39. Schweizerische Koloproktologie-Tagung

Samstag, 13. Januar 2018

Bern

Komplikationen und Katastrophen

Kolonkarzinom-Update

HELIOS Kliniken

Jeder Moment ist Medizin

Hereditäre Kolonkarzinome

Gabriela Möslein

Kolo**rektale** Karzinome

- Sporadisch (ca. 70%)
  - Höheres Lebensalter
  - Multiple somatische Mutationen
- Familiär (ca. 20%)
  - Polygenetisch
  - Exogene Faktoren
- Hereditär (10%)
  - pathogene Keimbahnmutation
  - Gen und Gender, individualisiertes Vorgehen,

    hohes Präventionspotential in der Familie!

Paradigmenwechsel

Das aktuelle Dilemma:

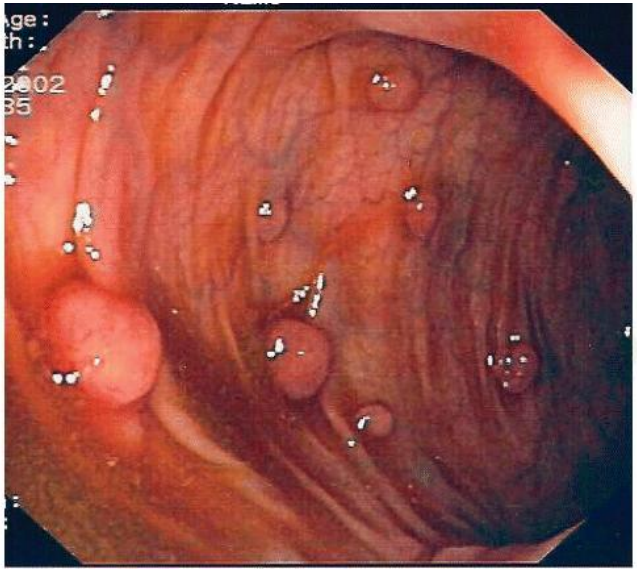
- Familienanamnestische Selektionskriterien sind unzulänglich
- Phänotypische Selektionskriterien sind unzulänglich
- Präventionspotential unterschätzt
- Chancen einer individualisierten Therapie werden nicht genutzt

Wie erkennen?

3 Szenarien

- Phänotypische Merkmale
- Systematische Testung
- Bekannte Mutationsträger

Wie erkennen?



Adenome

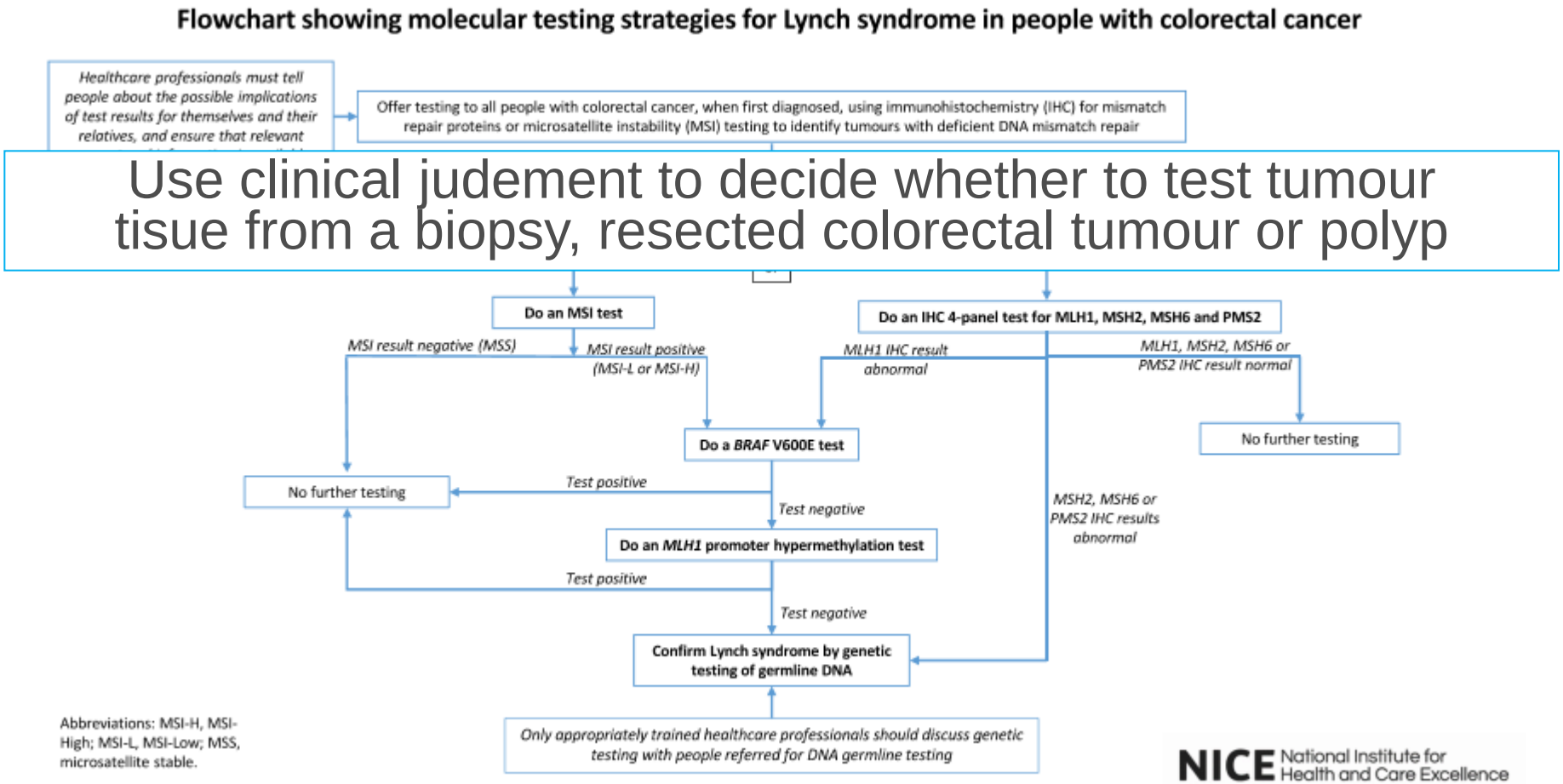
- Familiäre adenomatöse Polyposis (FAP)
- **MUTYH-assoziierte Polyposis (MAP)**
- **NTHL-1 assoziierte Polyposis (NAP)**
- **MSH-3 homozygot (rezessiv)**
- Hyperplastische Polyposis (HP)
- Oligopolyposis (Multiple Adenoma) MA
- Polymerase Proofreading-assoziierte Poly. (PPAP)
- Erblicher Darmkrebs ohne Polyposis (**HNPCC – Lynch-Syndrom**)

Wie erkennen?

3 Szenarien

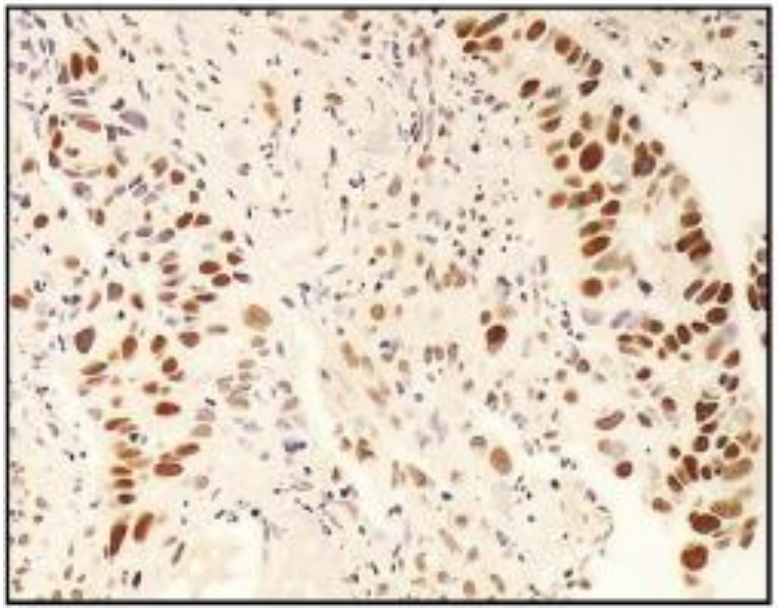
- Phänotypische Merkmale
- Systematische Testung
- Bekannte Mutationsträger

22. Februar 2017 !!!

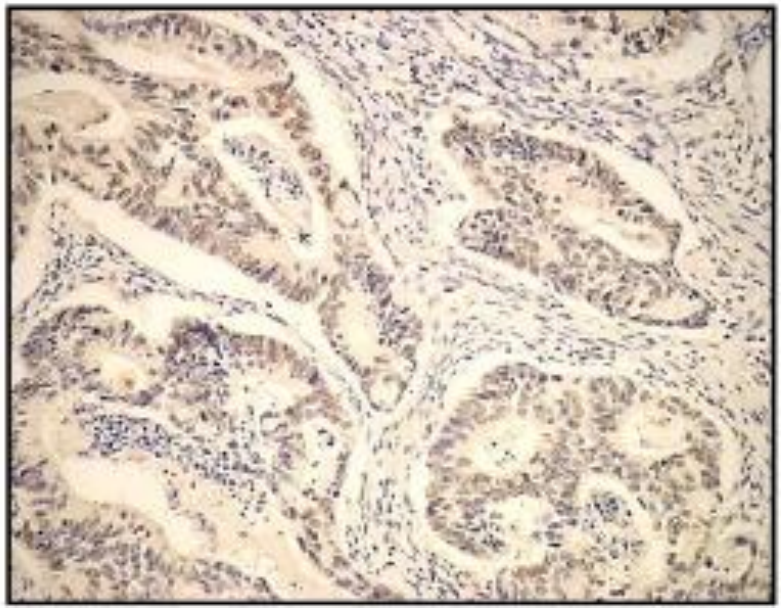


Non-Polyposissyndrome
Lynch-Syndrom und HNPCC
Vilkin A et al. Human Pathology 2015: 1705-1711

PMS2 Endoscopic biopsy



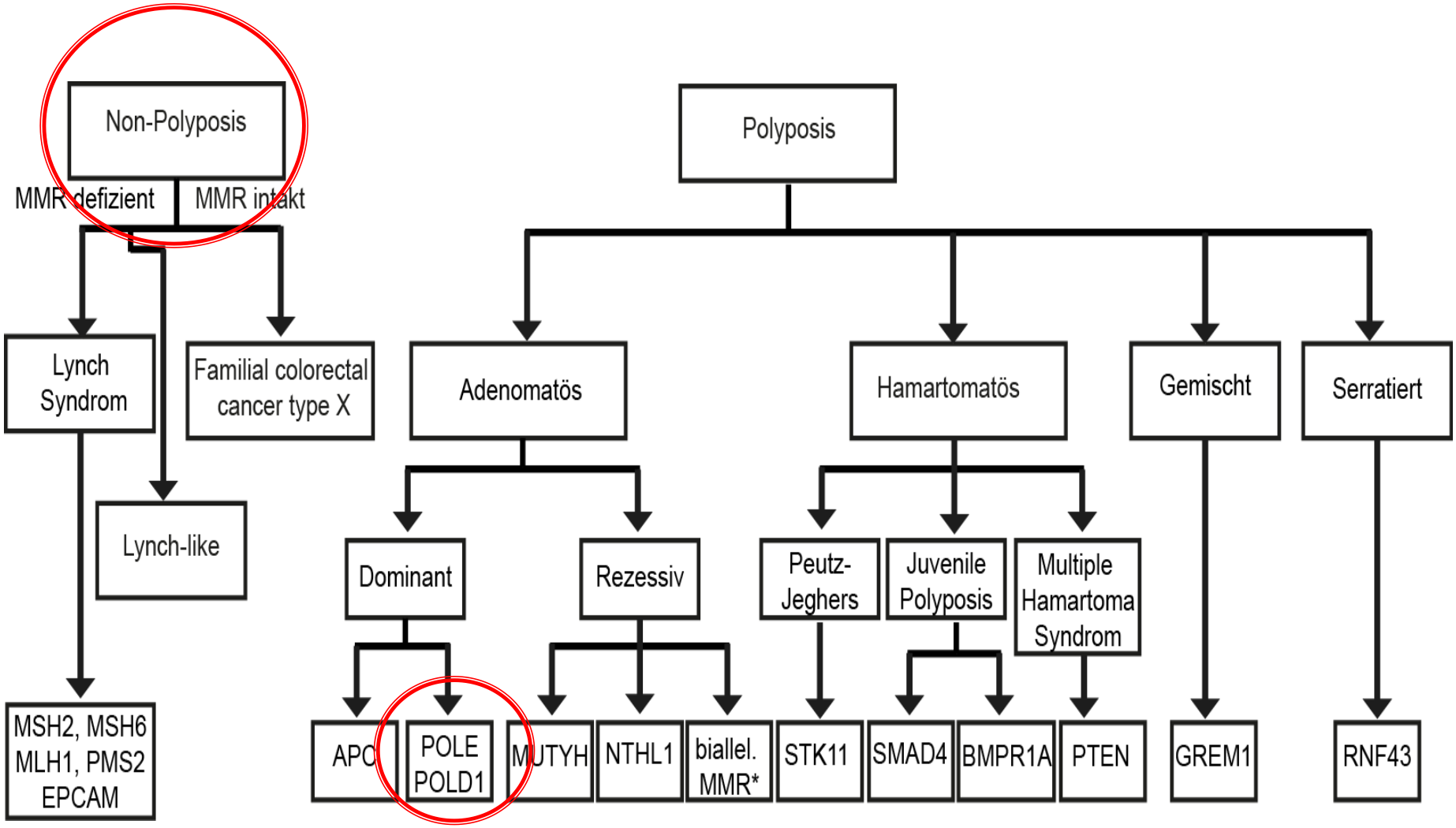
PMS2 Surgical material



Immunohistochemistry staining for PMS2 on endoscopic biopsies and surgical specimens from the same tumor

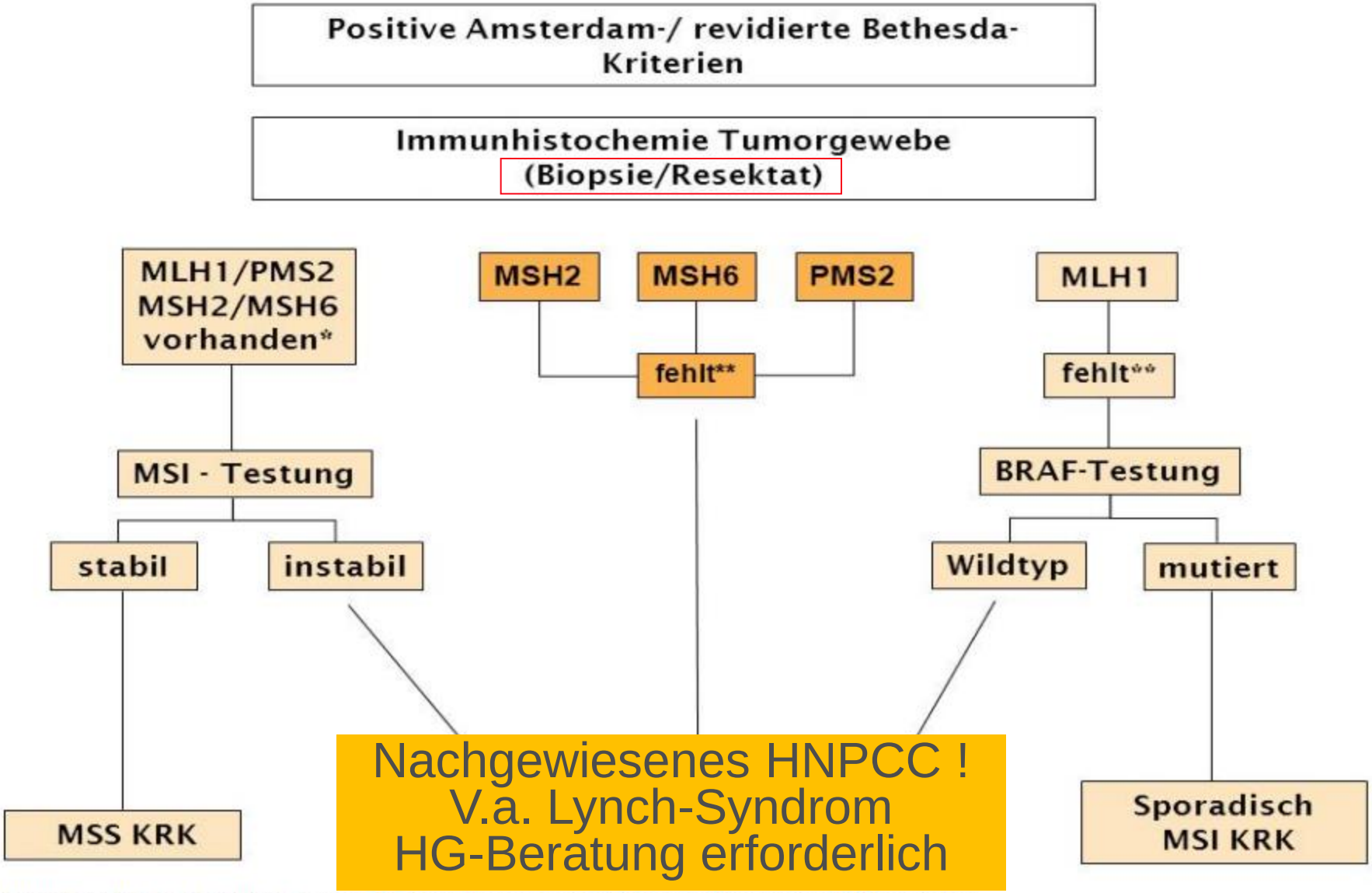
Hereditäre kolorektale Karzinome

Valle L. Recent Discoveries in the Genetics of Familial Colorectal Cancer and Polyposis. Clin Gastroenterol Hepatol 2016.



Bestimmung der Mikrosatelliteninstabilität

Aktuelle Deutsche S3-Leitlinie



Revised Bethesda-Criteria

(Umar et al., 2004)

Medscape® www.medscape.com

Tumors from individuals should be tested for MSI in the following situations:

1. Colorectal diagnosed in a patient who is less than 50 years of age.
2. Presence of synchronous, metachronous colorectal, or other HNPCC-associated tumors*, regardless of age.
3. Colorectal cancer with the MSI-H† histology‡ diagnosed in a patient who is less than 60 years of age.§
4. Colorectal cancer diagnosed in one or more first-degree relatives with an HNPCC-related tumor, with one of the cancers being diagnosed under age 50 years.
5. Colorectal cancer diagnosed in two or more first- or second-degree relatives with HNPCC-related tumors, regardless of age.

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*HNPCC-associated tumors include colorectal, endometrial, stomach, ovarian, pancreas, ureter and renal pelvis, biliary tract and brain (usually glioblastoma as seen in Turcot syndrome) tumors, sebaceous gland adenomas and keratoacanthomas in Muir-Torre syndrome, and carcinoma of the small bowel.

†MSI-H = microsatellite instability-high in tumors refers to changes in 2 or more of the five National Cancer Institute-recommended panels of

Limited sensitivity and specificity

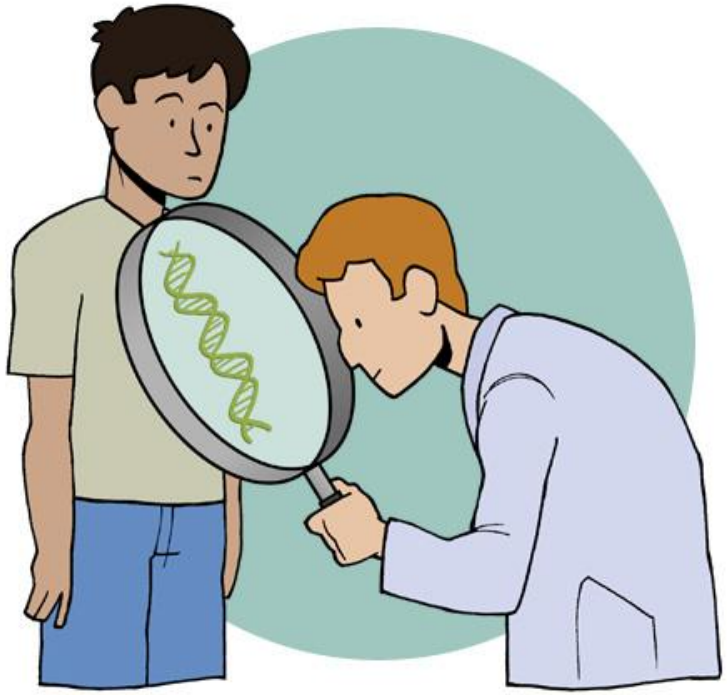
Wie erkennen?

medical
genetic testing

tests in people
who are ill

predictive
genetic testing

tests in people
who are well



Wie erkennen?

3 Szenarien

- Phänotypische Merkmale
- Systematische Testung
- Bekannte Mutationsträger

Wie behandeln?

- Syndromspezifisch
- Interdisziplinär
- Lebenslang
- …die ganze Familie
- Nach dem neuesten Erkenntnisstand
- Funktionalität + Lebensqualität
- Individuell, informed decision making!

Decision making in BRCA

Hereditäre kolorektale Karzinome

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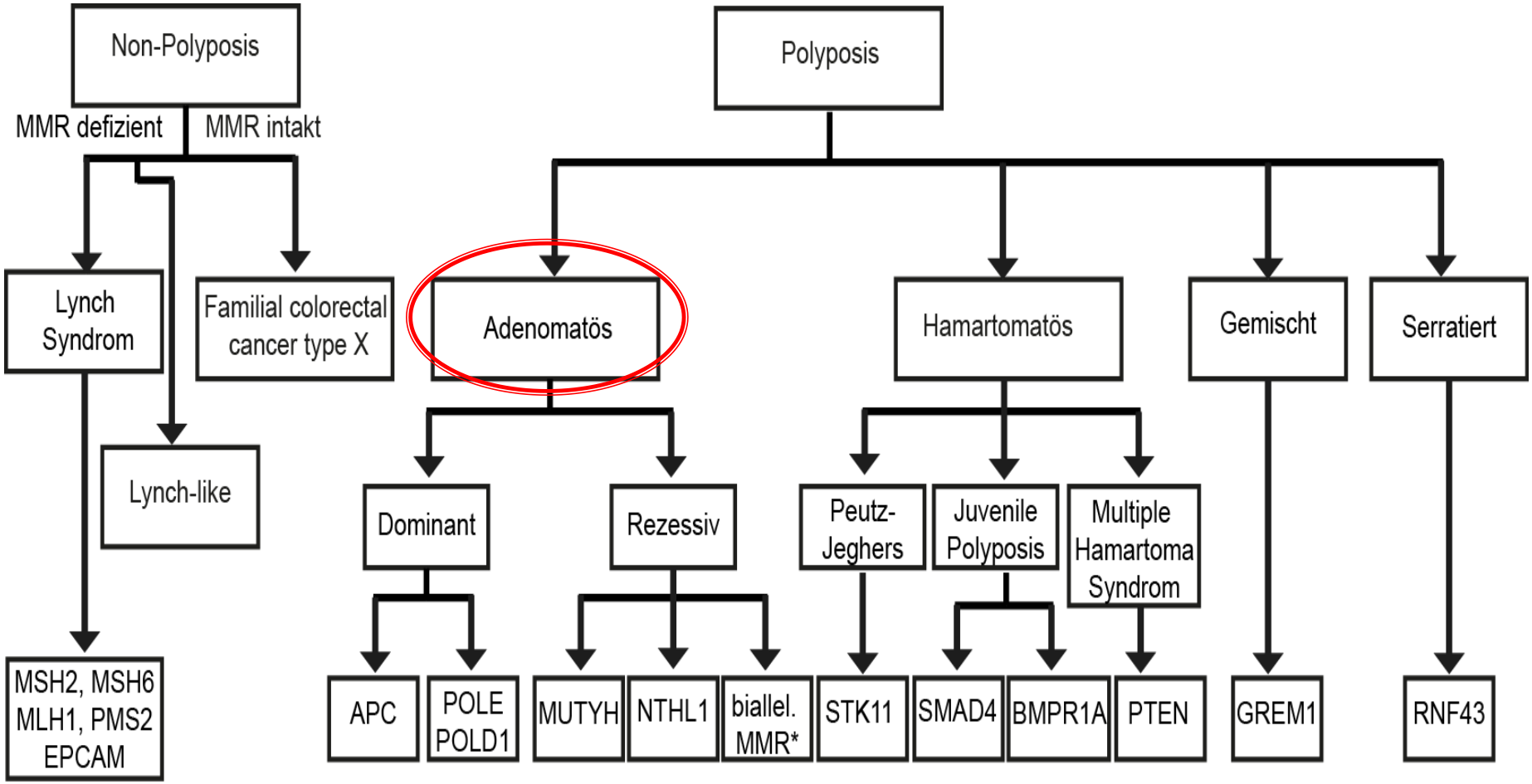


Adenomatöse Polyposis-Syndrome
FAP - *Klassische Variante*

State-of-the-Art

Kolorektum *(Chirurgische Therapie)*

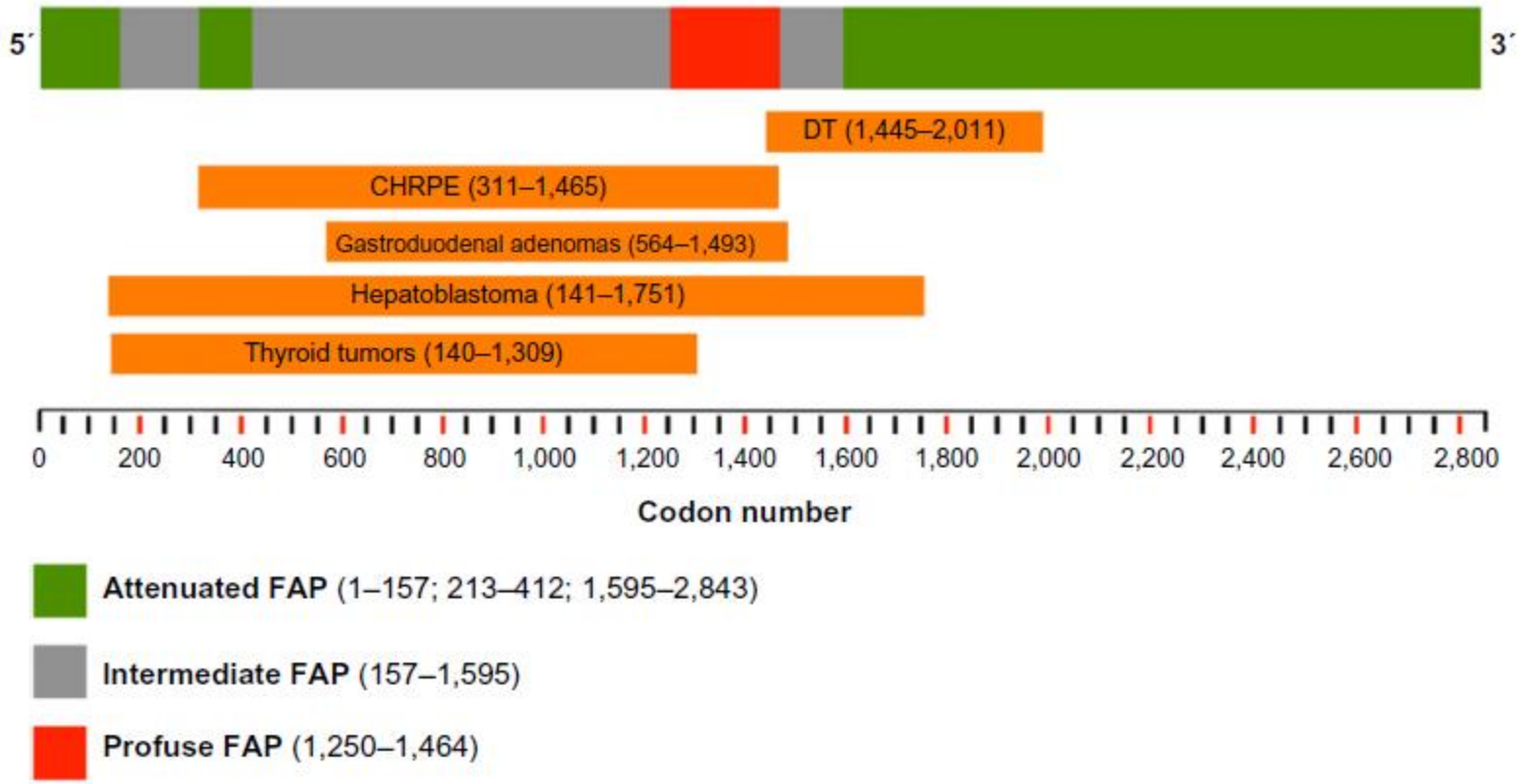
- Prophylaktische Proktokolektomie mit IAP (ileoanale Pouchanlage)

- Kriterien zur Indikationsstellung?
  - Größe, Zahl, Verteilungsmuster, Dysplasie?

Adenomatöse Polyposis-Syndrome
FAP - attenuierte *Variante*

- Weniger Adenome als bei der klassischen FAP (10-100)
- Späteres Erkrankungsalter bzgl. Adenomen (Mittel: 44 Jahre) und Karzinomen (56 Jahre)
- Autosomal-dominanter Erbgang
- APC-Gen-Mutation <Codon 1517 oder >Codon 1900 -> Gensequenzierung
- Rechtsbetonter Kolonbefall, Rektum eher selten betroffen -> Koloskopie, evtl. Chromoendoskopie
- Weniger extrakolonische Manifestationen
- Breite phänotypische Variabilität

APC – Gen (adenomatous polyposis coli)

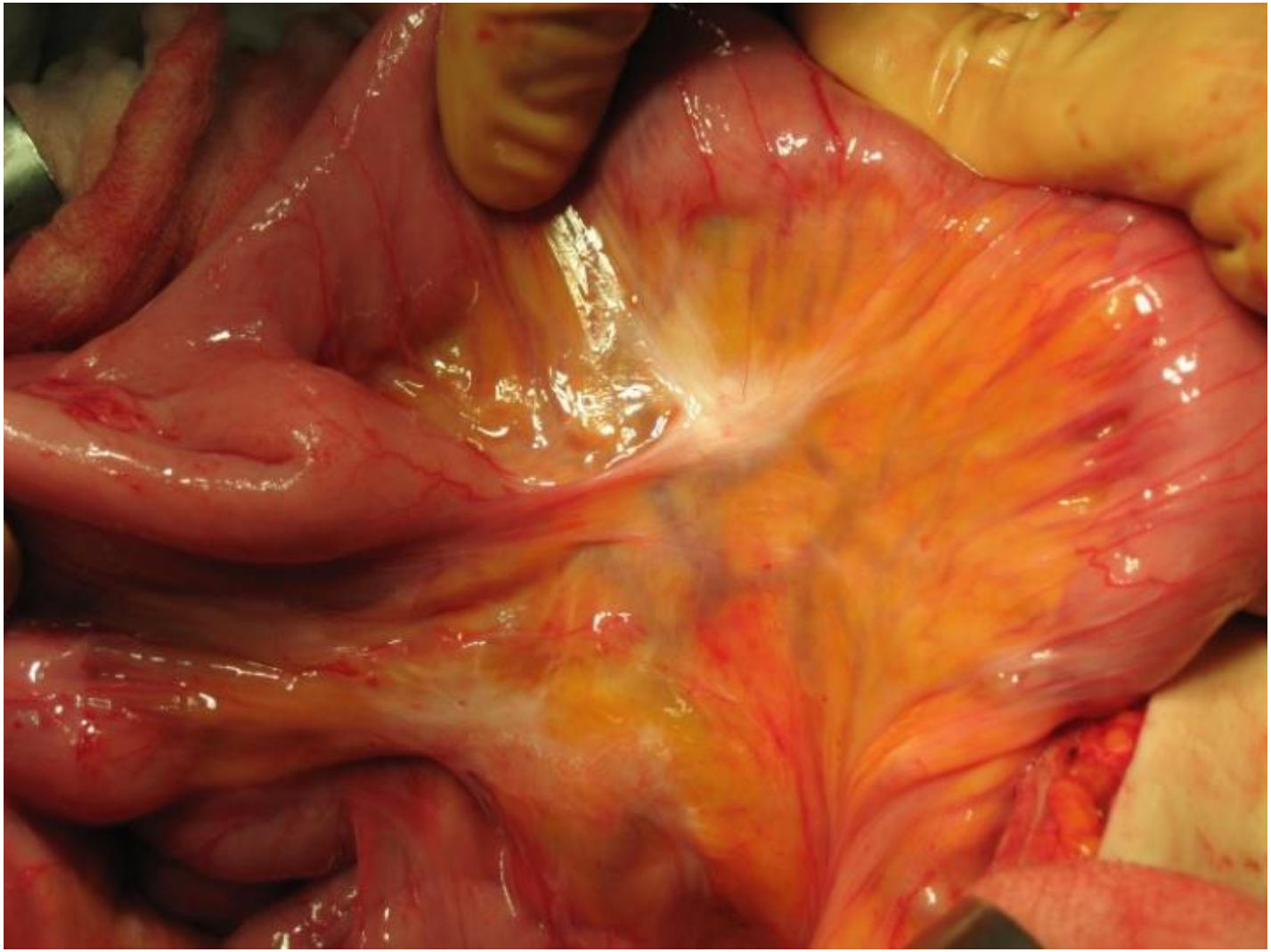


Extrakolonische Manifestationen

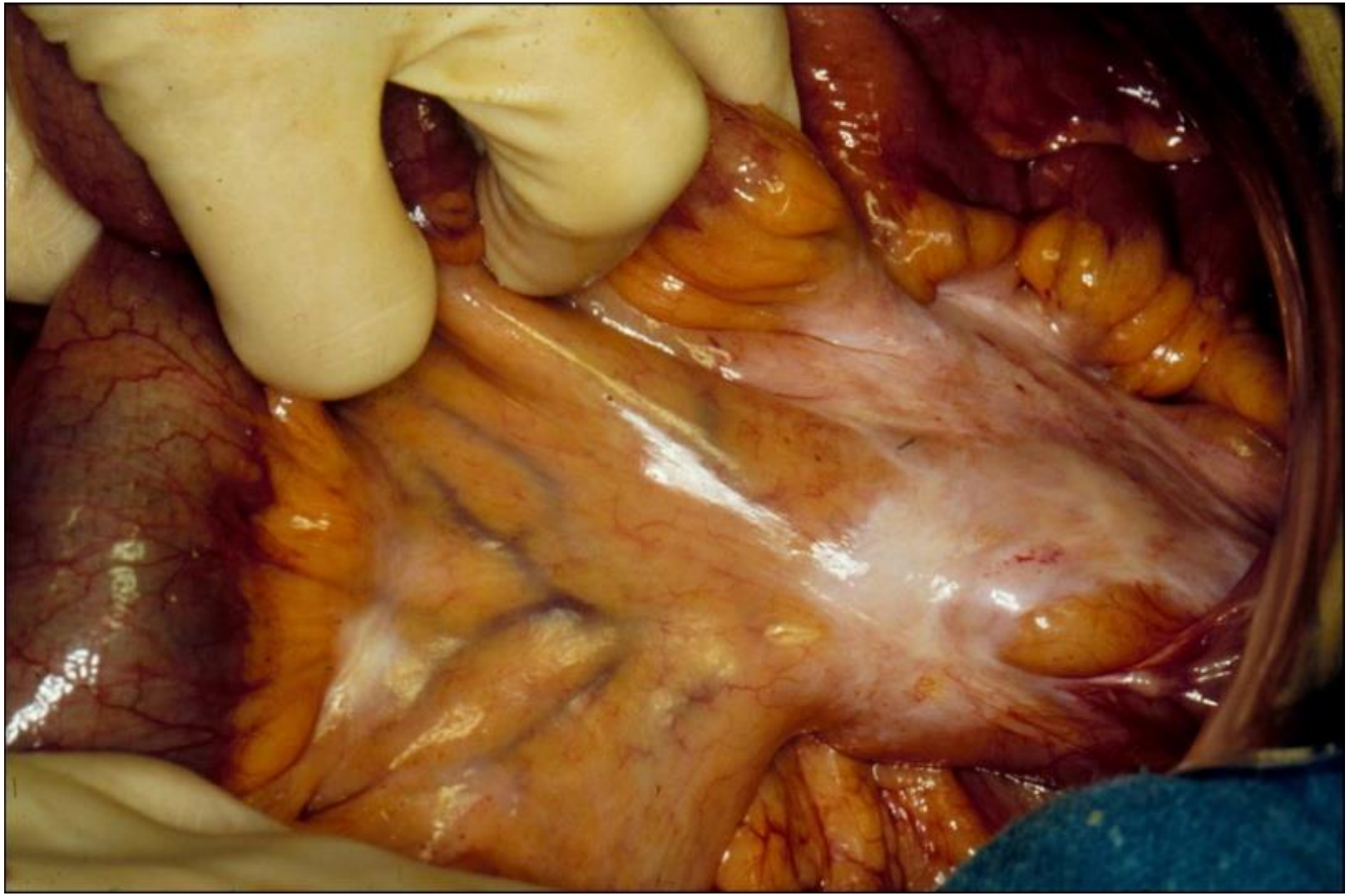
- Drüsenkörperzysten des Magens
- Adenome des Duodenums (und Jejunums)
- Extrakolonische Karzinome:
  - duodenale and periampulläre Tumore (5-10%)
  - Pankreas (2%)
  - Schilddrüse (2%)
  - Magen (0.5%)
- Osteome, und Weichgewebtumore der Haut (Fibrome, Atherome)
- Congenitale Hypertrophie des retinalen Pigmentepithels (CHRPE)

Hernegger et al. Dis Colon Rectum. 2002 Jan;45(1):127-136

Desmoid plaque als Vorläuferläsion



Desmoid Tumor



Wann operieren?

InSiGHT Polyposis Staging System-Rectum

Lynch PM et al. Gastrointestinal Endoscopy 2016;84:115-125.e114

Stage#	Polyp Description
0	0-10 polyps, all <5mm
1*	10-25 polyps most <5mm, none >1cm
2*	10-25 polyps, any >1cm, amenable to complete removal
3*	> 25 polyps amenable to complete removal, or any incompletely removed sessile polyp, or any evidence of HGD, even if completely excised
4	>25 polyps not amenable to complete removal, or any incompletely excised sessile polyp showing HGD; any invasive cancer

Clinical Intervention		Comments:
(A)	Repeat FS in 1 Year	
(B)	Ablate polyps; repeat sigmoidoscopy in 1 year	Chemo-preventive may be considered
(C)	Repeat sigmoidoscopy 6 months Polypectomy preferred	Removal of large polyps clearly necessary Chemo-preventive valuable
(D)	Repeat sigmoidoscopy 3-6 months; consider proctectomy	Large polyps must be removed; second opinion on polyp management helpful
(E)	Proctectomy / pouch revision +/- ileostomy clearly indicated within 3 months	Any decision to delay surgery must be highly individualized and based on compelling circumstances

*Presence of High-Grade Dysplasia Warrants Upstaging of Patient to Stage 4.

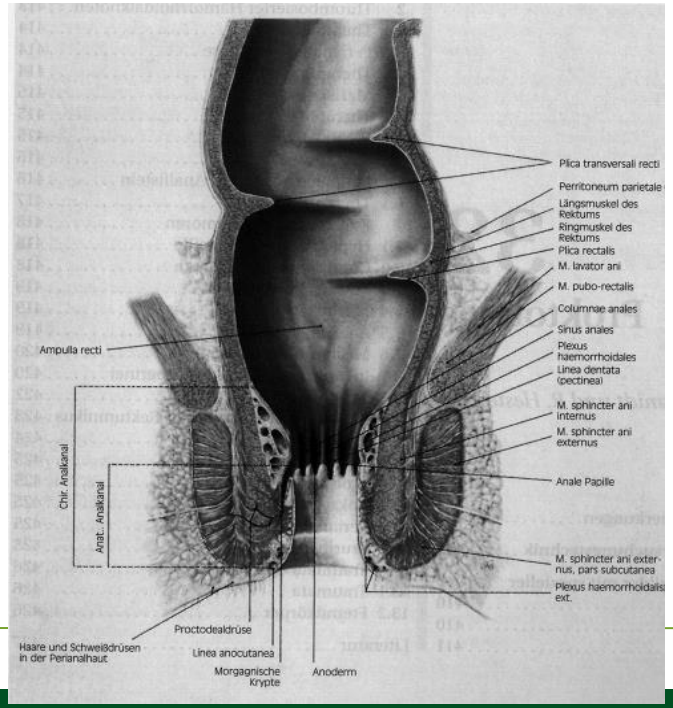
Patients who cannot be allotted a particular stage (e.g. patients with mix polyposis) call for an external discussion in a multidisciplinary specialty team.

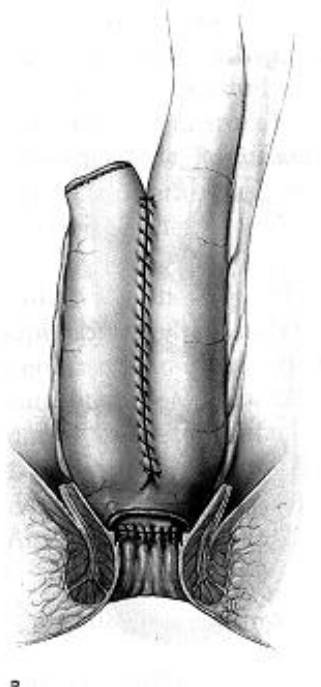
Wie operieren?

Prophylaktische Chirurgie

IRA
(ileorektale Anastomose)

IPAA
(ileopouchanale Anastomose)





Proktokolektomie und IPAA bei FAP

- Laparoskopisch
- Ohne protektive Loopileostomie
- TME als taTME

Proktokolektomie und IPAA bei FAP

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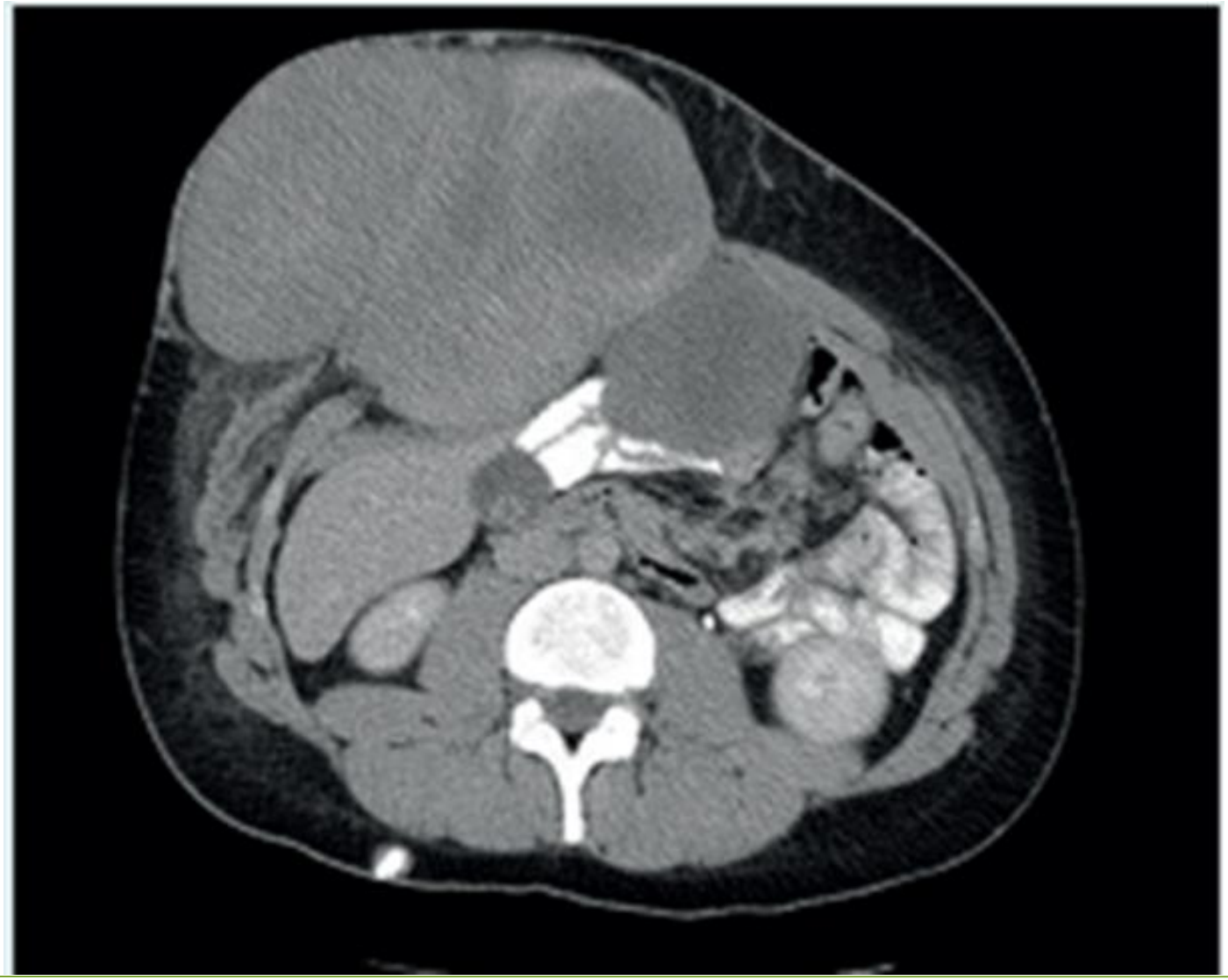
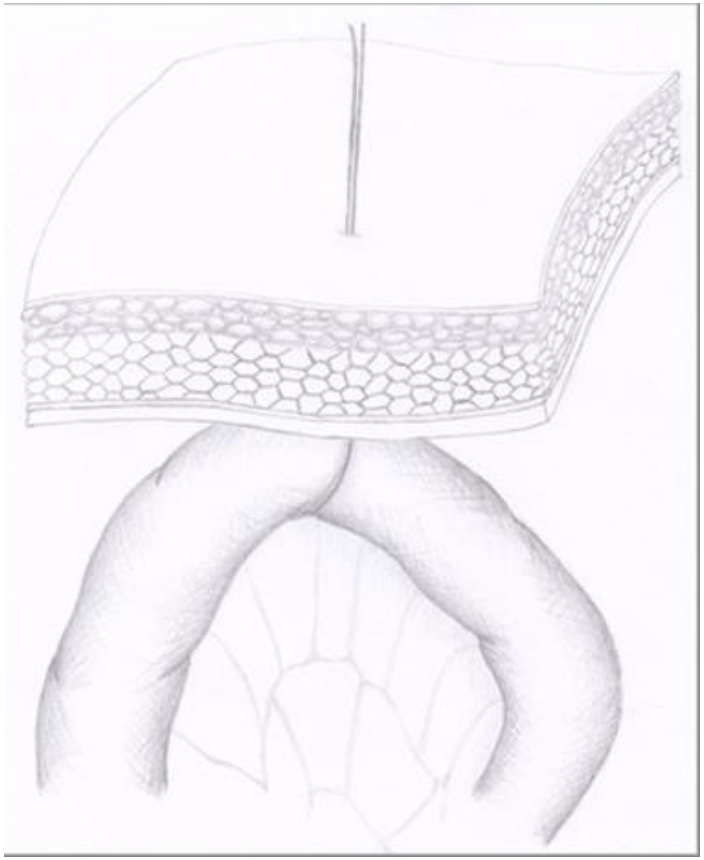
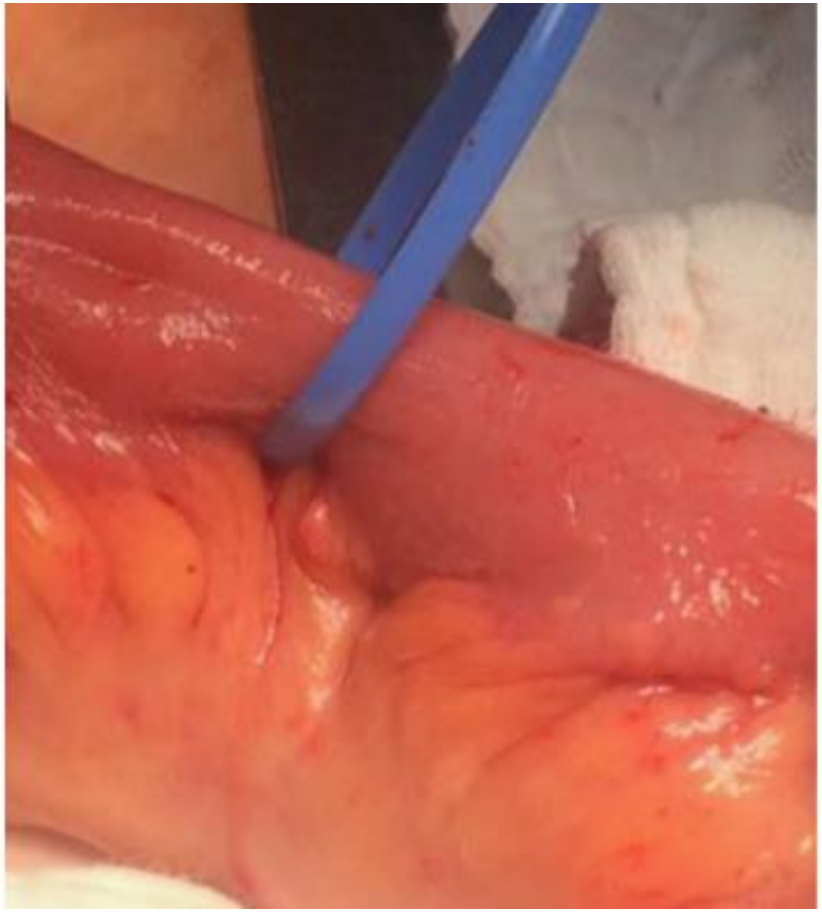
Proktokolektomie und IPAA bei FAP



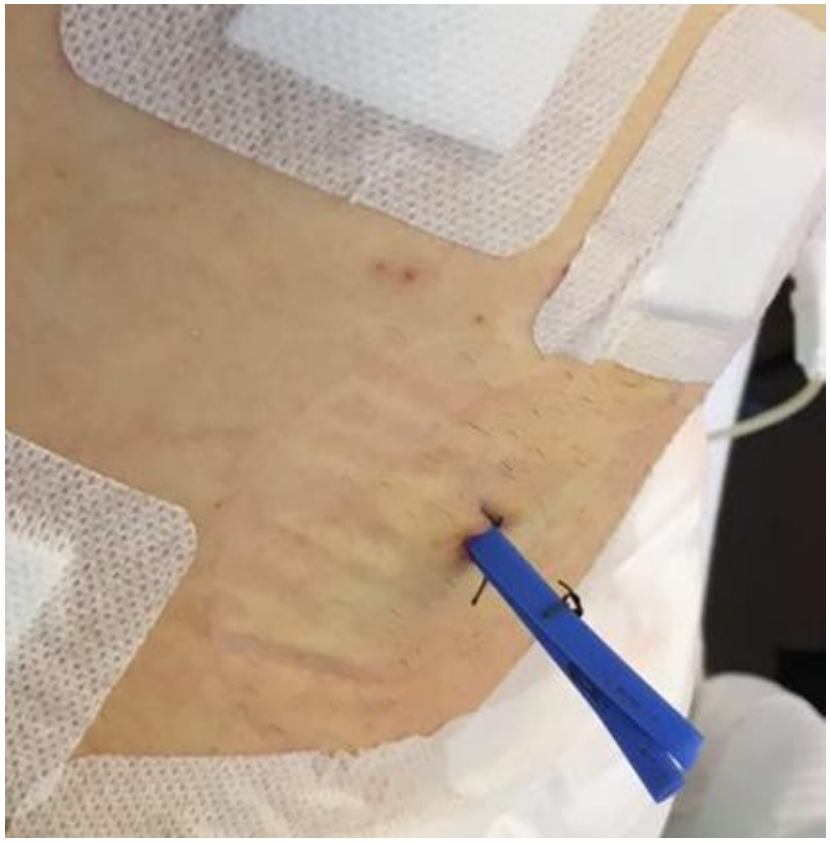
Virtual Ileostomy



Virtuelle Ileostomie



Virtuelle Ileostomie



Proktokolektomie und IPAA bei FAP

Laparoskopisch

Ohne protektive Loopileostomie

TME als taTME

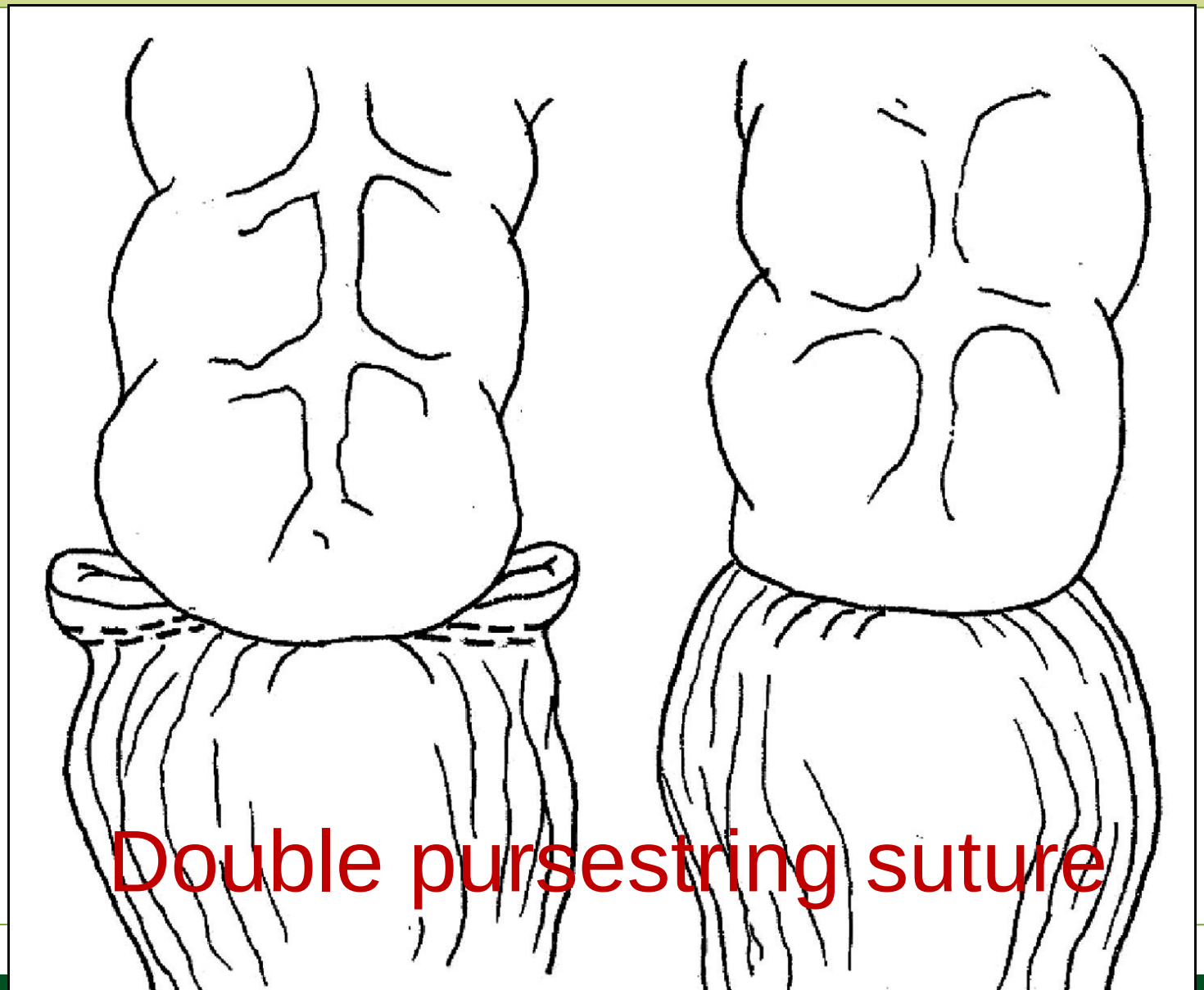
Techniques in Coloproctology (2017) 21:971–974
https://doi.org/10.1007/s10151-017-1730-9

ORIGINAL ARTICLE

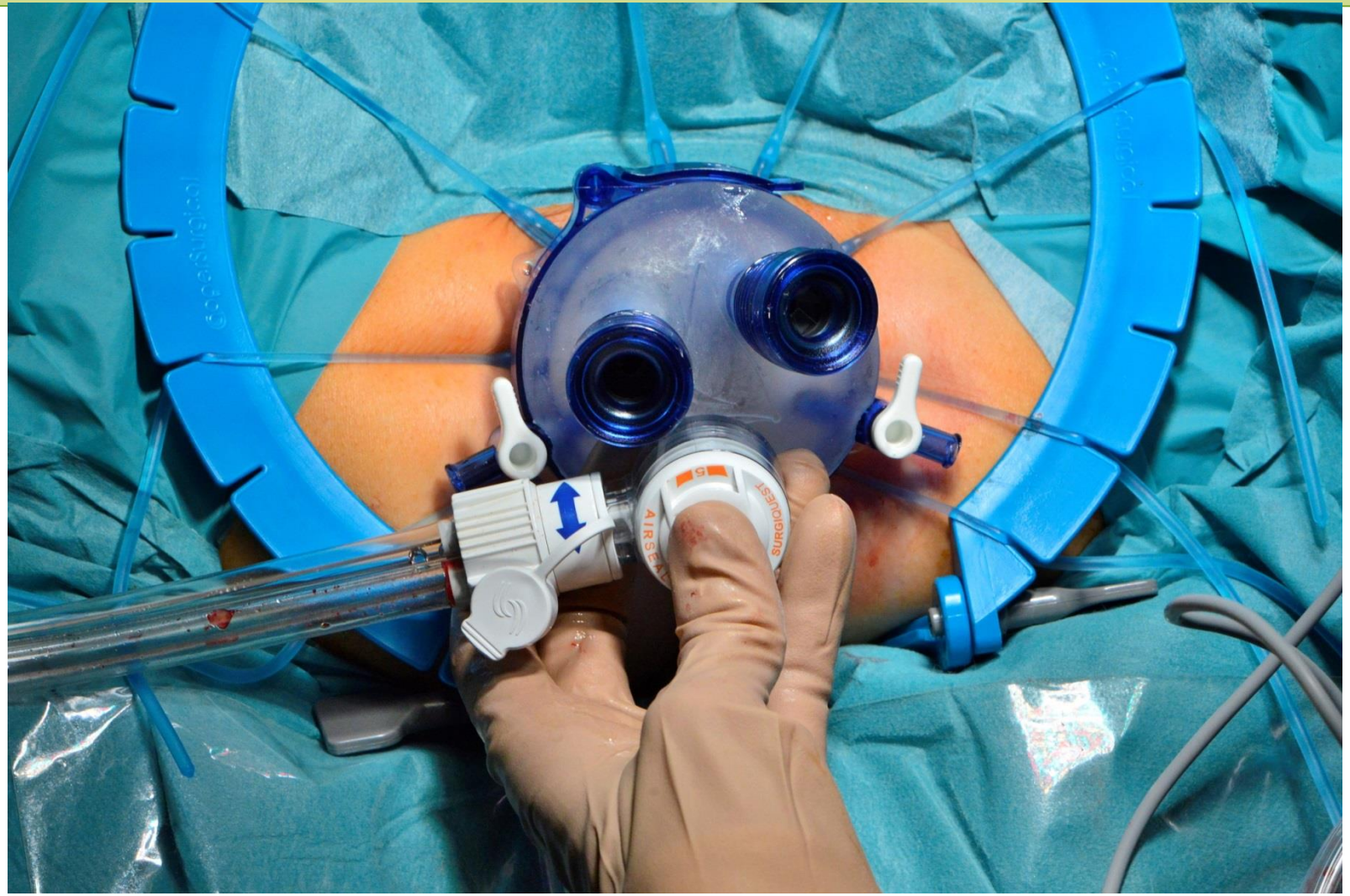
Initial experience with taTME in patients undergoing laparoscopic restorative proctocolectomy for familial adenomatous polyposis

P. C. Ambe[1,2] · H. Zirngibl[1] · G. Möslein[2]

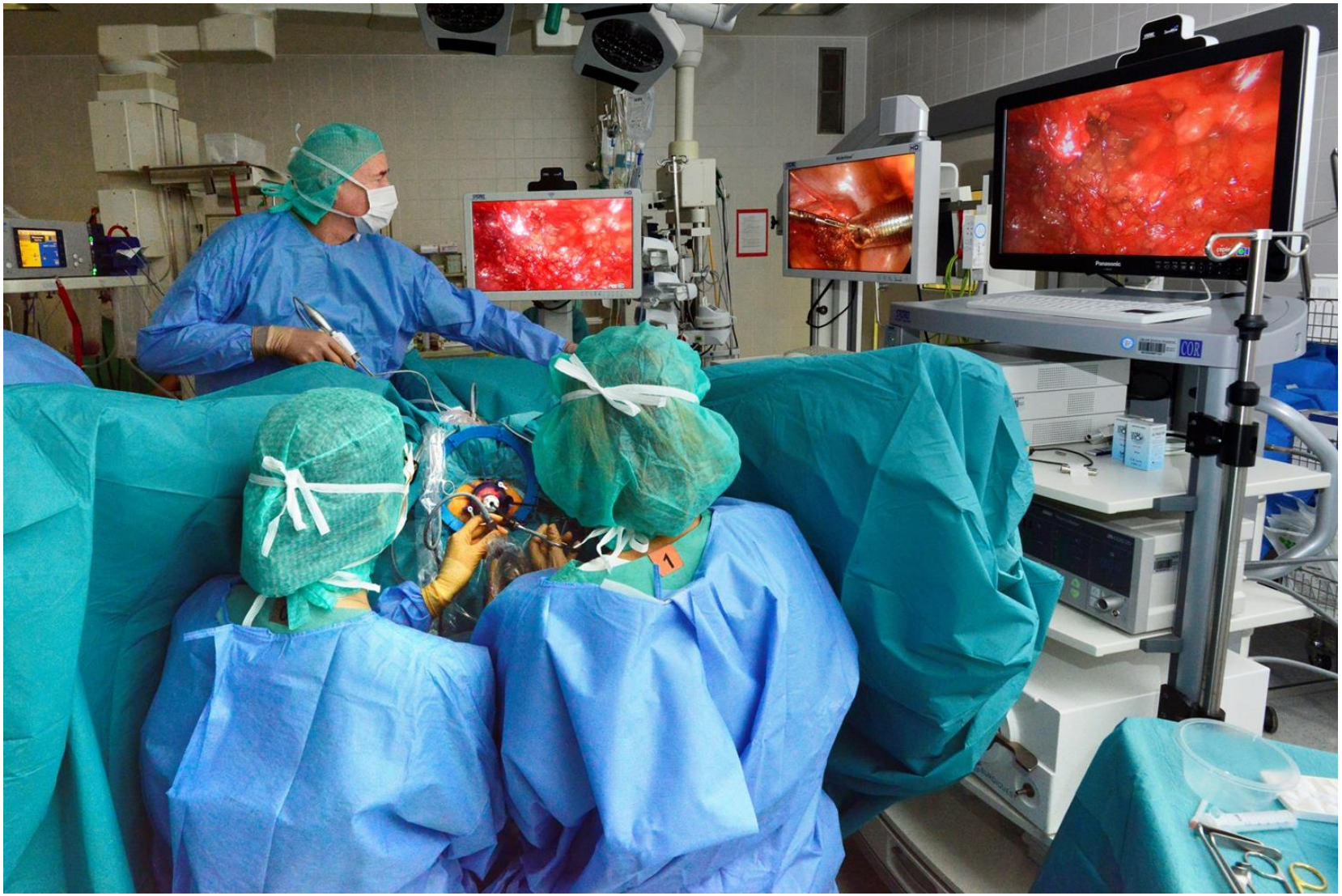
taTME = transanal total mesorectal excision



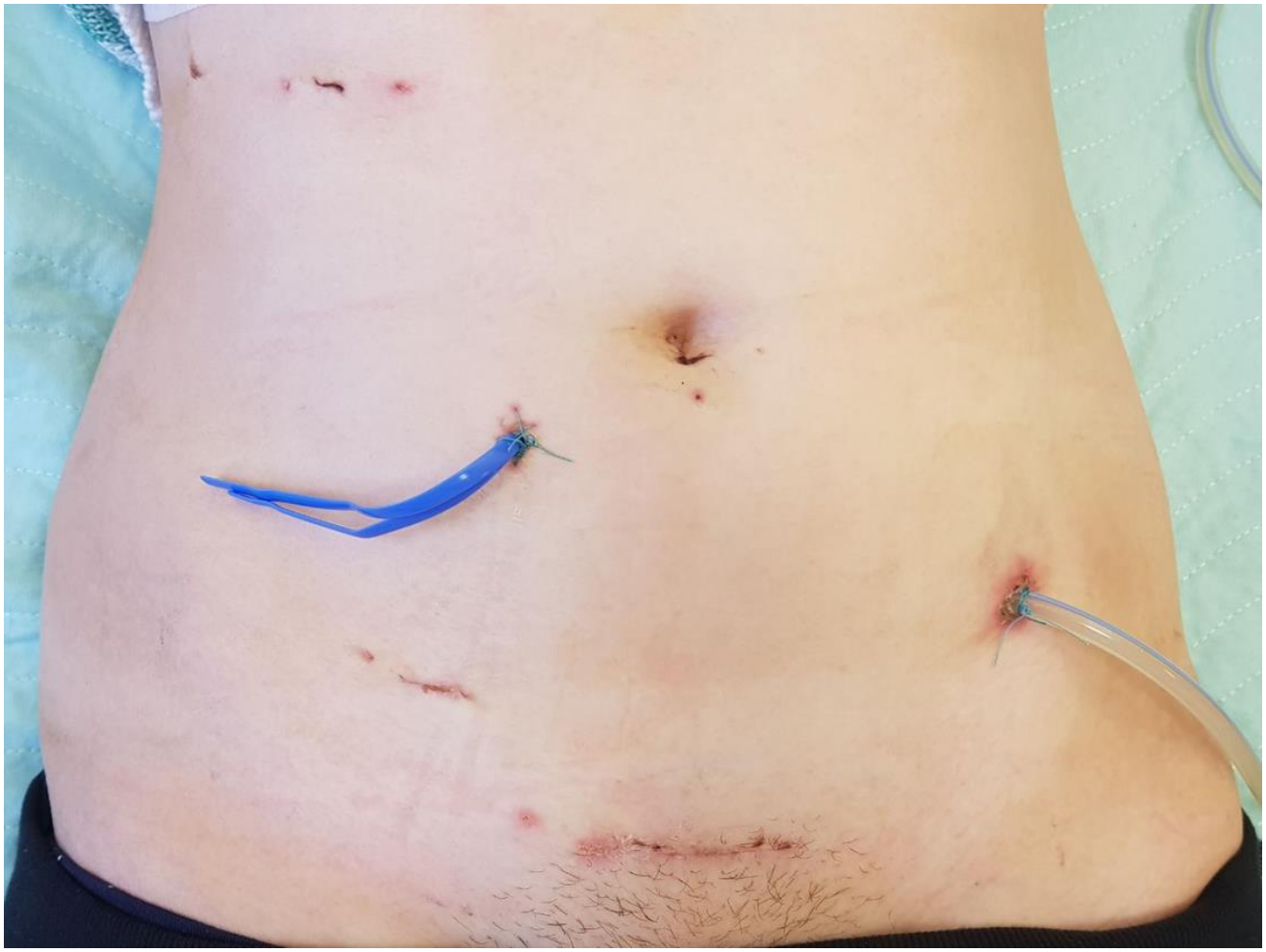
Platform und Airseal



Arbeiten mit 2 Teams!



Postoperatives Bild mit virtueller Ileostomie



Hereditäre kolorektale Karzinome

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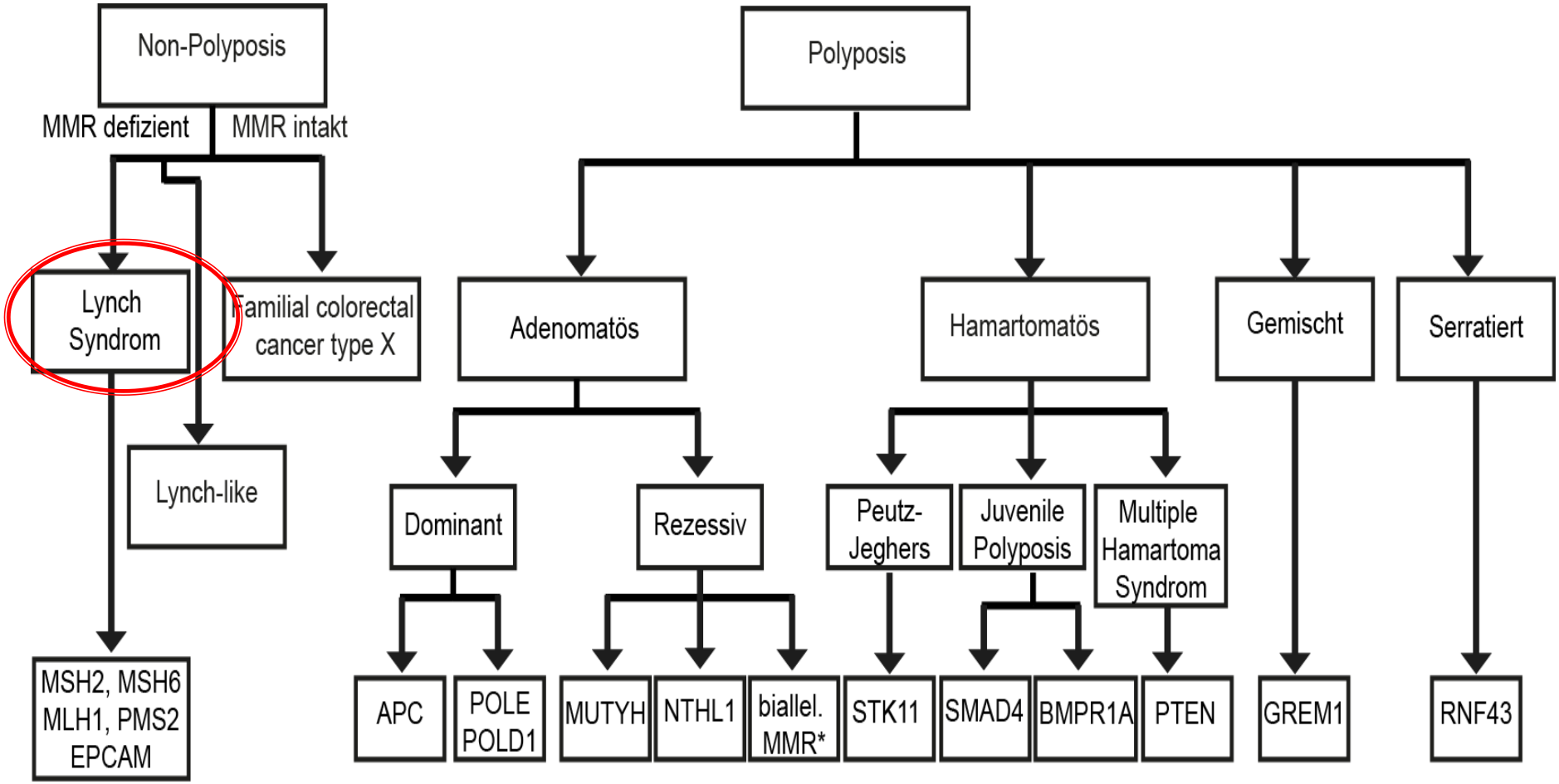


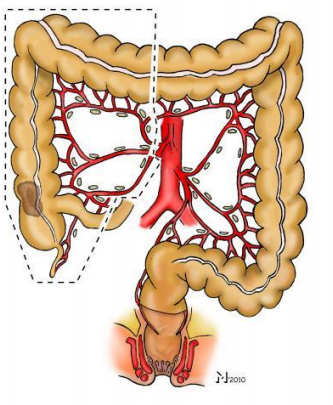
Non-Polyposissyndrome
Lynch-Syndrom und HNPCC
Aktuelle S3-Leitlinie

3.3.26	**Konsensbasierte Empfehlung**
GCP	Eine prophylaktische Kolektomie bzw. Proktokolektomie bei HNPCC-Mutationsträgern soll nicht durchgeführt werden. Eine subtotale Kolektomie bei Karzinom sollte nicht generell durchgeführt, aber individuell mit dem Patienten besprochen werden.
	Starker Konsens

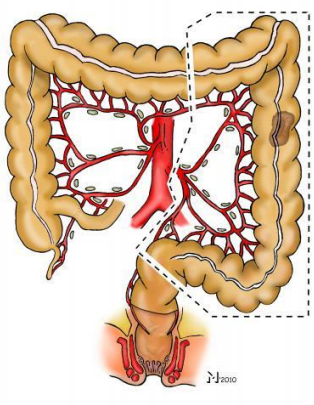
Non-Polyposissyndrome
Lynch-Syndrom und HNPCC
Aktuelle S3-Leitlinie

Onkologische Resektion

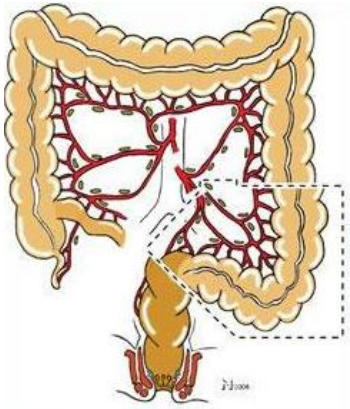
Kolektomie



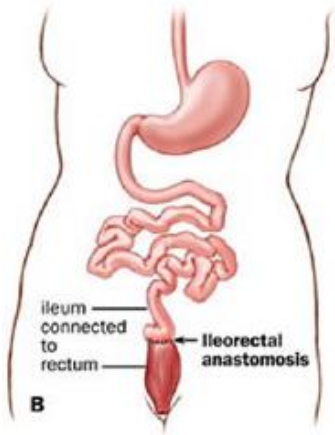
Hemikolektomie rechts



Hemikolektomie links



Sigmaresektion



Subtotale Kolektomie

- overall complication-free rate 75.4 versus 42.8 – 60%,p >.05

(You et al. Dis Colon Rectum 2008;51:1036-1042)

PLSD

Prospective Lynch Syndrome Database

Gut Online First, published on June 3, 2016 as 10.1136/gutjnl-2016-311403

OPEN ACCESS

ORIGINAL ARTICLE

Incidence of and survival after subsequent cancers in carriers of pathogenic MMR variants with previous cancer: a report from the prospective Lynch syndrome database

What are the new findings?

- This is the first comprehensive prospective study to provide empirically observed data on subsequent cancer incidence and survival in patients with Lynch syndrome who have survived previous cancer.
- The cumulative incidences for any subsequent cancer were 73% for path_*MLH1* and 76% for path_*MSH2* carriers. The incidence was lower in *MSH6* carriers.
- Colorectal cancer occurred frequently despite continued colonoscopic surveillance with removal of adenomas.
- Survival after subsequent cancer was good.

www.lscarisk.org

Prospective Lynch Syndrome Database | Carrier without previous cancer | Carrier with previous cancer | About

Calculation of cumulative risk for first cancer

Cancer type

Colorectal cancer

Current age

25 40 70

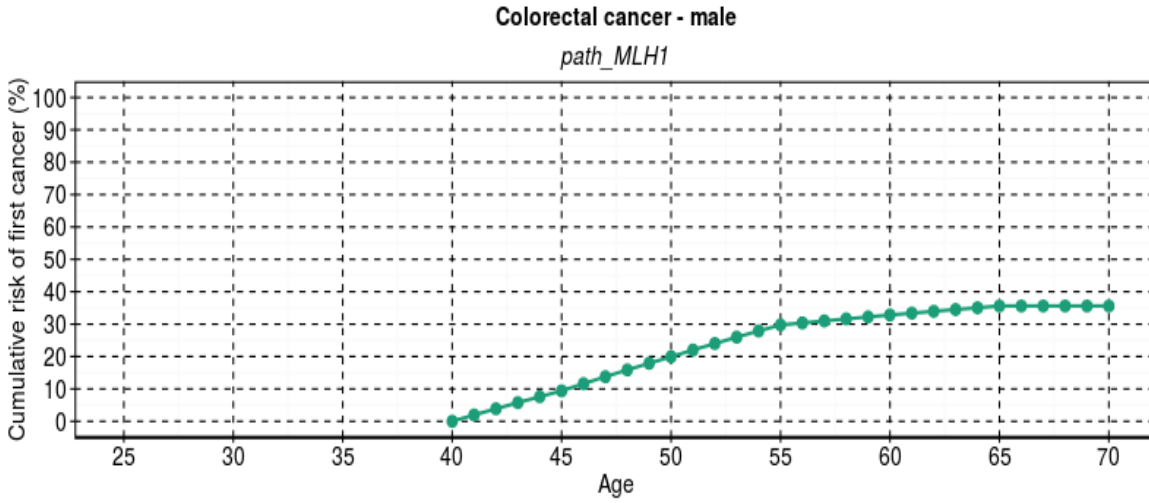
25 30 35 40 45 50 55 60 65 70

Gender

Male

Genetic variant

path_MLH1



Age	Risk (%)
40	0
50	20
60	33
70	36

www.lscarisk.org

Prospective Lynch Syndrome Database | Carrier without previous cancer | Carrier with previous cancer | About

Calculation of cumulative risk for first cancer

Cancer type

Colorectal cancer

Current age

25 40 70

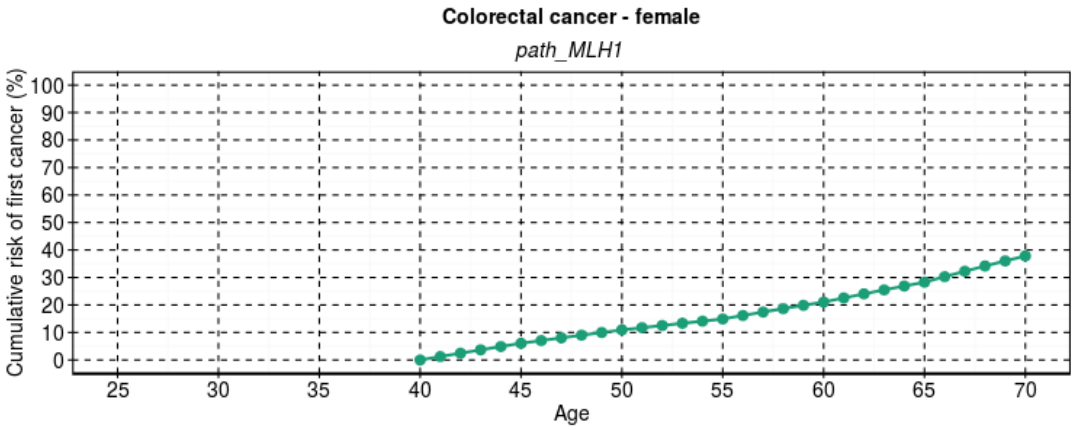
25 30 35 40 45 50 55 60 65 70

Gender

Female

Genetic variant

path_MLH1



Age	Risk (%)
40	0
50	11
60	21
70	38

www.lscarisk.org

Prospective Lynch Syndrome Database | Carrier without previous cancer | Carrier with previous cancer | About

Calculation of cumulative risk for first cancer

Cancer type

Colorectal cancer

Current age

25 40 70

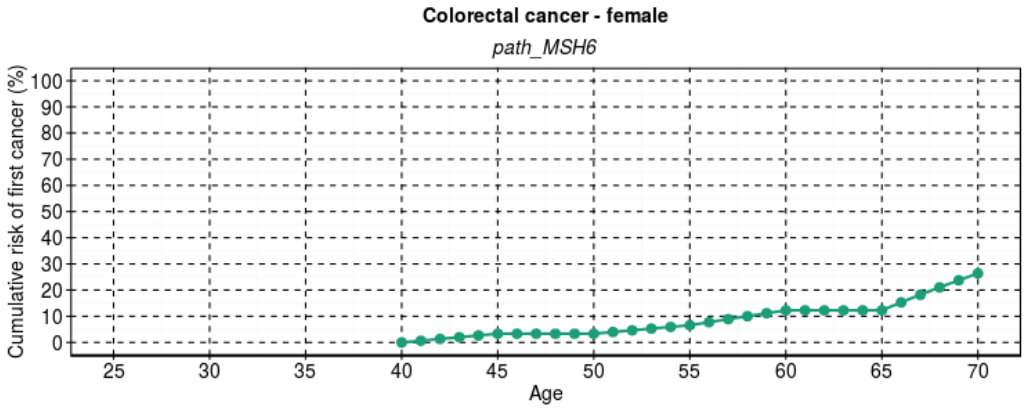
25 30 35 40 45 50 55 60 65 70

Gender

Female

Genetic variant

path_MSH6



Age	Risk (%)
40	0
50	3
60	12
70	26

www.lscarisk.org

Prospective Lynch Syndrome Database | Carrier without previous cancer | Carrier with previous cancer | About

Calculation of cumulative risk for first cancer

Cancer type

Colorectal cancer

Current age

25 40 70

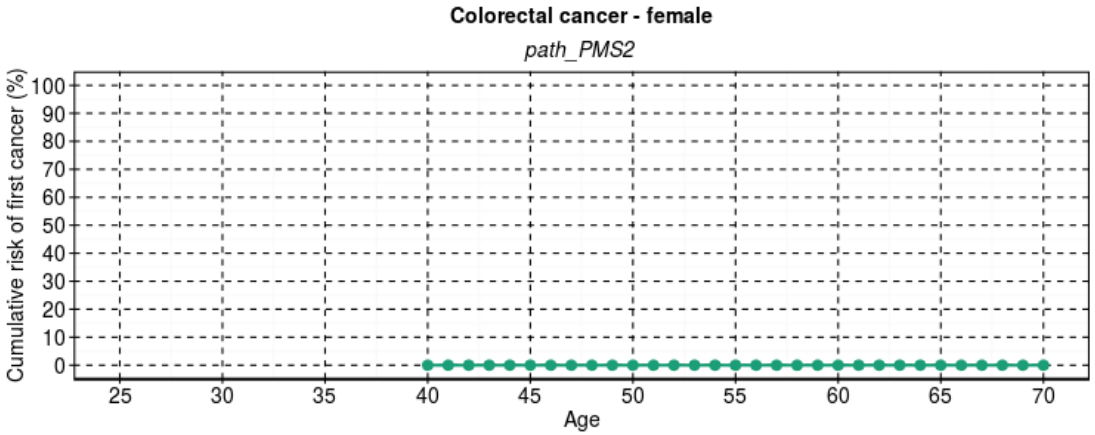
25 30 35 40 45 50 55 60 65 70

Gender

Female

Genetic variant

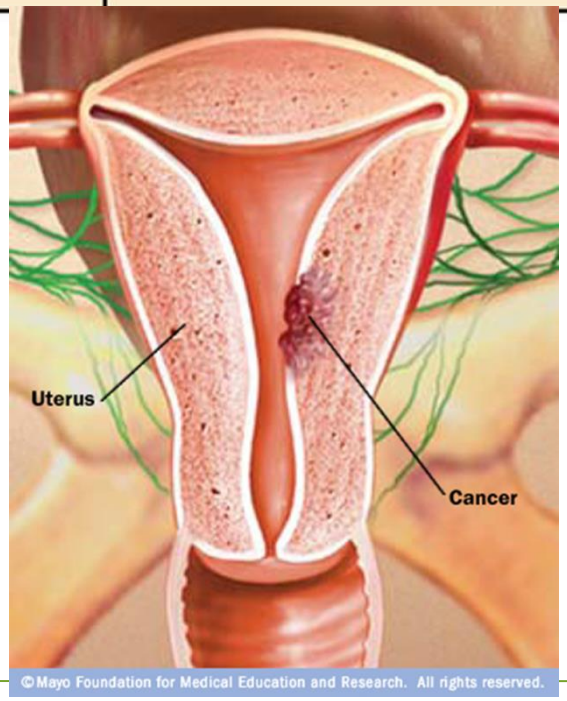
path_PMS2

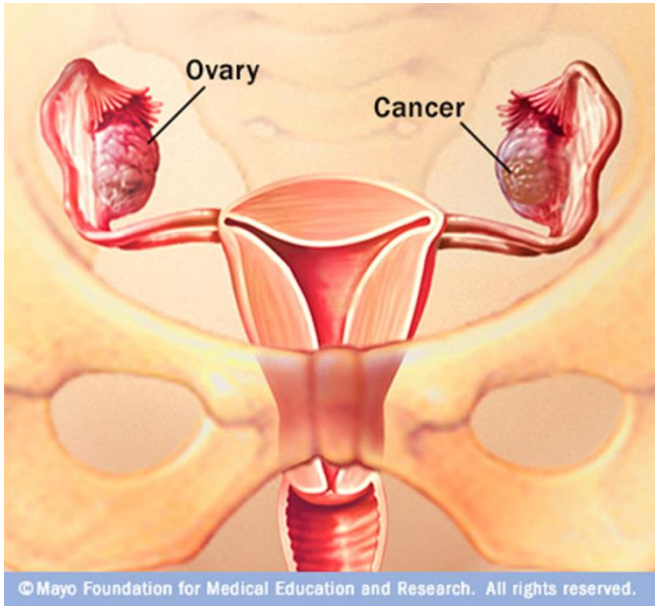


Age	Risk (%)
40	0
50	0
60	0
70	0

Chance einer simultanen Operation

3.3.28	Konsensbasierte Empfehlung
GCP	Mit Patientinnen mit Lynch- und HNPCC-Syndrom sollte mit 40 Jahren, bzw. fünf Jahre vor dem frühesten Erkrankungsalter in der Familie, eine prophylaktische Hysterektomie und ggf. eine Ovarektomie besprochen werden.
	Konsens





Hereditäre kolorektale Karzinome

10%

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Cancer Susceptibility Gene Mutations in Individuals With Colorectal Cancer

Matthew B. Yurgelun, Matthew H. Kulke, Charles S. Fuchs, Brian A. Allen, Hajime Uno, Jason L. Hornick, Chinedu I. Ukaegbu, Lauren K. Brais, Philip G. McNamara, Robert J. Mayer, Deborah Schrag, Jeffrey A. Meyerhardt, Kimmie Ng, John Kidd, Nanda Singh, Anne-Renee Hartman, Richard J. Wenstrup, and Sapna Syngal

Conclusion

Germline cancer susceptibility gene mutations are carried by 9.9% of patients with CRC. MSI/MMR testing reliably identifies LS probands, although 7.0% of patients with CRC carry non-LS mutations, including 1.0% with *BRCA1/2* mutations.

Published at ascopubs.org/journal/jco on January 30, 2017.

Paneldiagnostik


US Cancer Patients in Clinical Trials?


Gastric Bypass Surgery


Outcomes Named by Healthgrades


Insurance Exchanges

Medscape Medical News from the:

American College of Surgeons (ACS) 98th Annual Clinical Congress

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Medscape Medical News

Prophylactic Surgery: How Should Surgeons Respond?

Lara C. Pullen, PhD

Oct 10, 2012

Print Email

October 10, 2012 (Chicago, Illinois) — Most prophylactic surgeries performed in the United States are self-pay and occur in the South and Midwest, researchers reported here at the American College of Surgeons 98th Annual Clinical Congress.

As more and more women are turning to prophylactic surgery, surgeons are facing issues of access, awareness, and the quantification of benefits, according to study author Jessica Ryan, MD, from the Tufts University School of Medicine in Boston, Massachusetts.

Dr. Ryan noted that a significant increase in the awareness and

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Save the Date

SAVE THE DATE

1. Interdisziplinäres Symposium für hereditäre Tumorerkrankungen

Die unterschätzte Chance

Update für Niedergelassene und Kliniker

22. und 23. Juni 2018
Rheinterrasse Düsseldorf

Diagnostik, Therapie und Prophylaxe

Freitag, 22. Juni 2018

- Hereditäre Disposition zu Magen- und Dünndarmkarzinomen
- Hereditäre Disposition zu chronischer Pankreatitis und Pankreaskarzinom
- Retinoblastom
- MEN (Multiple endokrine Neoplasien)
- Hereditäre Disposition zu urologischen Karzinomen
- Hereditäre Disposition zu dermatologischen Karzinomen
- Diagnostische Marker in der Pathologie einschließlich Mikrosatelliteninstabilität (MSI)
  - Der Stellenwert einer systematischen Testung im Tumor
- Der Stellenwert einer systematischen NGS-Paneltestung – Falldarstellungen

Samstag, 23. Juni 2018

- Hereditäre Disposition zu Endometrium und non-BRCA Ovarial- und Mammatumoren
- Hereditäre Disposition zu kolorektalen Karzinomen
- Hereditäre Dispositionen zu Karzinomen im Kindesalter
- Das humangenetische Beratungsgespräch
- Individualisierte adjuvante und palliative Chemotherapie
- Immuntherapien einschließlich Vakzine
  Medikamentöse Prävention?
  - Bewegung, Ernährung, ASS and beyond?

Änderungen vorbehalten – Stand Oktober 2017

WISSENSCHAFTLICHE LEITUNG
Prof. Dr. med. Gabriele Möslein, Direktorin im Zentrum für Hereditäre Tumorerkrankungen, Spezielle Viszeralchirurgie
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ZERTIFIZIERUNG
Die Zertifizierung der Veranstaltung zur Anerkennung für das Fortbildungszertifikat der Ärztekammer Nordrhein ist beantragt.

VERANSTALTUNGSDATUM / -ORT
22. und 23. Juni 2018
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