

GRUPPO DI LAVORO SCREENING C.C.R.

WorkShop

NOVITÀ PER UN "PERCORSO PREFERENZIALE"

NELLE STRATEGIE DIAGNOSTICO-TERAPEUTICHE

DEL CANCRO COLORETTALE

Strategie di screening validate

Modalità alternative: colon TC e videocapsula

R. Marmo

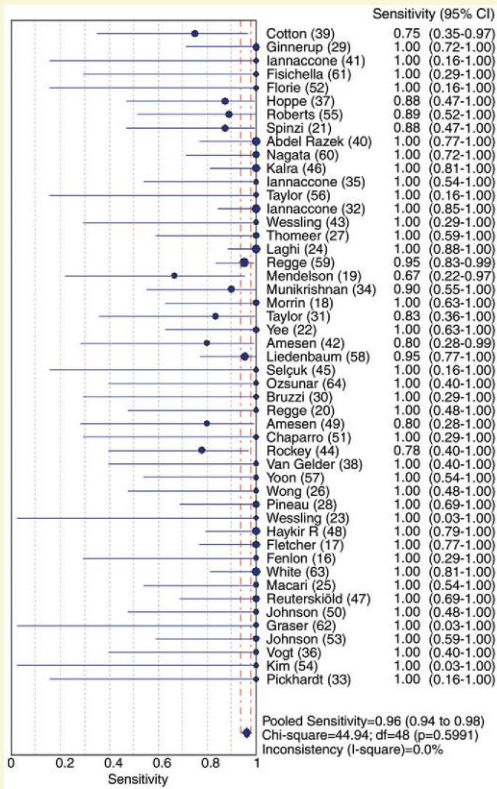
Colorectal Cancer: CT Colonography and Colonoscopy for Detection—Systematic Review and Meta-Analysis

Perry J. Pickhardt, MD
Cesare Hassan, MD
Steve Halligan, MD
Riccardo Marmo, MD

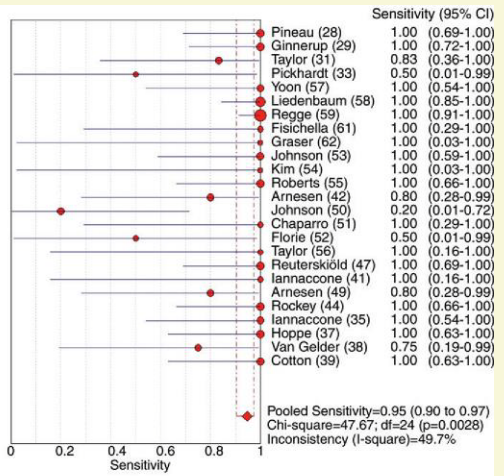
Conclusion:

CT colonography is highly sensitive for colorectal cancer, especially when both cathartic and tagging agents are combined in the bowel preparation. Given the relatively low prevalence of colorectal cancer, primary CT colonography may be more suitable than OC for initial investigation of suspected colorectal cancer, assuming reasonable specificity.

© RSNA, 2011



a.



b.

A 10-fold difference in cancer prevalence between asymptomatic screening 0.5% and symptomatic study populations 6%.

Given the relatively low prevalence of colorectal cancer, primary CT colonography may be more suitable than OC for initial investigation of suspected colorectal cancer, assuming reasonable specificity

In general,
despite an extensive literature investigating the
performance
of CT colonography, the test has limited impact on
CRC screening compliance.

CT colonography

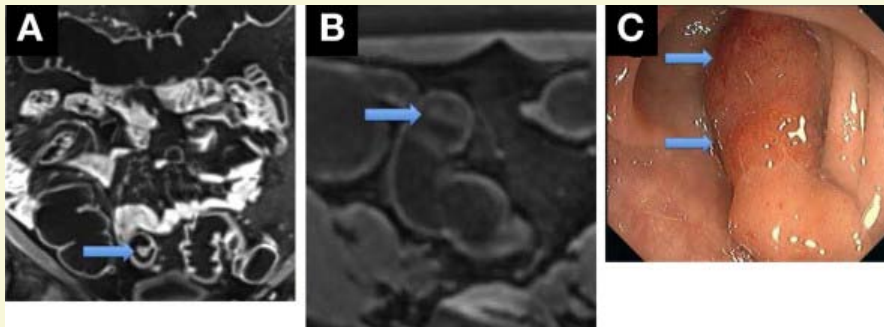
niche of patients who are concerned about the risks of colonoscopy.

We recommend that patients with polyps 6 mm in size at CT colonography undergo colonoscopy.

Magnetic Resonance Colonography for the Detection of Colorectal Neoplasia in Asymptomatic Adults



ANNO GRASER, ANJA MELZER, EVELYN LINDNER, DOROTHEA NAGEL, KARIN HERRMANN, PETRA STIEBER, JÖRG SCHIRRA, ULRICH ANSMANN, MAXIMILIAN F. REISER, BURKHARD GÖKE, and FRANK T. KOLLIGS



Sensitivity of Colonoscopy and MR Colonography for Adenomas and Advanced Neoplasia

133 pts

| Any size | Colonoscopy | MR colonography |
|--------------------|-------------------------------------|-----------------------------------|
| Adenoma | 98.5%; <small>(94.7–99.8)</small> | 32.3%; <small>(24.5–41.0)</small> |
| Advanced adenoma | 100.0%; <small>(83.2–100.0)</small> | 75.0%; <small>(50.9–91.3)</small> |
| Advanced neoplasia | 100.0%; <small>(83.9–100.0)</small> | 76.2%; <small>(52.8–91.8)</small> |

Sensitivity of Colonoscopy and MR Colonography
for Adenomas and Advanced Neoplasia

133 pts

Any size

Colonoscopy

**MR
colonography**

Adenoma detection
rate

29.4%

13.3%

Colon capsule endoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Guideline



C. Spada, C. Hassan, J. P. Galmiche, H. Neuhaus, J. M. Dumonceau, S. Adler, O. Epstein, G. Gay, M. Pennazio, K. Rex, R. Benamouzig, R. de Franchis¹, M. Delvaux, J. Devière, R. Eliakim, C. Fraser, F. Hagenmuller, J. M. Herrerias, M. Keuchel, F. Macrae, M. Munoz-Navas, T. Ponchon², E. Quintero, M. E. Riccioni, Rondonotti R. Marmo, J. J. Sung, H. Tajiri, E. Toth, K. Triantafyllou, A. Van Gossum, G. Costamagna

There is a lack of specific studies based in the setting of screening.

CCE screening may be cost-effective if it increases screening uptake compared with colonoscopy (Evidence level 4, Recommendation grade D)

Clinical Practice Guidelines for the Use of Video Capsule Endoscopy



Robert A. Enns, Lawrence Hookey, David Armstrong, Charles N. Bernstein, Steven J. Heitman, Christopher Teshima, Grigorios I. Leontiadis, Frances Tse, Daniel Sadowski

We recommend against the routine substitution of colon CE for colonoscopy.

Colon Capsule to Screen for Colorectal Neoplasia in Subjects with a Family History of Colorectal Cancer,



Andrea Parodi, Geoffroy Vanbiervliet, Cesare Hassan, Xavier Hebuterne, Antonella De Ceglie,
Rosa Angela Filiberti, Cristiano Spada, Massimo Conio,

Gastrointestinal Endoscopy, Available online 26 May 2017, ISSN 0016-5107,

Colon Capsule to Screen for Colorectal Neoplasia in Subjects with a Family History of Colorectal Cancer,



177 FDRs

CCE identified 51 of 56 FDRs with polyps ≥ 6 mm

Sensitivity 91%

correctly as negative 107 of 121 without lesions ≥ 6 mm

Specificity 88%;

CCE detected 24 of 27 patients with polyps ≥ 10 mm

Sensitivity 89%

Specificity 95%

Post-CCE referral rates to colonoscopy were 37% and 18%, respectively.

Gastrointestinal Endoscopy, Available online 26 May 2017, ISSN 0016-5107,

Colon Capsule to Screen for Colorectal Neoplasia in Subjects with a Family History of Colorectal Cancer,



Andrea Parodi, Geoffroy Vanbiervliet, Cesare Hassan, Xavier Hebuterne, Antonella De Ceglie,
Rosa Angela Filiberti, Cristiano Spada, Massimo Conio,

CCE is an accurate method to screen FDRs of CRC patients and could be offered as an alternative to those who decline or are unfit for colonoscopy screening.

Gastrointestinal Endoscopy, Available online 26 May 2017, ISSN 0016-5107,

Detection of up to 65% of Precancerous Lesions of the Human Colon and Rectum by Mutation Analysis of *APC*, *K-Ras*, *B-Raf* and *CTNNB1*

Mandy Schneider ^{1,†}, Bettina Scholtka ^{1,†,*}, Uwe Gottschalk ², Siegbert Faiss ³, Daniela Schatz ⁴, Kornelia Berghof-Jäger ⁴ and Pablo Steinberg ^{1,5,*}

Prospective pilot study on precancerous human colonic lesions, gene mutations

20 serrated lesions,

41 colorectal adenomas and

10 controls

Detection of precancerous lesions

| Tissue type | APC | K-Ras | B-Raf | CTNNB1 | Total detection rate |
|--------------|-------------|------------|-------------|------------|----------------------|
| Inflammation | 0/10 | 0/10 | 0/10 | 0/10 | 0/10 |
| Serrated | 2/20 (10%) | 4/20 (20%) | 10/20 (50%) | 0/20 (0) | 13/20 (65%) |
| Adenoma | 14/41 (34%) | 6/41 (15%) | 9/41 (22%) | 5/41 (12%) | 25/61 (61%) |



Contents lists available at [ScienceDirect](#)

Cancer Epidemiology

The International Journal of Cancer Epidemiology, Detection, and Prevention

journal homepage: www.elsevier.com/locate/canep



“ A gene marker panel covering the signaling pathways
allows to detect gene mutations
in 80% of early and > 90% of late stage CRC”

Caratteristiche del ColoScape

- Individuazione altamente sensibile delle forme mutate.
- Individuazione di lesioni in tutto il colon-retto.
- Sensibilita' per adenomi avanzati.
- Testabile su plasma e tessuto.

Conclusions

CT (MR) in patients who refuse colonoscopy and FIT.

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Capsule colonoscopy (if available) when patients decline :
colonoscopy, FIT,CT (MR) colonography, and flexible
sigmoidoscopy

Mutation Analysis for CRC screening must be proved

Caratteristiche del ColoScape

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CT in patients who refuse colonoscopy and FIT.

Individuazione di lesioni precancerose

- Almeno un gene era positivo in 65% delle lesioni serrate e 61% degli adenomi.

Specificity & Sensitivity from Internal Study

| | N | Specificity | Sensitivity |
|-------------------------------------|-----------|-------------|-------------|
| Cancer (Stages I-IV) | 35 | N/A | 100% |
| Non-Malignant | 22 | 95% | N/A |
| Overall (Exclude Pre-Cancer) | 57 | 95% | 100% |
| Overall (Include Pre-Cancer) | 67 | 95% | 91% |

Pre-cancer detection sensitivity is 60% (6 out of 10 samples)

Il cancro colorettales In Italia

- Seconda neoplasia per letalita' (dati AIRTUM 2016)

52.000

Nuove diagnosi

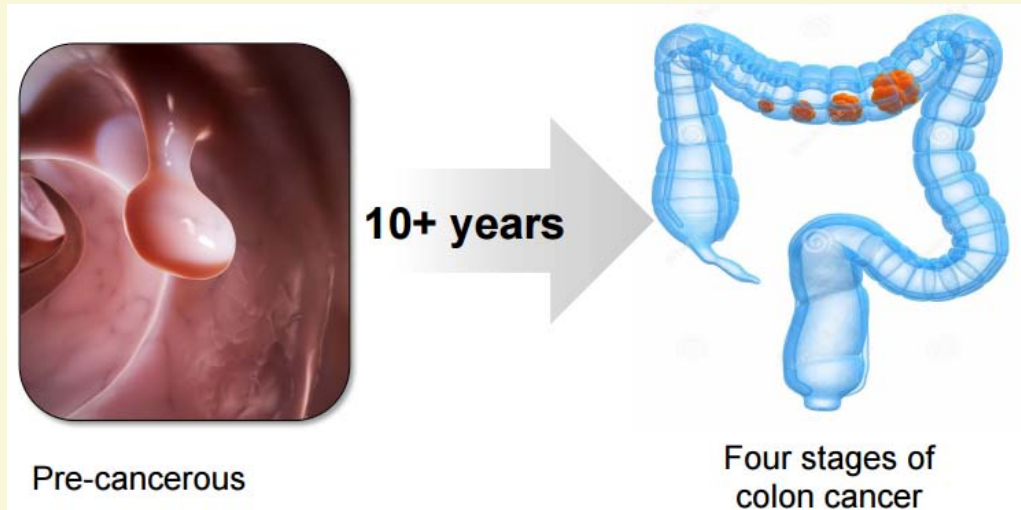
19.000

Decessi

Numero decessi per neoplasia

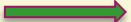


Overview of Colorectal Cancer (Cont')

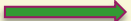


- Pre-cancer (adenoma) progresses to cancer slowly

Vie molecolari al cancro colorettaie (CCR)

1. Sequenza ADENOMA inattivazione bi-allelica del gene APC seguite da mutazioni oncogeniche a carico del K-Ras ,  inattivazione della Tp53 anche mutazioni del gene CTNNB1 , sebbene con una minore frequenza.

Vie molecolari al cancro colorettaie (CCR)

1. Sequenza ADENOMA inattivazione bi-allelica del gene APC seguite da mutazioni oncogeniche a carico del K-Ras ,  inattivazione della Tp53 anche mutazioni del gene CTNNB1 , sebbene con una minore frequenza.

2. SERRATED PATHWAY: caratterizzata da mutazioni “missense” del gene B-Raf, metilazione diffusa ed instabilita' microsatellitare..

3. FUSION PATHWAY (Jass et al.) : combina entrambe le vie : metilazione del gene di riparazione del DNA + mutazioni K-Ras + inattivazione Tp53 . B-Raf e K-ras si escludono a vicenda.

Sintesi delle vie molecolari al CCR

- Mutazioni possono essere individuate in tutti gli stadi della malattia (preneoplastico, neoplastico e metastatico)
- Mutazioni dei geni KRAS ed APC si trovano nella quasi totalita' dei CCR..
- La definizione di uno stato wild-type del KRAS e' ora un marker di risposta a certe terapie.
- Alcune mutazioni sembrano anticipare recidive organo-specifiche.
- Il gene BRAF si usa comunemente per la stratificazione prognostica.

ColoScape – Strategia di selezione dei geni

APC, CTNNB1 , B-RAF e K-RAS.

Sono coinvolti in tutte le pathways APC si trova in circa 60% ed KRAS ~ 40% dei CCR. BRAF si trova comunemente nelle lesioni serrate . La B-catenina e' un prodotto dell'espressione del gene CTNNB1 e si trova in ~ 50% dei CCR con instabilita' microsatellitare..

Facendo uso di questo panel genico si e' evidenziato che > 80% dei CCR (I-IV) e > 60% degli AA portavano ALMENO una forma mutata di uno dei 4 geni..

Gli studi sono stati condotti su TESSUTO da Bettina Scholtka e colleghi all' Universita' di Postdam (Germania) e confermati da studi di validazione interna anche su sangue e feci. ColoScape e' approvato CE-IVD per l'individuazione di mutazioni associate al CCR .

Sono ora necessari studi prospettici di validazione su plasma per possibili applicazioni nel triage pre- e post-colonoscopico nonche' nello screening.

Detection of precancerous lesions

| | Inflamed mucosa | | Serrated lesions | | Adenoma | |
|-----------------------|-----------------|------|------------------|------|---------|------|
| | N | % | N | % | N | % |
| LOCATION | 10 | 14.1 | 20 | 28.2 | 41 | 57.7 |
| Proximal colon | 1 | 10 | 8 | 40 | 21 | 51.2 |
| Distal colon | 4 | 40 | 6 | 30 | 13 | 31.7 |
| Rectum | 4 | 40 | 4 | 20 | 3 | 7.3 |
| Unknown | 1 | 10 | 2 | 10 | 4 | 9.8 |
| DYSPLASIA | | | | | | |
| LGD | | | | | 36 | 87.8 |
| HGD | | | | | 3 | 7.3 |
| Unknown | | | | | 2 | 4.9 |
| HISTOLOGIC TYPING | | | | | | |
| Tubular adenoma | | | | | 35 | 85.4 |
| Tubulovillous adenoma | | | | | 4 | 9.8 |
| Unknown | | | | | 2 | 4.9 |