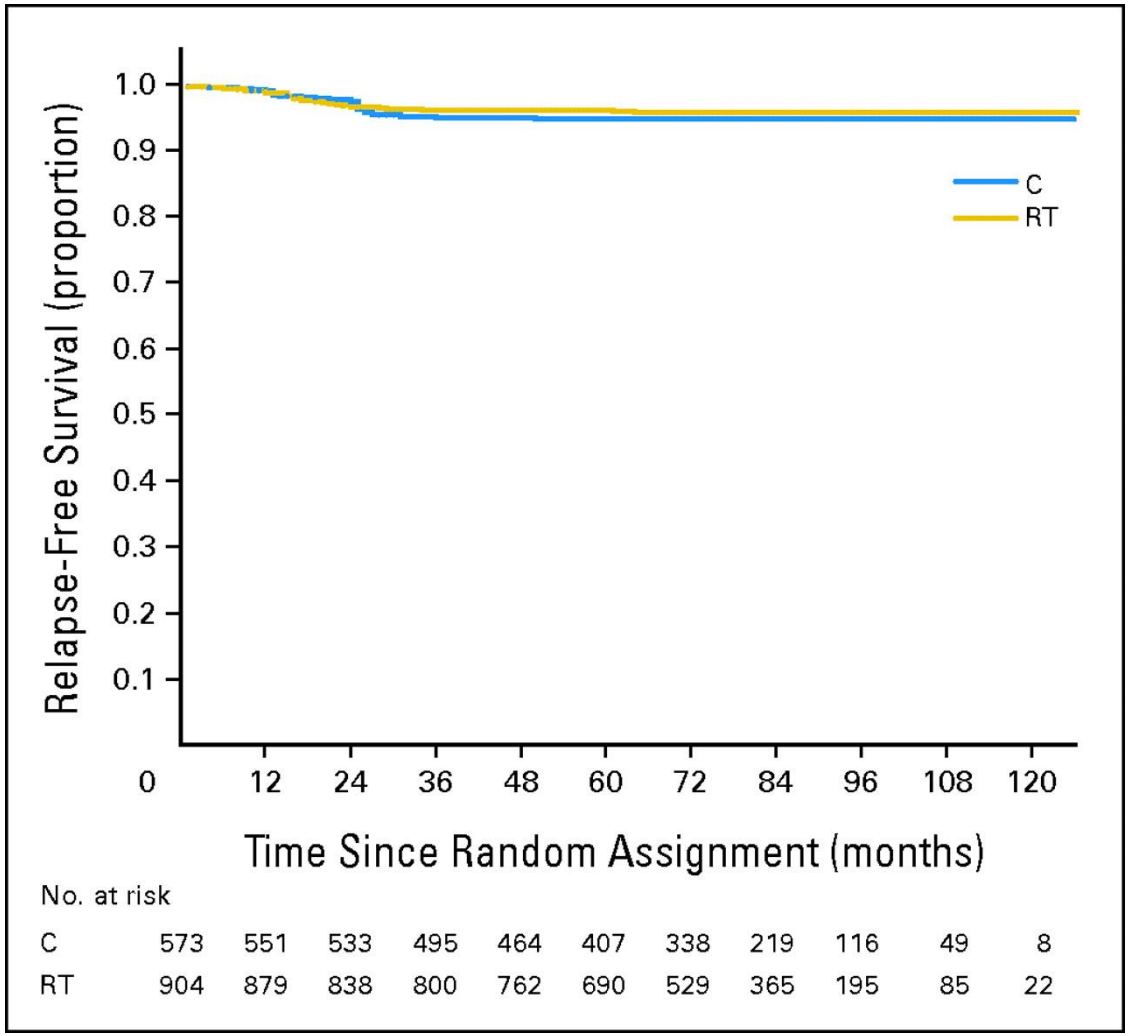
ST I Seminoma, sädehoito

Table 4. Adjuvant radiation therapy studies in stage I seminoma

Author	Years of study	No. patients	Relapse, %	Cause-specific survival, %
Bayens[23]	1975-1985	132	4.5	99%
Coleman[24]	1980-1995	144	4.2	100%
Fossa[25]	1989-1993	478	3.8	100%
Jones[26]	1995-1998	625	3.5	9.6%
Santoni[27]	1970-1999	487	4.3	99.4%
Warde[19]	1981-2002	283	5	100%

CUAJ 2010

Relapse-free rates (RFRs) by allocated treatment.



R. Timothy D. Oliver et al. JCO 2011;29:957-962

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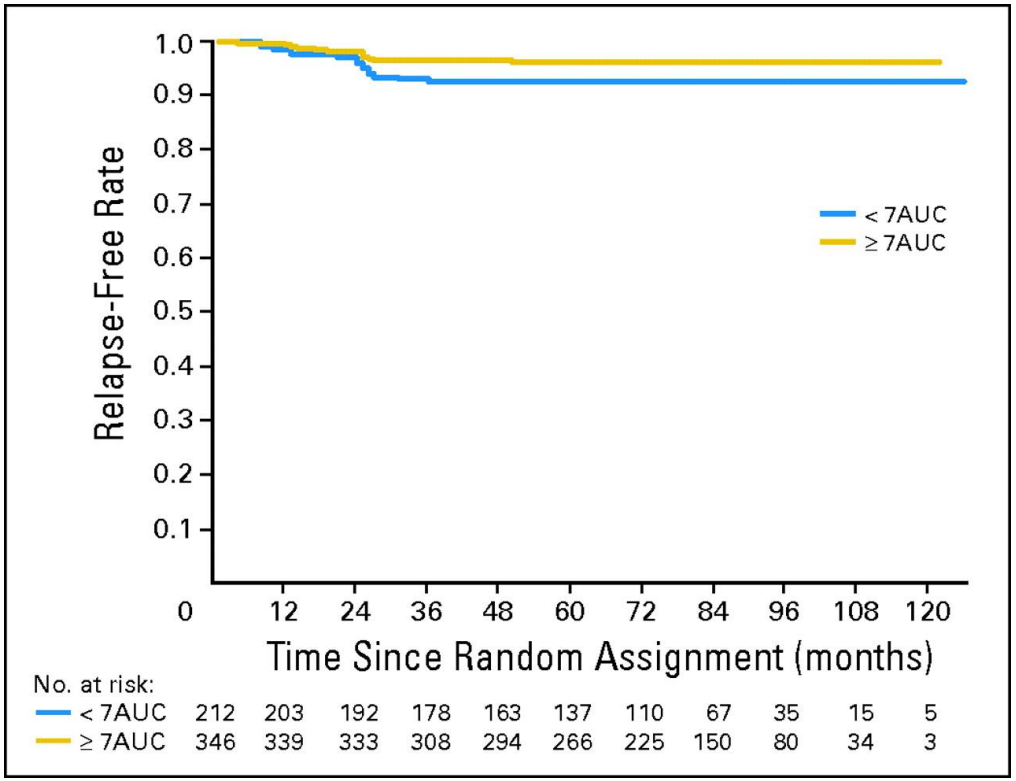
Karboplatiiniannoksen merkitys

Relapse-free rate (RFRs) by received carboplatin dose less than seven times area under the curve (AUC) compared with seven or more times the AUC. RFR at 5 years: carboplatin dose less than seven times AUC, 92.6% (95% CI, 88.0% to 95.5%; seven or more times ...



R. Timothy D. Oliver et al. JCO 2011;29:957-962

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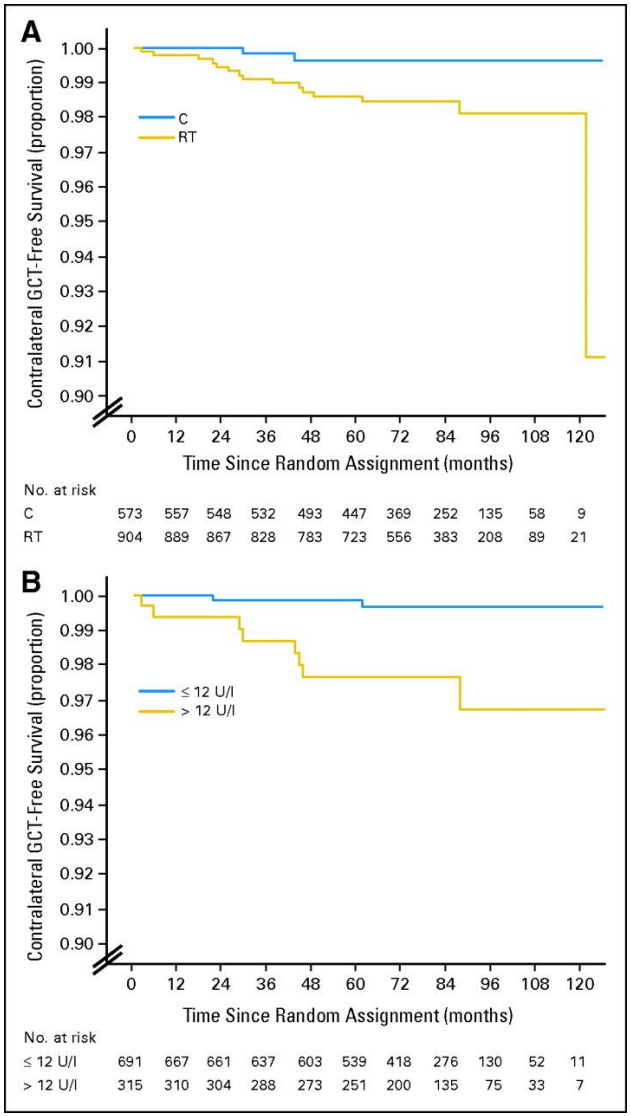
Karboplatiinia saaneilla vähemmän toisen kiveksen syöpää



(A) Contralateral germ cell tumor (GCT) rates by allocated treatment (truncated y-axis).

R. Timothy D. Oliver et al. JCO 2011;29:957-962

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JOURNAL OF CLINICAL ONCOLOGY ASCO

Aktiivisen seurannan aikaiset relapsit

(SWENOTECA ja British Columbia)

- ST I Seminoma N=1344
- ST I Non-seminoma N=1139
- Aktiivinen seuranta 1998-2010

- Relapseja:
- ST I seminoma N=173
- ST I non-seminoma N=221

Kollmannsberger ym. J Clin Oncol 2015;33:51-57

Mediaani aika relapsiin

- ST I non-seminoma LVI pos 4 kk (2-61 kk)
- ST I non-seminoma LVI neg 8 kk (2-77 kk)
- *ST I seminoma 14 kk (2-84 kk)*

Kollmannsberger ym. J Clin Oncol 2015;33:51-57

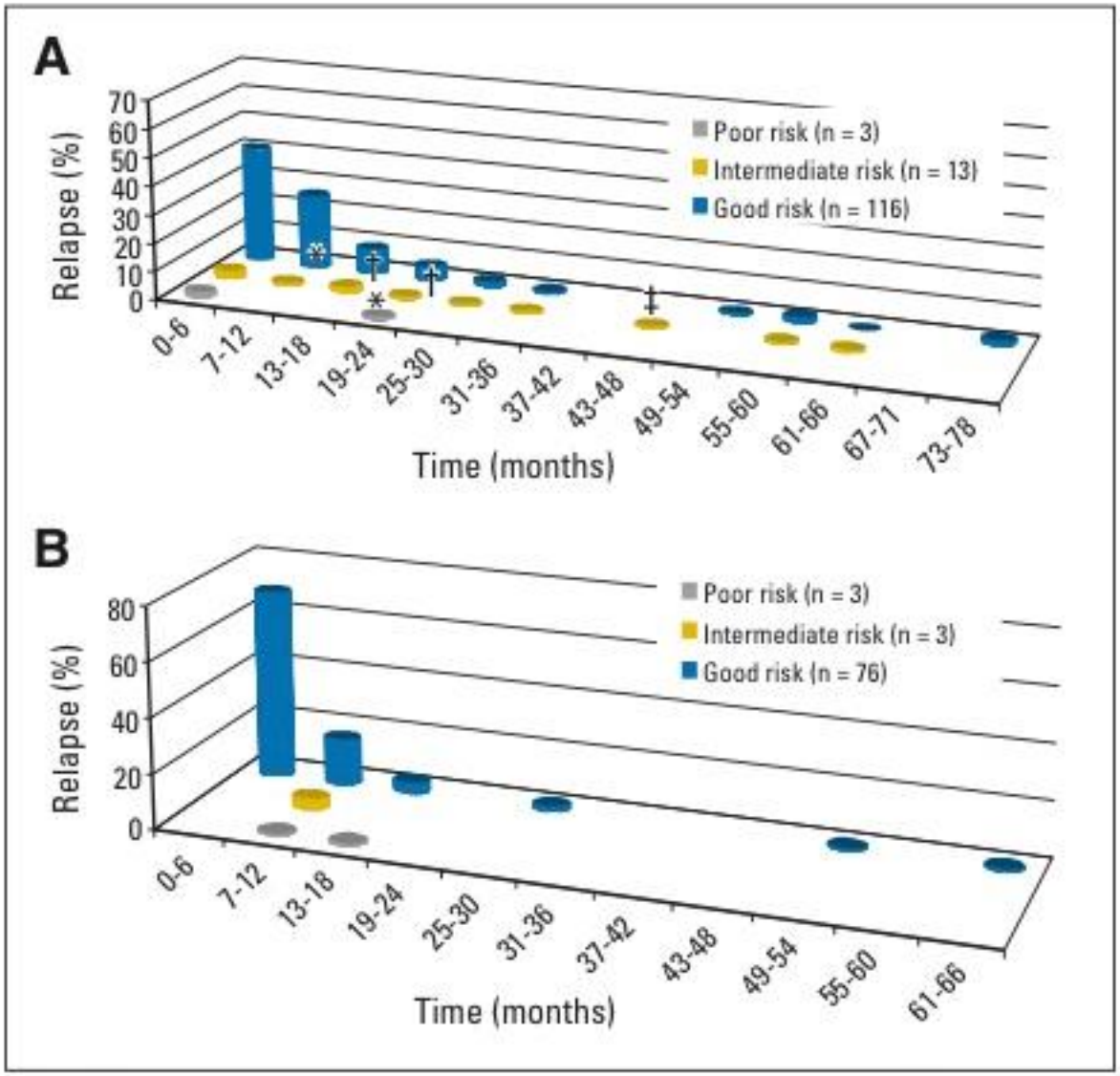

Fig 1. Prognostic group distribution and timing of relapses for (A) lymphovascular invasion (LVI) –negative and (B) LVI-positive relapses. (*) Dead of disease (DOD). (†) Death treatment-related. (‡) DOD (refused therapy).

Kollmannsberger ym. J Clin Oncol 2015;33:51-57

Kivessyövän uusiutuma todetaan oireiden perusteella vain harvoin

Table 2
Role of clinical examination in the detection of relapse

Study population	Number of patients	Relapses	Relapses detected by clinical examination	Reference
Stage I NSGCT (surveillance)	414	70	1	[12]
Stage I NSGCT (surveillance)	154	42	0	[13]
Stage I seminoma after para-aortic radiotherapy	409	13	0	[14]
Stage I germ cell tumours (relapsed cases only)	Not reported	494	1	[10]
Stage I NSGCT (surveillance, long-term follow-up)	453	100 (9 >2years)	0	[15]
Long-term population-based study of seminoma and NSGCT relapse (all stages)	1949	25 (>2 years)	3	[16]
Present study (stage I and post-treatment)	About 6000	69	0	Present study

NSGCT, non-seminomatous germ cell tumours.

Kuvantamisseuranta

Table 4. Authors' Recommendations for Surveillance Schedules Based on the Observed Patterns of Relapse and the Authors' Expert Opinion

	Frequency (months)			
Year	Physical Examination	Tumor Marker*	Chest X-Ray	CT/MRI Abdomen†
CSI-NONSEM				
Year 1	2	2	4, 8, 12	4, 8, 12
Year 2	3	3	18, 24	18, 24
Year 3	6	6	—	36‡
Year 4	6	6	—	—
Year 5	6	6	—	60‡
CSI-SEM				
Year 1	3	3	6, 12	6, 12
Year 2	6	6	18, 24	18, 24
Year 3	6	6	—	30, 36
Year 4	6	6	—	—
Year 5	6	6	—	60‡

Abbreviations: CSI-NONSEM, clinical stage I nonseminoma; CSI-SEM, clinical stage I seminoma; CT, computed tomography, MRI, magnetic resonance imaging.
*Alpha fetoprotein/human choriogonadotropin (lactate dehydrogenase is of questionable benefit in stage I).[22]
†MRI only in experienced centers.
‡Proposed by several authors.

Kollmannsberger ym. J Clin Oncol 2015;33:51-57

ST I Seminoma Kuvantamisen seurantasuositus:

6 kk välein ad 3 v + 5 v

=> 7 abdomen CT/MRI

Patterns of management and surveillance imaging amongst medical oncologists in Australia for stage I testicular cancer

Peter Grimison[1,2], Baerin Houghton[1,3], Mark Chatfield[1,3], Guy C. Toner[1,6,7], Ian D. Davis[1,8], Jarad Martin[1,4], Elizabeth Hovey[1,5] and Martin R. Stockler[1,2,3]

[1]Australian and New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group Ltd, [2]Sydney Cancer Centre and University of Sydney, [3]NHMRC Clinical Trials Centre, University of Sydney, Sydney, [4]Calvary Mater Newcastle, Waratah, [5]Prince of Wales Hospital, Randwick, NSW, [6]Peter MacCallum Cancer Institute, [7]University of Melbourne, [8]Ludwig Institute for Cancer Research, Joint Ludwig-Austin Oncology Unit, Austin Health, Melbourne, Vic., Australia

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Table 4 Consensus recommendations for number of imaging procedures during 5 years of surveillance.

Group (Year published)	Seminoma			Non-seminoma		
	Chest X-ray	CT Chest	CT Abdomen	Chest X-ray	CT Chest	CT Abdomen
MRC 1992 [25]	NS	NS	NS	22	4–8	4–8
Princess Margaret 2007 [34]	10	0	11 (also pelvis)	NS	NS	NS
Marsden 2008 [12]	7	0	7	18	0	3
ESMO 2010 [18,19]	7	0	7	18	0	3
European Association of Urology 2011 [16]	4	0	4 (also pelvis)	4	0	2 (also pelvis)
Swiss-German group 2011 [38]	6	0	4†	15	0	2†
NCCN 2012 [14]	NS	NS	7–10 (also pelvis)	21–27	0	8–12 (also pelvis)

EMSO, European Society of Medical Onocolgy, MRC, Medical Research Council; NCCN, National Comprehensive Cancer Network. †Also ultrasonography of the abdomen. NS, not specified.

Satunnaistettu tutkimus menossa kuvantamisseurannan järjestämisestä

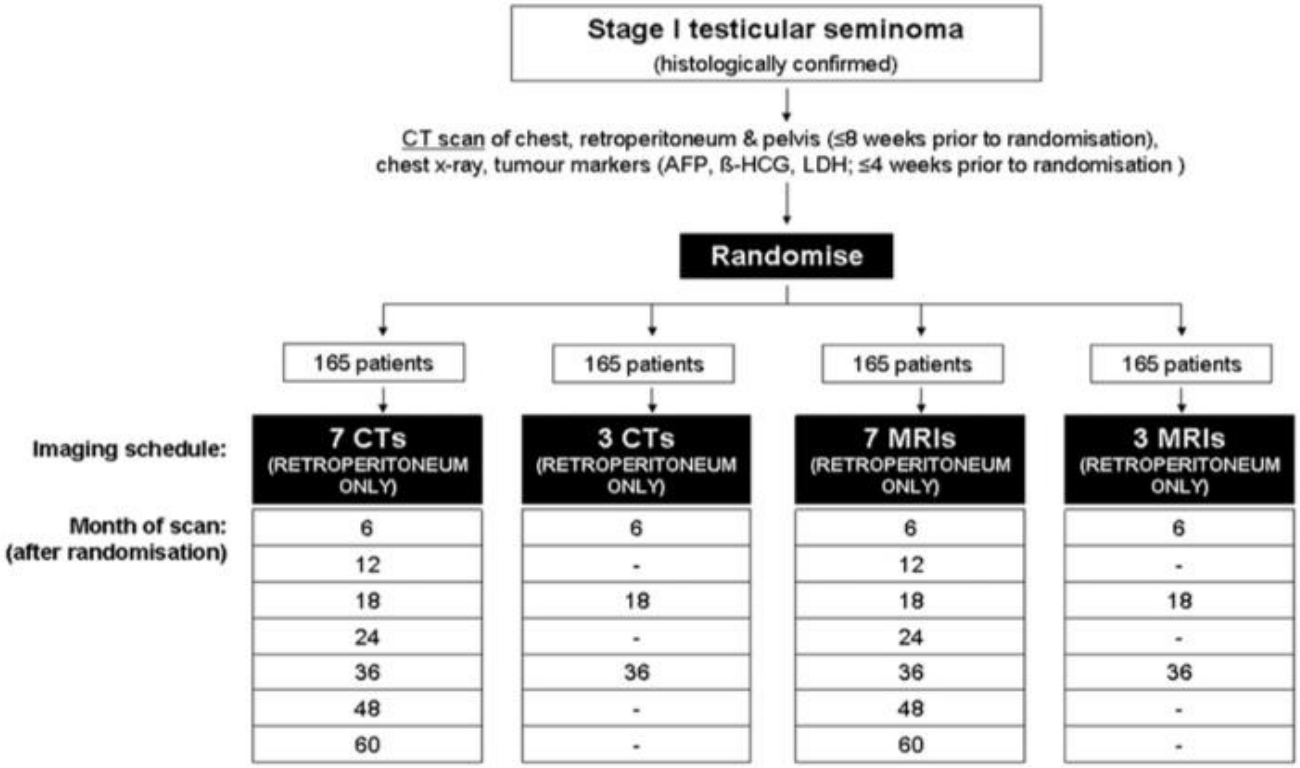


Fig 1. Trial of Imaging and Schedule in Seminoma Testis (TRISST).

F.H. Cafferty et al. / Clinical Oncology 24 (2012) 25–29

Ei näyttöä (ainakaan vielä) diagnostisten tutkimuksien aiheuttamista syövistä

VOLUME 29 · NUMBER 21 · JULY 20 2011

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Association of Diagnostic Radiation Exposure and Second Abdominal-Pelvic Malignancies After Testicular Cancer

Carl van Walraven, Dean Fergusson, Craig Earle, Nancy Baxter, Shabbir Alibhai, Blair MacDonald, Alan J. Forster, and Ilias Cagiannos

Conclusion

Second malignancies of the abdomen-pelvis are uncommon in men with low-grade testicular cancer. In this study, the risk of second cancer was not associated with the amount of diagnostic radiation exposure.

Seminoma ST I
SWENOTECA tulokset

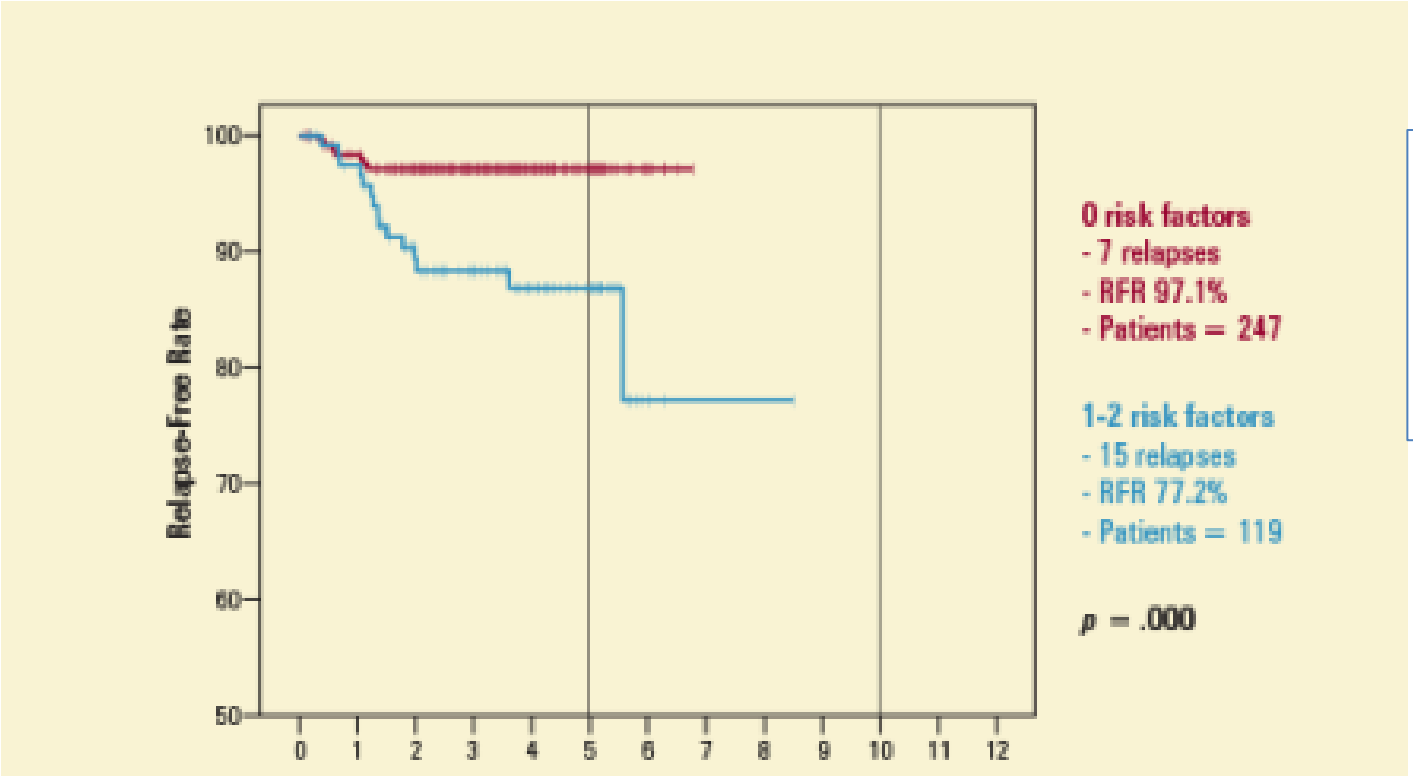
- V 2007-2010 prospektiivinen tutkimus
- Potilaille tarjottiin seurantaa tai single karbopl.
- Seurantaa suositeltiin, jos riskitekijöitä 0-1

  => 50 % halusi adjuvanttihoidon
- Karboplatiinia suositeltiin, jos 2 riskitekijää

  => 90 % sai hoidon
- Seurantaryhmässä N=391 (FU 3,6 v)
- Karbopl. hoidetussa ryhmässä N=447 (5,2 v)

Tandstad ym. SWENOTECA, ASCO 2014 #4508

Seminoma: pelkkä seuranta, riskitekijöiden merkitys



0 riskitekijää
Relapseja **3 %**

1-2 riskitekijää
Relapseja **23 %**

Riskitekijät:
- tuumori > 4 cm
- Rete testis inv.

Tandstad ym. ASCO 2014 Abstr. #4508

ST I Seminooma, karbopl annettu

- Karbopl. Hoidon sai N=669
- Relapseja N= 36 RFR 93,8 %
- Riskitekijät 0 => RFR 97,7 % (N=236)
- Riskitekijät 1-2 => RFR 90,6 % (N=337)

Relapseja:

2 %

9 %

- *”We recommend patient autonomy”*
- ***Jos ei riskitekijöitä => adj hoidosta ei hyötyä***

Yhteenveto:
ST I Seminoman hoito

Tuumorin koko < 4 cm, ei rete testis invaasiota:

- Aktiivi seuranta, adjuvanttihoidosta ei hyötyä (uusimisriski 3 %)

Jos 1-2 riskitekijää:

- Aktiivi seuranta tai karboplatiini, potilaan mielipide ratkaiseva (uusimisriski 23 % vs 9 %)
- Seminoma voi uusiutua pitkän ajan päästä

- MRI tulossa
- Aktiiviseurannassa potilaan sitoutuminen seurantaan keskeistä

Kiitos ja hyvää kevättä kaikille!

Kivessyöpäkoulutus pe 11.9.2015 Helsingissä