Leitlinienprogramm Onkologie

Leitlinienreport

S3-Leitlinie Kolorektales Karzinom

Version 1.1 – August 2014

AWMF-Registernummer: 021/007OL

Leitlinienreport

DKG Krebsgesellschaft · Deutsche Krebshilfe Helfen. Forschen. Informieren. · AWMF

Inhaltsverzeichnis

1. Informationen zum Leitlinienreport

Dieser Leitlinienreport ergänzt die Leitlinie zum kolorektalen Karzinom in der Fassung vom Juli 2013 (Version 1.0). Der Report bezieht sich ausschließlich auf die Aktualisierung der Leitlinie 2011/2012 im Rahmen des Leitlinienprogramms Onkologie.

1.1. Autoren des Leitlinienreports

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1.2. Herausgeber

Leitlinienprogramm Onkologie der Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e. V. (AWMF), Deutschen Krebsgesellschaft e.V. und Deutschen Krebshilfe e.V.

1.3. Federführende Fachgesellschaft

Deutsche Gesellschaft für Verdauungs- und Stoffwechselkrankheiten (DGVS)

Steuerungsgruppe für Planung und Durchführung über DGVS:
Univ.-Prof. Dr. Wolff Schmiegel
Dr. Christian P. Pox

1.4. Finanzierung der Leitlinie

Diese Leitlinie wurde von der Deutschen Krebshilfe im Rahmen des Onkologischen Leitlinienprogramms gefördert.

1.5. Kontakt

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1.6. Zitierweise

Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): S3-Leitlinie Kolorektales Karzinom, Leitlinienreport, Version 1.1, 2014 AWMF Registrierungsnummer: 021-007OL, http://leitlinienprogramm-onkologie.de/Leitlinien.7.0.html, [Stand: TT.MM.JJJJ]

1.7. Bisherige Änderungen an der Version 1

Juli 2014 Version 1.1: Redaktionelle Änderungen, Ergänzung und Spezifikation der offengelegten Interessenkonflikte von Prof. Schmiegel in Tabelle 11.

1.8. Dokumente zur Leitlinie

Die Langversion dieser Leitlinie wird in der Zeitschrift für Gastroenterologie veröffentlicht werden.

Die Langversion der S3-Leitlinie Kolorektales Karzinom“, wird auf den Homepages des Leitlinienprogramms Onkologie (www.leitlinienprogramm-onkologie.de), der AWMF (www.awmf.org), der Deutschen Krebshilfe (www.krebshilfe.de), der Deutschen Krebsgeellschaft (DKG) (www.krebsgesellschaft.de) und der DGVS (www.dgvs.de) sowie direkt über folgende Links zugänglich sein:

http://www.awmf.org/leitlinien/aktuelle-leitlinien.html

http://www.leitlinienprogramm-onkologie.de/OL/leitlinien.html

http://www.krebsgesellschaft.de/wub_llevidenzbasiert,120884.html

http://www.dgvs.de/508.php

Neben der Langversion gibt es folgende ergänzende Dokumente:

- Kurzversion
- Leitlinienreport
- Übersetzung (englisch)
- Patientenleitlinie
- Externer Evidenzbericht

Alle diese Dokumente werden ebenfalls auf den oben genannten Homepages abrufbar sein.

Der externe Evidenzbericht wurde zum Themenkomplex II und Teilen des Themenkomplexes V von einer Kooperation der Universität Witten/ Herdecke (Institut für Forschung in der Operativen Medizin) mit der Universität Duisburg/ Essen (Alfried Krupp von Bohlen und Halbach Stiftungslehrstuhl für Medizinmanagement) erstellt.

Die Erstellung der Patientenleitlinie und die Übersetzung der Langversion ins Englische werden mit Fertigstellung der Leitlinie in Auftrag gegeben.

Eine flächendeckende Verbreitung dieser evidenzbasierten, aktuellen Verhaltensempfehlungen ist insbesondere für die Steigerung der Qualität bei Patienteninformation und –versorgung notwendig. Mit Hilfe standardisierter Methoden wurden von den Empfehlungen Qualitätsindikatoren abgeleitet. Diese dienen neben der Implementierung in erster Linie der Qualitätssicherung und –steigerung der patientenrelevanten Prozesse.

1.9. Verwendete Abkürzungen

Abkürzung	Erläuterung
APE	abdominoperineal excision
APR	abdominoperineal resection
AR	anterior resection
ASS	Acetylsalicylsäure
BMI	Body Mass Index
CC	Colon Cancer
CI	Confidence Interval
CJP	Colonic J-Pouch
CMI	Circumferential Margin Involvement
CT	Computer Tomography
CTC	CT-Kolonographie
CTV	Klinisches Zielvolumen
CRC	Colorectal Carcinoma
CRM	circumferential resection margin
CU	Colitis Ulcerosa
EUS	Endoluminal Ultrasound
FAP	Familiäre Adenomatöse Polyposis
FFQ	Food Frequency Questionaire
FOBT	Fecal Occult Blood Test
FU	Follow Up
GTV	Gross tumor volume
HALS	Hand Assisted Laparoscopic Surgery
HNPCC	hereditäres kolorektales Karzinom ohne Polyposis
HR	Hazard Ratio
iFOBT/ FIT	Immunologischer FOBT
IGAM	inferior gluteal artery myocutaneous
IHC	Immunhistochemischen Untersuchung
KRK	Kolorektales Karzinom
LITT	Laserinduzierte interstitielle Thermotherapie
LL	Leitlinie
LoE	Level of Evidence
LRA	Low Colo-rectal Anastomosis
MDCT	Multidetector CT
MSA	Mikrosatellitenanalyse
MSI	Mikrosatelliteninstabilität

Abkürzung	Erläuterung
MSI-H	Mikrosatelliteninstabilität hoch (high)
MSI-L	Mikrosatelliteninstabilität gering (low)
MSS	Mikrosatellitenstabilität
NPV	Negative Predictive Value
OR	Odds Ratio
PET	Positron Emission Tomography
PJS	Peutz-Jeghers-Syndrom
PPV	Positive Predictive Value
PTV	Planungszielvolumen
RAM	rectus abdominus
RC	Rectal Cancer
RCT	Randomisierte, kontrollierte Studie
RFA	Radiofrequenzablation
RR	Relative Risk
SCA	Straight Coloanal Amastomosis
SIRT	Selective Internal Radiation Therapy
SR	Systematische Übersichtsarbeit
SRRE	Summary Relative Risk Estimate
STE	Side To End
(T)CP	(Transverse) Coloplasty
TME	Totale Mesorektumexzision
TRUS	Transrectal US
US	Ultrasonography

2. Geltungsbereich und Zweck

2.1. Adressaten

Diese Leitlinie richtet sich vorrangig an

- Ärztinnen und Ärzte, die in der Prävention und Behandlung des KRK im ambulanten und stationären Sektor tätig sind
- Kooperationspartner der Ärzteschaft (Fachbereiche im Gesundheitswesen)
- Kostenträger

2.2. Zielsetzung

Das Kolorektale Karzinom (KRK) ist mit über 73.000 Neuerkrankungen und ca. 27.000 Todesfällen pro Jahr in Deutschland einer der häufigsten malignen Tumoren. 1999 wurde erstmalig von der DGVS in Zusammenarbeit mit der Deutschen Krebsgesellschaft eine S3-Leitlinie für das KRK veröffentlicht, die flächendeckend eine standardisiert hochwertige Patientenversorgung auf dem Boden evidenzbasierter Medizin erreichen sollte. Um die Empfehlungen auf dem neuesten Stand wissenschaftlicher Erkenntnisse zu halten, wird die Leitlinie seitdem in enger Zusammenarbeit mit der AWMF regelmäßig aktualisiert (2004 komplett und 2008 die Themenkomplexe IV, VI und VII). Die aktuelle Überarbeitung betrifft die Themenkomplexe I, II, III, V und VIII, sowie einzelne Kapitel aus VI und VII.

3. Zusammensetzung der Leitliniengruppe

Redaktioneller Hinweis:
Dieser Leitlinienreport bezieht sich ausschließlich auf die Aktualisierung im Jahr 2012 der S3-Leitlinie Kolorektales Karzinom.

3.1. Beteiligte Fachgesellschaften, Institutionen und Patientenvereinigungen

Die Fachexpertengruppe für die Überarbeitung dieser Leitlinie setzte sich aus insgesamt 53 Mandatsträgern und nicht stimmberechtigten Experten folgender Fachgesellschaften, Berufsverbände und Patientenvereinigungen zusammen:

3.1.1. Fachgesellschaften

DKG (Deutsche Krebsgesellschaft)

- **ASORS** (AG der DKG "Supportive Maßnahmen in der Onkologie, Rehabilitation und Sozialmedizin")
- **PRIO** (AG der DKG Prävention und integrative Medizin in der Onkologie)
- **PSO** (AG der DKG: Dt. Arbeitsgemeinschaft für Psychoonkologie)
- **KOK** (AG der DKG: Konferenz Onkologische Kranken- und Kinderkrankenpflege)

DGVS (Deutsche Gesellschaft für Verdauungs- und Stoffwechselkrankheiten)

DEGAM (Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin)

DEGRO (Deutsche Gesellschaft für Radioonkologie)

DGAV (Deutsche Gesellschaft für Allgemein- und Viszeralchirurgie)

- **CACP** (Chirurgische Arbeitsgemeinschaft für Colo-Proktologie)
- **CAMIC** (Chirurgische Arbeitsgemeinschaft für Minimal Invasive Chirurgie)
- **CAO-V** (Chirurgische Arbeitsgemeinschaft für Onkologie)

DGCH (Deutsche Gesellschaft für Chirurgie)

DGEM (Deutsche Gesellschaft für Ernährungsmedizin)

DGHO (Deutsche Gesellschaft für Hämatologie und Onkologie)

DGIM (Deutsche Gesellschaft für Innere Medizin)

DGKL (Deutsche Gesellschaft für Klinische Chemie und Laboratoriumsmedizin)

DGN (Deutsche Gesellschaft für Nuklearmedizin)

DGP (Deutsche Gesellschaft für Pathologie)

DRG (Deutsche Röntgengesellschaft)

GfH (Deutsche Gesellschaft für Humangenetik)

3.1.2. andere Institutionen:

bng (Berufsverband Niedergelassener Gastroenterologen Deutschlands e.V.)

HÄV (Deutscher Hausärzteverband)

AQUA (Institut für angewandte Qualitätsförderung und Forschung im Gesundheitswesen)

ZI (Zentralinstitut der Kassenärztlichen Versorgung in der BRD)

Felix-Burda-Stiftung

Stiftung Lebensblicke

3.1.3. Patientenvereinigungen

DCCV (Deutsche Morbus Crohn/Colitis Ulcerosa Vereinigung)

Deutsche ILCO (Vereinigung für Stomaträger und für Menschen mit Darmkrebs)

3.2. Mandatsträger

Tabelle 1zeigt die Zusammensetzung der Leitliniengruppe 2011/2012 unter der Leitung von Prof. Dr. W. Schmiegel (DKG, DGVS)

Tabelle 1: Zusammensetzung der Leitliniengruppe 2011/2012

TK I: Prävention asymptomatische Bevölkerung	
Koordinator: J. Riemann	DGIM, DGVS, Stiftung Lebensblicke
Mitglieder: S. C. Bischoff	DGEM, DGVS
F. Kolligs	DGVS
J. Ockenga	DGEM, DGVS
W. Scheppach	DGEM, DGVS
TK II: Früherkennung/ Vorsorge asymptomatische Bevölkerung	
Koordinatoren: C. Pox A. Sieg	 DGVS DGVS
Mitglieder: L. Altenhofen	ZI
H-J. Brambs	DRG, DGAM
H. Brenner	Experte (nicht stimmberechtigt)
P. Engeser	HÄV
A. Theilmeier	bng, DGVS
TK III: Risikogruppen	

Koordinatoren:	
N. Rahner	GfH
K. Schulmann	DGVS
G. Baretton	DGP
B. Bokemeyer	bng, DGVS
J. Epplen	DGHG
U. Melle	DGVS
R. Porschen	DGVS
J. Weitz	DGAV
C. Witte	DCCV
TK V: Präoperative Diagnostik und Chirurgie	
Koordinatoren:	
W. Hohenberger	DKG, DGAV
S. Post	DKG, DGAV, CACP
M. Anthuber	DGAV
W. Bechstein	DGAV
U. Graeven	DGVS
M. Haß	Dt. ILCO
M. Heike	DGHO
K-W. Jauch	DGAV
T. Kirchner	DGP
H. Lang	DKG, DGAV, CAO-V
K-H. Link	DKG, DGAV
P. Pereira	DRG
H-R. Raab	DGAV
A. Reinacher-Schick	DGVS
C. Rödel	DEGRO
M. Sailer	DGAV
R. Sauer	DEGRO
K. Scheidhauer	DGN
A. Tannapfel	DGP
T. Vogl	DRG
C. Wagener	DGKL
M. Walz	DGAV, CAMIC
C. Wittekind	DGP
TK VIII: Nachsorge	
Koordinator:	
A. Holstege	DGVS

Mitglieder: P. Heußner	PSO
T. Höhler	DGHO
J. Hübner	DKG, PRIO
J. Körber	DKG, ASORS
M. Landenberger	DKG, KOK
H. Link	DKG, ASORS
Plenum	
S. Ludt	AQUA
P. Lux	Autor (nicht stimmberechtigt)
C. Maar	Felix-Burda-Stiftung

3.2.1. Die Koordinatoren bei der Überarbeitung der Themenkomplexe IV, VI und VII 2007/2008 waren:

TKIV: Endoskopie: Durchführung und Polypenmanagement
Koordinatoren: J. Riemann, W. Schmitt

TK VI: Adjuvante und neoadjuvante Therapie
Koordinatoren: R. Porschen, R. Sauer

TK VII: Therapeutisches Vorgehen bei Metastasierung und in der palliativen Situation
Koordinatoren: U. Graeven, H-J. Schmoll

4. Fragestellungen und Gliederung

4.1. Gliederung

Die Leitlinie ist in acht Themenkomplexe gegliedert:

Tabelle 2: Gliederung der Leitlinie

Themenkomplex	Bezeichnung	Jahr der Überarbeitung
I	Prävention asymptomatische Bevölkerung	2011/ 12
II	Früherkennung/ Vorsorge asymptomatische Bevölkerung	2011/ 12
III	Risikogruppen	2011/ 12
IV	Endoskopie: Durchführung und Polypenmanagement	2007/ 08
V	Präoperative Diagnostik und Chirurgie	2011/ 12
VI	Adjuvante und neoadjuvante Therapie	2007/ 08 *
VII	Therapeutisches Vorgehen bei Metastasierung und in der palliativen Situation	2007/ 08 *

VIII	Nachsorge	2011/ 12

* die aktuelle Überarbeitung betraf einzelne Kapitel aus VI und VII

4.2. Schlüsselfragen/ Themen für die Überarbeitung

Die Schlüsselfragen und die Art der Recherche wurden bei einer Kick off-Veranstaltung am 15.01.2011 von den anwesenden Mandatsträgern verabschiedet.

Tabelle 3: Erläuterung der Recherchearten

Art der Recherche	Erklärung	In der Leitlinie
Leitlinienadaptation	Systematische Literatursuche Inhalt wird wörtlich übernommen	Empfehlung
De Novo	Systematische Literatursuche ohne zeitliche Begrenzung Ergebnisse in Evidenztabellen extrahiert	Empfehlung/ Statement
Evidenz aus Aktualisierungsrecherche	Recherche mit eingeschränktem Zeitintervall (ab 2003, entsprechend dem Endpunkt der de novo-Suche für die letzte Aktualisierung)	Empfehlung/ Statement
Handsuche	Keine Systematische Literatursuche	GCP

Tabelle 4: Schlüsselfragen/ Themen für die Überarbeitung

TK	Schlüsselfrage/ Schlüsselthema	Art der Recherche
I	Wird das sporadische KRK Risiko durch Körperliche Bewegung beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK Risiko durch Körpergewichtsregulierung beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK Risiko durch ballaststoffreiche Kost beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK Risiko durch ballaststoffreiche Kost beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK Risiko durch Fleisch beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK Risiko durch Obst und Gemüse beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK Risiko durch Alkohol beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK Risiko durch Fisch beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK durch Nahrungszubereitung (Fast-food/Fette/ Fettsäuren) beeinflusst?	De Novo
I	Wird das sporadische KRK Risiko durch die Einnahme von Acrylamid beeinflusst?	De Novo
I	Einfluss von Coffein, Teein, grüner Tee auf die KRK-Entstehung	Expertenkonsens[1]
I	Wird das sporadische KRK Risiko durch sonstige Ernährungsgewohnheiten im Allgemeinen beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK Risiko durch die Einnahme von Folsäure beeinflusst?	De Novo
I	Wird das sporadische KRK Risiko durch die Einnahme von Vitaminen beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK Risiko durch die Einnahme von Calcium beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK Risiko durch die Einnahme von Magnesium beeinflusst?	De Novo
I	Wird das sporadische KRK Risiko durch die Einnahme von Selen beeinflusst?	De Novo
I	Wird das sporadische KRK Risiko durch COX-2 Inhibitoren beeinflusst?	De Novo
I	Wird das sporadische KRK Risiko durch die Einnahme von Statine beeinflusst?	Evidenz aus Aktualisierungsrecherche
I	Wird das sporadische KRK Risiko durch die Einnahme von ASS beeinflusst?	Leitlinienadaptation
I	Wird das sporadische KRK Risiko durch die Einnahme von Hormonersatz beeinflusst?	Leitlinienadaptation

[1] Die dem Expertenkonsens zugrunde liegenden Quellen wurden per Handsuche gefunden

TK	Schlüsselfrage/ Schlüsselthema		Art der Recherche
II [2]	CT-Kolonographie	In wieweit wird die KRK bedingte Mortalität durch CTC gesenkt? In wie weit wird die Inzidenz kolorektaler Karzinome durch CTC gesenkt? Was sind die Testeigenschaften von CTC im Vergleich zum Referenzstandard (Koloskopie)?	De Novo
II	Sonstige Tests (Test auf okkultes Blut im Stuhl (FOBT), M2-PK, Stuhl-DNA, Kapselendoskopie, Sigmoidoskopie)	In wie weit wird die KRK bedingte Mortalität durch sonstige Tests gesenkt? In wie weit wird die Inzidenz kolorektaler Karzinome durch sonstige Tests gesenkt? Was sind die Testeigenschaften sonstiger Tests im Vergleich zum Referenzstandard (Koloskopie)?	De Novo
III	Wie ist der psychologische Effekt der genetischen Testung (Differenzierung prädiktiv, diagnostisch)?		Expertenkonsens
III	Vorsorgeuntersuchungen und -intervall bei Patienten mit pos. Amsterdamkriterien aber MSS		Expertenkonsens
III	Gibt es eine effektive medikamentöse Prävention bei HNPCC-Anlageträgern?		Expertenkonsens
III	Sollte man HNPCC-Anlageträgern eine subtotale Kolektomie oder eine prophylaktische Hysterektomie/Ovarektomie anbieten?		Abgleich S3-LL Ovarialkarzinom
III	Wie sollte man bei FAP-Patienten mit Duodenaladenomen vorgehen? Indiktation zur Papillektomie und OP?		Expertenkonsens
III	Wie sollte man Desmoide bei FAP-Patienten behandeln?		Expertenkonsens
III	Wie ist der psychologische Effekt der genetischen Testung (Differenzierung prädiktiv, diagnostisch)?		Expertenkonsens
III	Wann sollte auf das Vorliegen einer MUTYH-Mutation getestet werden?		Expertenkonsens
III	Was für Vorsogergeuntersuchungen sollten bei MUTYH-Trägern durchgeführt werden? Beginn? Für welche Familienmitglieder?		Expertenkonsens
III	Wie hoch ist das Tumorrisiko bei MUTYH-Anlageträgern?		Expertenkonsens
III	Welche Rolle kommt der endoskopischen Vorsorge zu?		Expertenkonsens
III	Für welche Tumorerkrankungen besteht ein erhöhtes Tumorrisiko?		Expertenkonsens
III	Effektivität des Beginns einer früheren Vorsorge bei Patienten mit erhöhtem Risiko; Vorsorgeintervall		Expertenkonsens
III	Für welche Tumorerkrankungen besteht ein erhöhtes Tumorrisiko bei		Expertenkonsens

[2] Die Recherche für den Themenkomplex II wurde nach extern an eine Kooperation folgender zwei Institute vergeben: Universität Duisburg Essen, Alfried Krupp von Bohlen und Halbach Stiftungslehrstuhl für Medizinmanagement Universität Witten/Herdecke, Institut für Forschung in der Operativen Medizin (IFOM)

TK	Schlüsselfrage/ Schlüsselthema		Art der Recherche
	HNPCC-Anlageträgern? (Hautmanifestation Muir-Torre-Syndrom)		
III	Gibt es eine effektive medikamentöse Prävention bei FAP Patienten	für kolorektale Adenome	Expertenkonsens
		für Duodenaladenome?	
III	Welche Vorsorgeuntersuchungen sollten bei HNPCC-Anlageträgern durchgeführt werden? (ÖGD ? Endometriumkarzinomvorsorge ?)		Expertenkonsens
III	Welches Vorgehen sollte zum Ausschluss einer HNPCC-Anlage gewählt werden: Immunhistochemie oder Mikrosatelliteninstabiltät?		Expertenkonsens
III	Bei welchen Patienten sollte man eine Untersuchung auf HNPCC durchführen: Bethesda vs. Generell?		Expertenkonsens
III	Für welche Tumorerkrankungen besteht ein erhöhtes Tumorrisiko?		Expertenkonsens
III	Welche Rolle kommt der endoskopischen Vorsorge zu?		Expertenkonsens
III	Wann und wie häufig sollte eine Untersuchung des Dünndarms vorgenommen werden? Mit welcher Methode?		Expertenkonsens
III	Ist eine Pankreaskarzinomvorsorge sinnvoll?		Expertenkonsens
III	Ist eine Vorsorge des Urogenitaltrakts sinnvoll?		Expertenkonsens
III	Gibt es eine effektive medikamentöse Prävention?		Expertenkonsens
V	Wie ist der Stellenwert des präoperativen lokalen Stagings durch CT, MRT beim Kolonkarzinom bzgl. lokaler Ausbreitung?		Expertenkonsens
V	Wie ist der Stellenwert von Endosonographie, CT und MRT beim prätherapeutischen lokalen Staging des Rektumkarzinoms ?		De Novo
V	Wie ist der Stellenwert bildgebender Verfahren (CT, MRT, Endosonographie, PET, andere) beim Rektumkarzinom zum Restaging nach erfolgter Radiochemotherapie bzw. Radiotherapie?		De Novo
V	Welche Verfahren sind bei der Primärbehandlung des Kolorektalen Karzinoms zur Abklärung von Fernmetastasen anzuwenden (außer PET)?		Expertenkonsens
V	Wie ist der Stellenwert des PET-CT zur Primärdiagnostik des kolorektalen Karzinoms?		De Novo
V	Wie ist der Stellenwert des PET/ PET-CT vor einer Metastasenresektion?		De Novo
V	Welche Tumormarker sind im Rahmen der Primärdiagnostik im Serum zu erheben (CEA; CA 19-9; CA 125) ? (CA 19-9, CA 125, Mikrometastasen, zirkulierende DNA; Aussage in den Fließtext)		Expertenkonsens
V	Welchen Stellenwert hat die intraoperative Sonographie der Leber ?		Expertenkonsens
V	Wie sind metastasenverdächtige Läsionen der Leber histologisch zu sichern?		Expertenkonsens
V	Gibt es eine Indikation für die intraoperative Sentinel-Node-Biopsie im Rahmen der Chirurgie des Kolorektalen Karzinoms?		Expertenkonsens
V	Wie ist das strategisches Vorgehen bei Tumorkomplikationen (Perforation, Ileus)?		Expertenkonsens
V	Sollen simultane Lebermetastasen synchron oder metachron		De Novo

TK	Schlüsselfrage/ Schlüsselthema	Art der Recherche
	reseziert werden?	
V	Wie ist das Vorgehen bei ausgedehnter Fernmetastasierung und asymptomatischem Primärtumor?	De Novo
V	Behandlung der Peritonealkarzinose → HIPEC und Peritonektomie: Indikation und Technik	De Novo
V	Dokumentation der TME- Qualität durch den Chirurgen (im Fließtext)	Expertenkonsens
V	Ausmaß der Lymphknoten-Dissektion?	Expertenkonsens
V	Welche Bedeutung hat die komplette mesokolische Exzision (CME)?	Expertenkonsens
V	Welchen Stellenwert hat die laparoskpische Resektion des Kolonkarzinoms ? (Datenaktualisierung; Im Fließtext: Zugangswege, Robotic, NOTES)	Leitlinienadaptation de Novo
V	Was ist die Rolle der laparoskopischen Chirurgie in der Behandlung des Rektumkarzinoms?	de Novo
V	Welche der folgenden Rekonstruktions-Verfahren sollten bei der tiefen anterioren Rektumresektion eingesetzt werden: a) Bildung eines J-Pouch b) Bildung einer transversen Koloplastik c) Seit-zu-End-Anastomose?	de Novo
V	Technik der abdomino-perinealen Rektumexstirpation und Defektdeckung bei Rektumkarzinomen	de Novo
V	Verfahrenswahl zur Exstirpation vs Kontinenzerhalt nach neoadjuvanter Therapie abhängig von der ursprünglichen Einschätzung oder einer Reevaluation?	de Novo
V	Sollte ein protektives Stoma zur Senkung der postoperativen Anastomoseninsuffizienz nach Rektumresektion angelegt werden? Gibt es ein differenziertes Vorgehen?	Expertenkonsens
V	Lokale Therapie des Rektumkarzinoms: Indikationen für lokale Exzision	Expertenkonsens
V	Sondersituationen: Vorgehen bei komplettem Response nach neoadjuvanter Therapie beim Rektumkarzinom	Expertenkonsens
V	Minimale Resektionsgrenze vom kaudalen makroskopischen Tumorrand - bei Karzinomen im oberen Rektumdrittel - bei Karzinomen im mittleren Rektumdrittel - bei Karzinomen im unteren Rektumdrittel	Expertenkonsens
V	Radikalchirurgische Therapie des Rektumkarzinoms (inkl. Ausmaß der kranialen und lateralen Lymphadenektomie im Bereich der Art mesenterica inferior und /oder im Bereich der Art. iliaca interna) (Einschränkung auf Dissektion der Art. Iliaca interna)	Expertenkonsens
V	Hat die präoperative Markierung des Patienten im Sitzen/ Stehen und Liegen zur Festlegung möglicher Stellen für eine geplante oder eventuelle Stomaanlage Auswirkungen auf eine gute Stomaversorgungsmöglichkeit und damit auf die Lebensqualität?	Expertenkonsens
V	Können frühzeitig – also schon in der Klinik – erfolgte fachkundige Beratung und Anleitung zur Selbstversorgung durch Stomatherapeuten spätere Fehlversorgung und Komplikationen	Expertenkonsens

TK	Schlüsselfrage/ Schlüsselthema	Art der Recherche
	verhindern oder verringern (z. B. Hautreizungen, Hautentzündungen, unnötiger Materialverbrauch?	
V	Können frühzeitig – also schon in der Klinik – erfolgte fachkundige Beratung und Anleitung zur Selbstversorgung durch Stomatherapeuten die Selbstständigkeit des Stomaträgers bei der Durchführung seiner Stomaversorgung erhöhen oder beschleunigen?	Expertenkonsens
V	Wirkt sich eine frühzeitige Selbstständigkeit in der Stomaversorgung auf die Lebensqualität des Stomaträgers aus?	Expertenkonsens
V	Werden Zeiten notwendiger Fremdpflege (durch ambulante Pflegedienste) reduziert oder verhindert?	Expertenkonsens
V	Hat die prominente/ nicht prominente Anlage eines Colostomas Auswirkungen auf die Stomaversorgungsmöglichkeit und damit auf die Lebensqualität des Stomaträgers? Wie prominent sollte ein Colostoma angelegt werden?	Expertenkonsens
V	Wie prominent sollte ein Ileostoma angelegt werden?	Expertenkonsens
V	Lebensqualität nach Therapie des Rektumkarzinoms	Expertenkonsens
V	Behandlung von Therapiefolgen beim Rektumkarzinom	Expertenkonsens
V	Was ist die optimale Anzahl an zu untersuchenden LK im OP-Präparat?	Leitlinienadaptation Expertenkonsens
V	Welche Bedeutung hat die Angabe der Qualität des TME-Präparats?	Expertenkonsens
V	Welche Bedeutung hat der Abstand vom circumferentiellen Resektionsrand (CRM-Klassifikation) beim Rektumkarzinom?	Expertenkonsens
V	Welche Bedeutung hat der Tumorabstand zur Resektionsfläche des Mesokolons beim Kolonkarzinom?	Expertenkonsens
V	Welche Bedeutung haben morphometrische Untersuchungen des Kolonpräparates ?	Expertenkonsens
V	Wie soll der MSI-Status für die Graduierung der Tumortypen muzinöses Adenokarzinom, Siegelringzellkarzinom und undifferenziertes Karzinom in der Routinediagnostik methodisch bestimmt werden (Immunhistochemie oder MSI-Analyse)? Zu welchem Zeitpunkt ist die Bestimmung sinnvoll?	Expertenkonsens
VII	Nutzen und Risiken lokalablativer/regionaler Verfahren in der kurativen Behandlung von Lebermatastasen (RFA, SIRT, LITT)	De Novo
VIII	Wie hoch ist die Effektivität einer Nachsorge und der Nachsorgemethoden?	De Novo
VIII	Ist eine Nachsorge bei Stadium I Patienten sinnvoll?	Expertenkonsens
VIII	Wie oft sollten Koloskopien im Rahmen der Nachsorge durchgeführt werden?	De Novo
VIII	Hat das PET/ PET-CT eine Bedeutung bei der Nachsorge?	De Novo
VIII	Wann beginnt die Nachsorge bei adjuvanter Therapie (OP/Abschluss der Chemotherapie)?	Expertenkonsens
VIII	Rehabilitation	De Novo
	Tertiärprävention	Expertenkonsens

5. Methodik

Methodische Unterstützung im gesamten Überarbeitungsprozess erhielt die Leitliniengruppe durch Ina Kopp und Markus Follmann vom Leitlinienprogramm Onkologie.

5.1. Evidenzbasierung

Redaktioneller Hinweis:

Die Recherche für den Themenkomplex II und das Kapitel Lokalablative Verfahren des TK V wurde nach extern an eine Kooperation folgender Institute vergeben:

- Universität Duisburg Essen, Alfried Krupp von Bohlen und Halbach
- Stiftungslehrstuhl für Medizinmanagement Universität Witten/Herdecke, Institut für Forschung in der Operativen Medizin (IFOM).

Der Evidenzreport ist als gesondertes Dokument veröffentlicht worden.
Die Literaturrecherche und Evidenzbewertung für die Themenkomplexe I, III, V und VIII wurde innerhalb der Leitliniengruppe aufgeteilt (siehe 5.1.3.3). Für diese gilt dieser Report.

Recherchestrategie:

Suchebene 1: Leitliniensuche in den Datenbanken Guidelines International Network (g-i-n) und Pubmed/MEDLINE

Suchebene 2: Suche nach Sekundärliteratur in der Cochrane Database of Systematic Reviews und in Pubmed/MEDLINE

Suchebene 3: Suche nach Primärliteratur in Pubmed/MEDLINE

Ergänzend wurden Handsuchen in den Literaturverzeichnissen der identifizierten Leitlinien und Sekundärliteratur, in der Cochrane Clinical Trials Database und in EMBASE durchgeführt.

5.1.1. Suchebene 1

5.1.1.1. Recherche

g-i-n: “colorectal cancer”
Trefferzahl 99, Suchdatum: 20.06.2010

Pubmed/MEDLINE: (("colorectal neoplasms"[MeSH Terms] OR ("colorectal"[All Fields] AND "neoplasms"[All Fields]) OR "colorectal neoplasms"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields]) OR "colorectal cancer"[All Fields]) AND "guideline"[Publication Type]) AND ("2003/06"[PDAT] : "2010/06"[PDAT])
Trefferzahl 121, Suchdatum: 18.06.2010

5.1.1.2. Auswahl der Leitlinien

Tabelle 5: Ein- und Ausschlusskriterien für Leitlinien

Einschlusskriterien	
Publikationstyp	Leitlinie
Zeitraum	Ab 2000
Tumorentität: Kolorektales Karzinom	
Publikationssprache: deutsch, englisch	
Studie am Menschen	
Volltext beschaffbar	
Ausschlusskriterien	
Leitlinie abgelaufen, im Entstehungsprozess oder under review	
Andere Tumorentität	

5.1.1.3. Leitlinienbewertung

Bewertung nach dem deutschen Instrument zur methodischen Leitlinienbewertung (DELBI/ Version 2008) durch zwei Methodiker. (http://www.awmf.org/fileadmin/user_upload/Leitlinien/Werkzeuge/delbi05kurz.pdf) Eingeschlossen wurden die Leitlinien, welche bei der Methodikbewertung (Domäne 3) einen Wert ≥ 0,4 erhalten haben.

5.1.1.4. eingeschlossene Quellleitlinien

Tabelle 6: eingeschlossene Leitlinien, den Themenkomplexen zugeordnet

Leitlinie	**DW[3]:**	**Themenkomplex**				
		I	**II**	**III**	**V**	**VIII**
Routine aspirin or nonsteroidal anti-inflammatory drugs for the primary prevention of CRC U.S. Preventive Services Task Force, veröffentlicht 2007, Stand der Literatursuche 11/2004	0,57	X				
Hormone therapy for the prevention of chronic conditions in postmenopausal women U.S. Preventive Services Taks Force, veröffentlicht 2005, Stand der Literatursuche 2004	0,5	X				
Hormontherapie in der Peri- und Postmenopause (HT) DGGG (AWMF Register Nummer 015/062) veröffentlicht 2009, Stand der Literatursuche 2008		X				
Asia Pacific consensus recommendations for colorectal	0,41		X			

3 Domänenwert (DW): Durchschnittswert der Bewertung der Domäne 3 nach DELBI durch zwei Methodiker

Leitlinie	DW[3]:	Themenkomplex				
		I	II	III	V	VIII
cancer screening Asia Pacific Working Group on Colorectal Cancer, veröffentlicht 2008, Stand der Literatursuche 2007						
Screening for colorectal cancer U.S. Preventive Task Force, veröffentlicht 2008; Stand der Literatursuche 2008	0,69		X			
Peutz-Jeghers syndrome: a systematic review and recommendations for management Working group, veröffentlicht 2010, Stand der Literatursuche 5/2009	0,57			X		
Genetic testing strategies in newly diagnosed individuals with colorectal cancer aimed at reducing morbidity and mortality from Lynch syndrome in relatives Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group, veröffentlicht 2009	0,43			X		
Laparascopic surgery for colorectal cancer NICE (UK), veröffentlicht 2006, Stand der Literatursuche 2005	0,71				X	
Optimization of surgical and pathology quality performance in radical surgery for colon and rectal cancer: margins and lymph nodes Cancer Care Ontario (CA), veröffentlicht April 2008, Stand der Literatursuche Februar 2007	0,57				X	
Colon cancer National working group on GI Cancers (NL) veröffentlicht 2008, Stand der Literatursuche 02/2006	0,45				X	X
Rectal cancer National working group on GI Cancers (NL) veröffentlicht 2008, Stand der Literatursuche 02/2006	0,45				X	X

5.1.1.5. weitere genutzte Leitlinien

Für das Thema der psychonkologischen Betreuung wurde die „Interdisziplinäre S3-Leitlinie für die Diagnostik, Therapie und Nachsorge des Mammakarzinoms“ (AWMF Register Nummer 032/045OL) eingeschlossen, welche bei der initialen Suche aufgrund der falschen Tumorentität ausgeschlossen worden war.

Für Kapitel 5.3 „Chronisch entzündliche Darmerkrankungen“ wurden die deutschen S3-Leitlinien zur Colitis ulcerosa (AWMF-Registernummer: 021/009) und Morbus Crohn (AWMF-Registernummer: 021/004) eingeschlossen, welche bei der initialen Suche nicht gefunden worden war, da es sich nicht um eine primär maligne Erkrankungen handelt.

Außerdem wurden Leitlinien zum Lynchsyndrom [1] und zur familiären adenomatösen Polyposis (FAP) [2] sowie die zeitgleich im Rahmen des OL entwickelte S3-Leitlinie zum Ovarialkarzinom (AWMF-Registernummer: 032/035OL) berücksichtigt.

5.1.1.6. Adaptierungsprozess

Bei der Leitlinienadaptation werden sowohl der Wortlaut, als auch die Stärke der Empfehlungen unverändert übernommen.

5.1.2. Suchebene 2

Die Suche nach Systematic Reviews und Metaanalysen erfolgte

- in den Datenbanken der Cochrane Library
- Pubmed (für jeden Themenkomplex gesondert)

Die Auswahl der Literatur erfolgte anhand definierter Ein- und Ausschlusskriterien (siehe Tabelle 5.2).

Die eingeschlossenen Texte wurden in den Evidenztabellen (siehe Kapitel 15.3) den extrahierten Einzelpublikationen vorangestellt.

5.1.3. Suchebene 3

5.1.3.1. Recherche

Die Suchstrategiennach Einzelpublikationen wurde in Pubmed/MEDLINE durchgeführt. Ergänzend wurden Handsuchen in den Datenbanken Cochrane Clinical Trials Database, in den Literaturverzeichnissen der identifizierten Leitlinien und Sekundärliteratur durchgeführt.

Bei der Suche in Pubmed wurden für jede Schlüsselfrage/ jedes Schlüsselthema zielgerichtete Suchen generiert, wobei sowohl das Suchthema als auch die Art der Recherche berücksichtigt wurde (siehe Kapitel 15.3).

Die Suche in der Cochrane Clinical Trials Database war unspezifisch mit dem Suchbegriff „kolorektales Karzinom“. Die erzielten Treffer wurden gesichtet und dem jeweiligen Themenkomplex zugeordnet.

Die Literatursuche, Evidenzbewertung und Erstellung von Evidenztabellen fand zwischen Oktober 2010 und Dezember 2011 statt.

5.1.3.2. Auswahl der Evidenz

Die in den Recherchen identifizierte Literatur der Suchebene 2 und 3 wurde von den Experten auf dem jeweiligen Themengebiet einem Titel- und Abstract- Screening unterzogen. Die ausgewählten Abstracts wurden im Volltext bestellt und nach erneuter Sichtung und Kommentierung durch Fachexperten eingeschlossen, wenn die Volltexte als relevant und methodisch geeignet bewertet wurden. Die Gründe für das Ausschließen bestimmter Studien können im Leitliniensekretariat angefragt werden.

Tabelle 7: Ein-und Ausschlusskriterien der Suchebenen 2 und 3

Einschlusskriterien		
Publikationstyp	Suchebene 2	Metaanalysen, systematische Übersichtsarbeit, HTA auf Basis der genannten Studienarten
	Suchebene 3	randomisierte kontrollierte Studien, Fallkontroll-Studien, prospektive Kohortenstudien
Zeitraum	Für neue Fragestellung	Keine zeitliche Einschränkung
	Für Update	Ab 2003 (Rechercheende für die letzte Aktualisierung der betroffenen TK)
Tumorentität: Kolorektales Karzinom		
Publikationssprache: deutsch, englisch		
Studie am Menschen		
Volltext beschaffbar		
Ausschlusskriterien		
Andere Tumorentität		
Nicht Fragestellung		
Anderer Publikationstyp: z.B. Editorial, Brief, Fall-Serie (Ausnahme: TK III, bei dem auch Fallserien berücksichtigt wurden)		
Mehrfachpublikation mit identischem Inhalt		

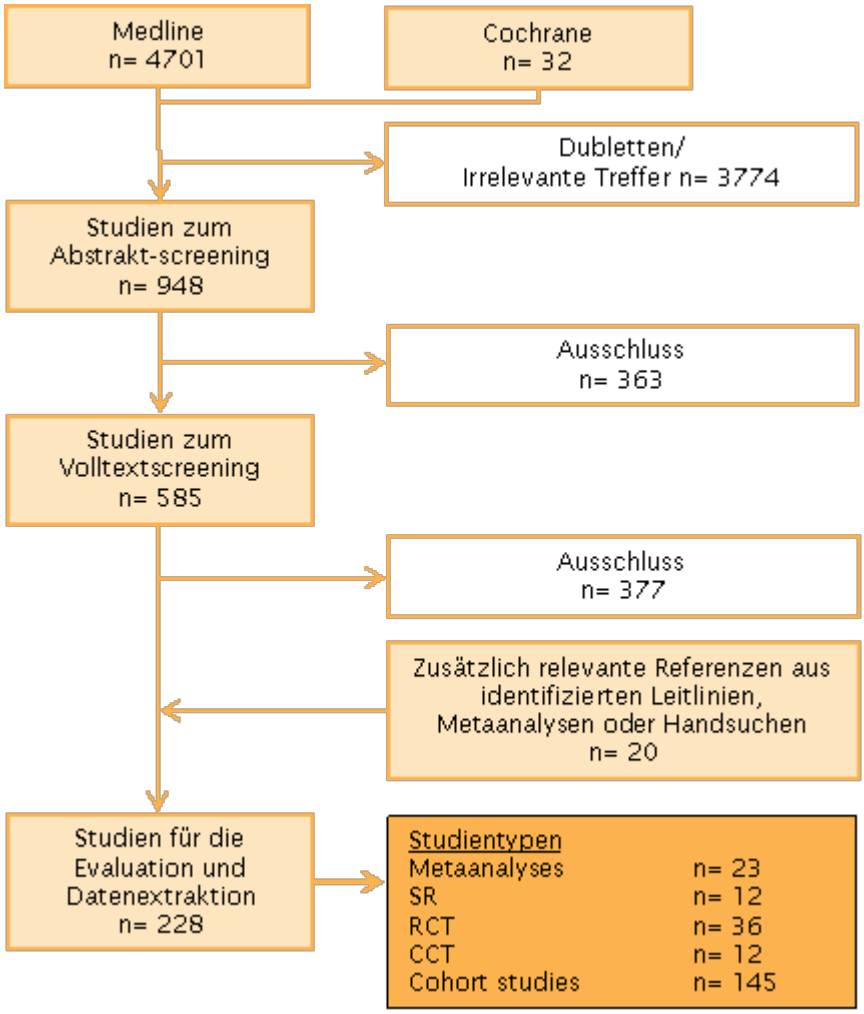

Abbildung 1: Überblick über die in diesem Report dargestellte systematische Recherche

5.1.3.3. Bewertung der Evidenz

Die Ergebnisse der systematischen Recherchen wurden themenspezifisch den Koordinatoren/ Fachexperten der Arbeitsgruppen als Listen mit bibliographischen Angaben und als Volltexte zur Verfügung gestellt. Die eingeschlossenen Studien wurden in Evidenztabellen extrahiert. Auf dieser Grundlage erfolgte die formal methodische Bewertung der Evidenz und Zuordnung nach den Kategorien des Oxford Centre for Evidence-based Medicine Levels of Evidence (2009) (siehe 13.1) durch:

TK I: C. Pox
TK II: Externes Institut
TK III: N. Rahner, K. Schulmann
TKV: W. Hohenberger, S. Post, J. Hardt, P. Lux, C. Pox, A. Reinacher-Schick, Externes Institut
TK VIII: A. Holstege, C. Pox.

5.1.3.4. Evidenzsynthese

Die Evidenztabellen sind in Kapitel 12.1dargestellt.

5.2. Formulierung der Empfehlung und formale Konsensusfindung

5.2.1. Formales Konsensusverfahren

Das Leitlinienprogramm Onkologie sieht zur formalen Konsensfindung Konferenzen vor, bei denen die beteiligten Fachgesellschaften, Institutionen und Patientenvertretungen durch ihre Mandatsträger vertreten sind. Zur Vorbereitung auf die Konferenzen haben die Koordinatoren der Themenkomplexe Empfehlungen und Hintergrundtexte formuliert und Empfehlungsgrade vorgeschlagen. Diese Vorarbeit wurde an alle Mitglieder der jeweiligen AG mit Bitte um Sichtung und Stellungnahme verschickt.

5.2.1.1. Konsensuskonferenzen

Für die Aktualisierung gab es zwei Konsensuskonferenzen (siehe Tabelle 8 und

Tabelle 9) unter der Leitung von Prof. Dr. W. Schmiegel, welche von Prof. Dr. I. Kopp moderiert wurden. Die Methodik von Konsensuskonferenzen sieht ein zweistufiges System vor. In Kleingruppen, welche von zwei zertifizierten externen Leitlinienberatern (Prof. Dr. I. Kopp, Dr. M. Follmann) moderiert wurden, fanden in einem Nominalen Gruppenprozess folgende Arbeitsschritte statt:

- Jeder Teilnehmer äußert sich zu den vor der Konferenz erhaltenen Unterlagen (Empfehlung, Empfehlungsstärke, Hintergrundtext)
- Der Moderator sammelt alle Kommentare und fasst inhaltliche Überschneidungen zusammen
- Alle Äußerungen werden diskutiert
- Änderungen werden in den Entwurf aufgenommen
- Der neue Entwurf wird zur Diskussion gestellt und gegebenenfalls nochmal modifiziert

Der zweite Konferenzteil erfolgte im Plenum und umfasste folgende Arbeitsschritte:

- Vorstellung der endgültigen Vorschläge zu Empfehlungen, Empfehlungsgrad und Hintergrundtexten durch die AG-Koordinatoren
- Klärung/ Diskussion von Rückfragen zur Evidenzgrundlage, Empfehlungsgrad, Wortlaut und Hintergrundtext
- Diskussion und Einarbeitung der Änderungsvorschläge
- Abstimmung über die endgültige Formulierung und ihre Graduierung
- Bei fehlendem Konsens erneute Diskussion
- Finale Abstimmung

Die Abstimmung erfolgte bei der ersten Konsensuskonferenz anonym per TED-System und bei der zweiten Konferenz per Handzeichen.

Infolge der Erstellung der Qualitätsindikatoren wurde die nachträgliche Änderung einer Empfehlung notwendig. Dies geschah im DELPHI-Verfahren. Am 09.07.12 wurde allen Mandatsträger das DELPHI-Formular per Email zugestellt. Zum Stichtag am 16.07.12 gab es 37 Zustimmungen, eine Enthaltung und eine Ablehnung. Die Ablehnung enthielt als Gegenvorschlag die ursprüngliche Empfehlung. Somit erhielt die geänderte Empfehlung einen „Konsens".

Tabelle 8: Informationen zur 1. Konsensuskonferenz

Erste Konsensuskonferenz	
Leitung Moderation	W. Schmiegel I. Kopp
Ort Datum	Bochum 01./02.04.2011
Inhalt	TK I, III, V, VIII
Teilnehmer	G. Baretton, W.-O. Bechstein, B. Bokemeyer, P. Engeser, J. Epplen, W. Fischbach, M. Follmann, U. Graeven, M. Hass, M.Heike, T. Höhler, W. Hohenberger, A. Holstege, J. Hübner, K.-W. Jauch, F. Kolligs, J. Körber, M. Landenberger, H. Lang, K.-H. Link, H. Link, S. Ludt, P. Lux, C. Maar, U. Melle, J. Ockenga, R. Porschen, S. Post, C. Pox, H.-R. Raab, N. Rahner, A. Reinacher-Schick, J. Riemann, R. Sauer, S. Stemmler, W. Scheppach, K. Schulmann, A. Tannapfel, T. Vogl, C. Wagener, J. Weitz, C. Witte, C. Wittekind

Tabelle 9: Informationen zur 2. Konsensuskonferenz

Zweite Konsensuskonferenz	
Leitung Moderation	W. Schmiegel I. Kopp
Ort Datum	Bochum 01.02.2012
Inhalt	TK II, einzelne Kapitel bzw. Nacharbeiten aus TK V, VI, VII und VIII
Teilnehmer	L. Altenhofen, H.-J. Brambs, H. Brenner, M. Follmann, M. Haß, T. Höhler, W. Hohenberger, A. Holstege, J. Hübner, M. Landenberger, S. Ludt, P. Lux, C. Maar, S. Post, C. Pox, N. Rahner, A. Reinacher-Schick, J. Riemann, K. Scheidhauer, K. Schulmann, A. Sieg, A. Tannapfel, A. Theilmeier, T. Vogl, C. Witte

5.2.1.2. Empfehlungsgraduierung

Die Festlegung der Empfehlungsgrade erfolgte im Rahmen der Konsensuskonferenzen durch die beteiligten Experten. In der Regel bestimmt der Evidenzgrad den Empfehlungsgrad. Bei der Formulierung der Empfehlungen kann so zwischen drei Modalitäten unterschieden werden (A: "soll", B: "sollte", 0: "kann", siehe Abbildung 5.1).

Berücksichtigt wurden zudem Faktoren wie die Studienqualität, die klinische Relevanz der Studienendpunkte und die ökonomische Umsetzbarkeit im Versorgungsalltag, aber auch Patientenpräferenzen und ethische Aspekte fanden Eingang in die Überlegungen. In einigen Fällen kam es daher zu Abweichungen zwischen Evidenz- und Empfehlungsgrad, die im Hintergrundtext zu den Empfehlungen erläutert werden.

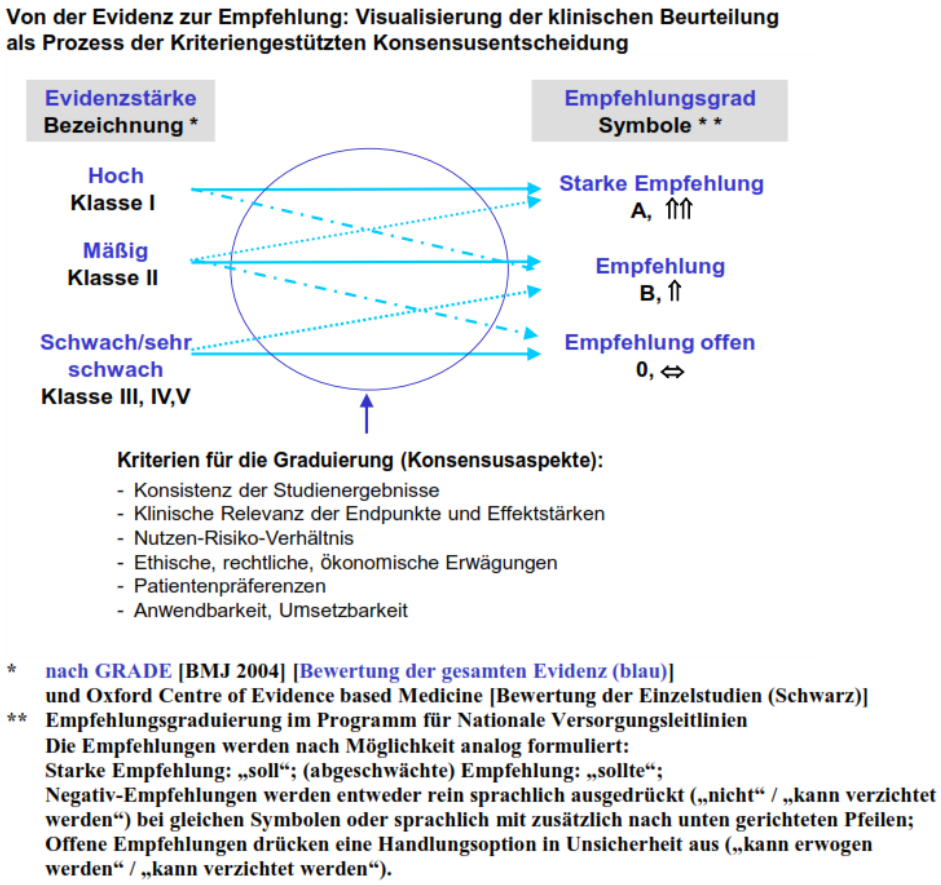

Abbildung 2: Zusammenhang zwischen Evidenz und Empfehlung [3]

5.2.1.3. Konsensusstärke

Um die Konsensusstärke festzustellen, wurde der prozentuale Anteil der den Empfehlungen zustimmenden Teilnehmer sowie die absolute Zahl der Zustimmungen ermittelt. (Bei der ersten Konferenz per TED, bei der zweiten Konferenz per Handzeichen). Wurde kein Konsens erzielt, sind die Gründe bzw. unterschiedlichen Positionen im Text dargelegt. Die Klassifizierung der Konsensusstärke ist in Tabelle 10: Klassifizierung der Konsensstärke [4] dargestellt.

Tabelle 10: Klassifizierung der Konsensstärke [4]

Konsensusstärke	Prozentuale Übereinstimmung
Starker Konsens	Zustimmung von >95% der Teilnehmer
Konsens	Zustimmung von >75% - 95% der Teilnehmer
Mehrheitliche Zustimmung	Zustimmung von >50 - 75% der Teilnehmer

Kein Konsens	Zustimmung von <50% der Teilnehmer

5.2.2. Darstellung der Kernaussagen im Leitlinientext

In der Langfassung der Leitlinie sind die Kernaussagen in Form von Empfehlungskästen dargestellt. So heben sie sich stark vom Hintergrundtext ab. Es gibt Kästen für Empfehlungen, für Statements (Erläuterung spezifischer Sachverhalte oder Fragestellungen) und für konsensbasierte Empfehlungen/ Statements- (GCP). Je nach Kasten enthalten sie Zusatzinformationen wie Empfehlungsgrad, Evidenzstärke, Konsensstärke und zugrunde liegende Literatur. Die aktualisierten Kernaussagen stehen in orangefarbenen Kästen, die unveränderten Empfehlungen in gelben.

Für Zusatzinformationen und für die übersichtliche Darstellung komplexer Zusammenhänge wurde die Tabellenform gewählt oder Schaubilder generiert.

6. Qualitätsindikatoren

Zur Ableitung bzw. Entwicklung von Qualitätsindikatoren wurden für diese Leitlinie folgende in Deutschland bereits bestehende bzw. geplante Datenerhebungen im Vorfeld berücksichtigt:

- Basisdatensatz der klinischen Krebsregister mit der organspezifischen Ergänzung Kolorektales Karzinom

(Quelle: http://www.tumorzentren.de/onkol-basisdatensatz.html)

- Qualitätsindikatorenset des AQUA-Instituts für die sektorenübergreifende Qualitätssicherung

(Quelle: http://www.sqg.de/sqg/downloads/Entwicklung/Abschlussberichte/KRK/Abschlussbericht_Kolorektales_Karzinom.pdf)

Die Generierung der neuen Qualitätsindikatoren aus der überarbeiteten Leitlinie wurde in folgenden Schritten durchgeführt:

1. Bestandsaufnahme: Zusammenstellung und Analyse der oben genannten Quellen

2. Soweit möglich wurden im Vorfeld des Anwesenheitstreffens aus den starken Empfehlungen der aktuellen Leitlinienversion mögliche Indikatoren mit Definition von Zähler und Nenner abgeleitet. Es wurden sowohl evidenzbasierte als auch Expertenkonsens basierte starke (A-) Empfehlungen berücksichtigt.

3. In einem Treffen der Mitglieder der Leitlinienkommission und Vertretern der klinischen Krebsregister, des Zertifizierungssystems und des AQUA-Instituts am 05.06.2012 wurden die bereits bestehenden bzw. geplanten Datenerhebungen (ADT, AQUA) als potentielle Basis für die zu entwickelnden QI der Leitlinie zu Grunde gelegt. In dem Treffen wurden den Teilnehmern der Prozessablauf der QI-Erstellung sowie das Bewertungsinstrument des OL erläutert.

Die unter 2. generierte Zusammenstellung aus den Empfehlungen der Leitlinie wurde diskutiert und entschieden, ob aus der Empfehlung ein potentieller QI generiert werden könne. Für die potentiellen QI, für die bereits Daten aus den Kennzahlen des Zertifizierungssystems der zertifizierten Darmkrebszentren vorlagen, wurden die

Jahresauswertungen 2012 im Rahmen des Treffens gezeigt (Jahresbericht 2012: http://www.onkozert.de/downloads/dz_allgemein_benchmarking_2012%28120525%29-A16.pdf). Die Auswertungen der Kennzahlen verdeutlichen das Verbesserungspotential der konsentierten QI 5, 6 und 7. Folgende Ausschlusskriterien kamen bei diesem ersten Screening zur Anwendung:

Gründe für einen Ausschluss der Empfehlung aus der Liste der potenziellen QI:		
Empfehlung ist nicht operationalisierbar (Messbarkeit nicht gegeben)	Fehlender Hinweis auf Verbesserungspotential	Sonstiges (mit Freitexteingabe in Liste der Empfehlungen)

4. Dieses vorselektierte Set von potentiellen QI wurde mit dem Bewertungsinstrument des Leitlinienprogramms Onkologie mittels eines standardisierten Bogens durch das interdisziplinäre Gremium der Leitliniengruppe bewertet (in Anlehnung an Ärztliches Zentrum für Qualität in der Medizin (ÄZQ), Expertenkreis Qualitätsindikatoren für Nationale VersorgungsLeitlinien. Programm für Nationale VersorgungsLeitlinien von BÄK, KBV und AWMF. Qualitätsindikatoren – Manual für Autoren . äzq Schriftenreihe Band 36, Make a Book, Neukirchen, Zugriff 27.06.2012). Als angenommen galten Indikatoren mit mind. 75% Zustimmung („Trifft eher zu“ und „Trifft zu“ und „Nein, kein Risiko für nicht korrigierbare Fehlsteuerung) bei jedem Kriterium.

	1 Trifft nicht zu	2 Trifft eher nicht zu	3 Trifft eher zu	4 Trifft zu
1. Kriterium: Bedeutung des mit dem QI erfassten Qualitätsmerkmals für das Versorgungssystem (Bedeutung) Folgende Aussage wird bewertet: "Der Indikator erfasst wesentliche Aspekte der Lebensqualität, Morbidität oder Mortalität.“				
2. Kriterium: Klarheit der Definitionen Folgende Aussage wird bewertet: "Der Indikator ist klar und eindeutig definiert.“				
3. Kriterium: Beeinflussbarkeit der Indikatorausprägung Folgende Aussage wird bewertet: „Der Qualitätsindikator bezieht sich auf einen Versorgungsaspekt, der von den genannten Akteuren beeinflusst werden kann.“				
	Ja		**Nein**	
4. Kriterium: Berücksichtigung potenzieller Risiken / Nebenwirkungen. Folgende Fragestellung ist zu beantworten (Teilaspekt): „Gibt es Risiken zur Fehlsteuerung durch den Indikator, die nicht korrigierbar sind?“				

5. Nach der schriftlichen Bewertung erfolgte eine methodisch moderierte Telefonkonferenz (12.07.12), in der die Ergebnisse der Bewertung diskutiert wurden. Bereits in dem Anwesenheitstreffen hatte die Leitlinienkommission beschlossen, nicht nur Strukturqualitätsziele, sondern auch Ergebnisqualitätsziele zu berücksichtigen, für die es keine starke Empfehlung in der Leitlinie gibt. Die Experten waren sich einig,

dass die Erhebung der Daten für Anastomoseninsuffizienzen Rektumkarzinom und Kolonkarzinom einen erheblich Mehrwert für die klinische Versorgung darstellen, da gerade in diesen Bereichen deutliche Qualitätsunterschiede bestehen und somit ein großes Potential für eine Qualitätsverbesserung mithilfe von Qualitätsindikatoren. Darüber hinaus wurde von Seiten der Patientenvertreter auf die Wichtigkeit eines Qualitätsindikators für die adäquate präoperative Stomaanzeichnung hingewiesen. Der Text der entsprechenden Empfehlung wurde diskutiert und geändert, sodass eine konsensfähige starke Empfehlung entstand. Diese wurde im standardisierten Umlaufverfahren (DELPHI) konsentiert. Am Ende der Telefonkonferenz wurde vereinbart, dass für die 3 Themenbereiche 3 mögliche QI beschrieben werden.

6. Analog den Schritten 4-5 wurden die 3 zusätzlichen QI bewertet und in einer zweiten Telefonkonferenz am 14.08.2012 das finale Set von 10 Qualitätsindikatoren konsentiert.

Das Set der konsentierten Qualitätsindikatoren findet sich in der Langversion und Kurzversion der Leitlinie.

Die Primärliste der potentiellen Qualitätsindikatoren, die o.g. Basisdatensätze als auch die Ergebnisse der schriftlichen Bewertung sind auf Anfrage im Leitliniensekretariat erhältlich.

7. Externe Begutachtung und Verabschiedung

Die fertige Langfassung ist allen Mitgliedern der Leitlinienüberarbeitung zur Kommentierung zugegangen.

Inhaltlich geprüft wurden Lang- und Kurzversion und Leitlinienreport von den Vorständen der beteiligten Fachgesellschaften, Institutionen und Patientenvereinigungen.

8. Redaktionelle Unabhängigkeit und Interessenkonflikte

Die Aktualisierung der Leitlinie erfolgte in redaktioneller Unabhängigkeit von der finanzierenden Organisation, der Deutschen Krebshilfe. Für die ausschließlich ehrenamtliche Arbeit der Mandatsträger und Experten, ohne die die S3-Leitlinie nicht zu realisieren gewesen wäre, ist ihnen zu danken.

Alle Mitglieder der Leitliniengruppe haben ein Formblatt der AWMF zur Interessenkonflikterklärung erhalten und ausgefüllt. Die Relevanz des Themas wurde bei Veranstaltungen und per Email wiederholt dargelegt. Das Formblatt (siehe 13.2) beinhaltet die eigene Bewertung, ob durch die jeweiligen Interessenkonflikte die erforderliche Neutralität für die Tätigkeit als Experte in Frage gestellt ist. Die Inhalte der Interessenkonflikterklärungen sind in Tabelle 11 tabellarisch dargestellt. Die Erklärungen sind von den Leitlinienkoordinatoren geprüft worden. Die Berater- und Gutachtertätigkeiten vieler Mandatsträger bei diversen Firmen gab Anlass zur Diskussion. Da sich die vorliegende Leitlinienaktualisierung jedoch nicht auf die Themenkomplexe bezieht, welche medikamentöse Behandlungen beinhalten, wurden genannte Tätigkeiten nicht als möglicher Interessenkonflikt gewertet.

Prof. Schmiegel hat sich aufgrund eines möglichen Interessenskonfliktes bei den Abstimmungen zum FOBT/iFOBT, genetischer Stuhltests und M2-PK enthalten.

Weitere Ausschlüsse von Mandatsträgern aufgrund der Selbsterklärungen erfolgten nicht.

Die Gefahr der Beeinflussung durch Interessenkonflikte wurde umgangen, indem für die Recherche, Auswahl und Bewertung der Literatur politisch besonders brisanter Themen externe Institute beauftragt worden sind. Die formale Konsensbildung und die interdisziplinäre Erstellung sind weitere Instrumente, die Einflussnahme der Industrie zu minimieren.

9. Verbreitung und Implementierung

Die überarbeitete Leitlinie steht als Langversion, als Kurzfassung im Internet auf den Homepages der AWMF, der DKG, der DKH und der DGVS zum kostenlosen Download bereit. Zusätzlich wird eine Veröffentlichung in der Zeitschrift für Gastroenterologie erfolgen. Eine Veröffentlichung in weiteren Zeitschriften ist angestrebt.

Weiterhin wurde die Erstellung einer dreiteiligen Patientenleitlinie und die Übersetzung der Langfassung ins Englische beauftragt. Beides wird nach Fertigstellung auf den o. g. Homepages abrufbar sein.

In der Vergangenheit haben zudem sich die Darmkrebszentren als eine zentrale Maßnahme zur Implementierung der Leitlinie etabliert. Die im Rahmen der Aktualisierung definierten Qualitätsindikatoren werden in die Erhebungsbögen für Darmkrebszentren aufgenommen. Auch die vom AQUA-Institut entwickelten Qualitätsindikatoren bilden wesentliche Inhalte der S3-Leitlinie zur Diagnostik, Behandlung und Nachsorge von Patienten ab. Über die Bereitstellung von Indikatoren zu relevanten Prozessen kann die Qualitätssicherung die Umsetzung der Leitlinie unterstützen.

Als zusätzliches Instrument zur Verbesserung der Implementierung gelten Klinische Algorithmen. Diese wurden erstellt zur HNPCC-Diagnostik, ICH/ MSI zur Abklärung Mismatch-Reperatur-Defekt, Vorsorge HNPCC/ Lynch-Syndrom, Lokales Staging beim KRK und zum CRM. Diese Algorithmen sind in den entsprechenden Kapiteln der Langversion abgebildet.

10. Gültigkeitsdauer der Leitlinie

Die S3-Leitlinie Kolorektales Karzinom wird kontinuierlich aktualisiert. Die Gültigkeitsdauer der 2012 jetzt überarbeiteten Themenkomplexe I, II, III, V, und VIII wird auf 5 Jahre geschätzt, sie werden spätestens 2017 einer erneuten Revision unterzogen. Die Aktualisierung der verbleibenden Themenkomplexe IV, VI und VII ist für 2014 vorgesehen.

Das Aktualisierungsverfahren wird von der verantwortlichen Institution (Leitliniensekretariat) koordiniert. Neu erscheinende wissenschaftliche Erkenntnisse werden von den Mitgliedern der Leitliniengruppe beobachtet. Daraufhin werden einzelne Themenkomplexe gegebenenfalls vorzeitig überarbeitet. Alle Aktualisierungen werden gesondert publiziert (Addendum zur Internetversion, Fachzeitschriften) und anschließend in die Volltextversion der Leitlinie eingearbeitet.

Kommentare und Hinweise für den Aktualisierungsprozess aus der Praxis sind ausdrücklich erwünscht und können an das Leitliniensekretariat adressiert werden.

Leitlinienkoordination: Dr. Christian P. Pox
Leitliniensekretariat: Anjes Giuliani

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11. Ausblick

Im Rahmen dieser Aktualisierung wurden bereits Themen für die nächste Aktualisierung identifiziert. Dies sind sowohl bisher nicht in der Leitlinie besprochene Themen als auch bereits enthaltene Themen, zu denen Aktualisierungsbedarf gesehen wird:

- Indikation für die neoadjuvante Radiochemotherapie beim Rektumkarzinom
- Bedeutung von MSI für die Indikation zur adjuvanten Chemotherapie
- Indikation für die adjuvante Chemotherapie beim Kolonkarzinom im Stadium II
- Genderaspekte
- weitere Studien zur Bedeutung der bildgebenden Verfahren in der Nachsorge (CT, NMR, PET-CT vs Sonographie)
- Studien zur Wertigkeit von Reha-Maßnahmen nach kurativer Operation
- Dauer der Nachsorge nach adjuvanter Chemotherapie.

12. Literaturrecherche

12.1. Recherchestrategie / Evidenztabellen

12.1.1. Themenkomplex I

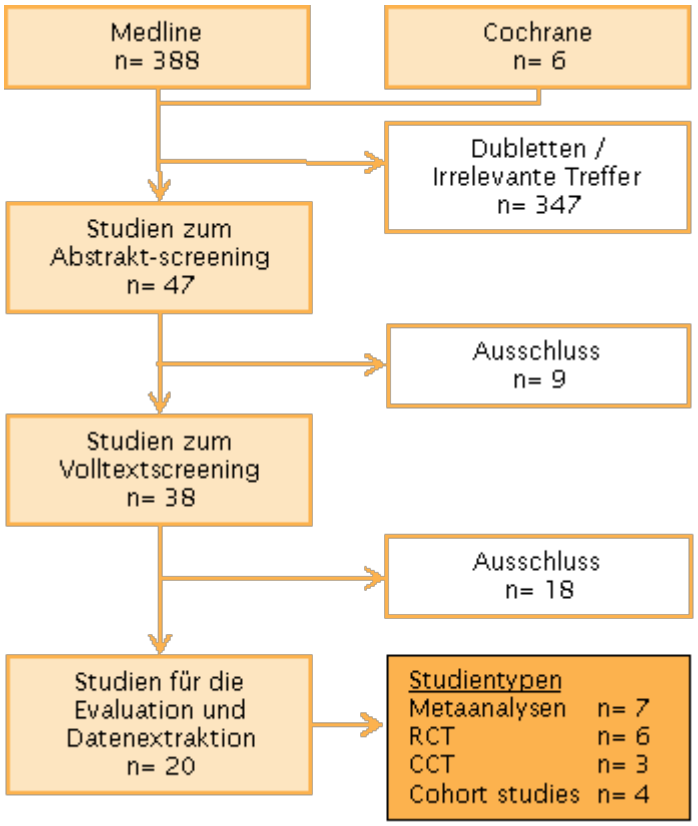

Abbildung 3: Ergebnisse der Recherchen zum Themenkomplex I

12.1.1.1. Suchebene 2: Meta-Analysen

Database	Suche	Datum	Treffer	Identifizierte abstracts	Eingeschlossene Volltexte
Cochrane Database of Systematic Reviews	“colorectal neoplasms” in Title, Abstract or Keywords and prevention in Title, Abstract or Keywords, from 2003 to 2010	28.09.2010	6	2	2
MEDLINE via Pubmed	"colorectal neoplasms"[MeSH Terms] AND ("prevention and control"[Subheading] OR ("risk"[MeSH Terms] OR "risk"[All Fields])) AND "Meta-Analysis "[Publication Type] AND ("humans"[MeSH Terms] AND (English[lang] OR German[lang]) AND ("2003/06"[PDAT] : "2010/06"[PDAT]))	04.10.2010	194	47	11

12.1.1.2. Suchebene 3: Primärliteratur

12.1.1.2.1. Ergebnisse der systematischen Literaturrecherche

Suchfragen	Suchzeitraum	Suchdatum	Treffer	Identifizierte Abstracts(nach Dubletten-abgleich)	Aus-geschlossene Abstracts	Identifizierte Volltext-publikationen	Ein-geschlossene Volltext-publikationen	Zusätzlich berücksichtigte Volltext-publikationen (Handsuche, Referenzen-recherche)
Nahrungszubereitung (Fette/ Fettsäuren)	Bis 09.03.2011	09.03.2011	95	12	9	3	3	0
Acrylamid	Bis 09.03.2011	09.03.2011	18	5	0	5	3	0
Magnesium	Bis 21.10.2010	21.10.2010	5	1	0	1	1	0
Selen	Bis 21.10.2010	21.10.2010	16	8	0	8	7	0
Folsäure	Bis 21.10.2010	21.10.2010	34	9	0	9	3	0
Cox-2	Bis 31.10.2010	31.10.2010	26	12	0	12	3	0

12.1.1.2.2. Suchstrategie und Evidenztabellen

12.1.1.2.2.1. Wird das sporadische KRK-Risiko durch Nahrungszubereitung (Fast-food/ Fette) beeinflusst?

Suchstrategie

#1 colorectal

#2 colonic

#3 sigmoid

#4 rectal

#5 #1 or #2 or #3 or #4

#6	neoplasms
#7	tumor
#8	carcinoma
#9	#6 or #7 or #8
#10	#5 and #9
#11	prevention and control
#12	risk
#13	#11 or #12
#14	#10 and #13
#15	fat intake
#16	animal fat
#17	dietary fat
#18	fast food
#19	#15 or #16 or #17 or #18
#20	#14 and #19
#21	#20, Limits: Humans, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Controlled Clinical Trial, English, German

Evidenztabelle

Referenz	Studientyp	Teilnehmer FU	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[5]	Meta-Analysis	6 prospective cohort studies (1070 CRC-cases) and 3 case-control studies FU 3-17 years	Association of animal fat intake and colorectal cancer risk		Colorectal cancer incidence	SRRE between highest and lowest intake for cohort studies: 1.04 (95% CI: 0.83, 1.31) for cohort and case-control studies: 1.15 (95%CI: 0.93, 1.42)	no association between animal fat consumption and colorectal carcinogenesis	2a
[6]	Combined Analysis	13 case-control studies (5,287 cases of colorectal cancer; 10,470 controls)	Association of dietary fat intake and colorectal cancer risk adjusted for total energy intake		colorectal cancer incidence	Odds ratio lowest to highest quintile all 0.92 (95% CI 0.77-1.10) Men 0.90 (0.72 – 1.13) Women 0.98 (0.73-1.32)	no energy-independent association between dietary fat intake and risk of colorectal cancer	3a
[7]	Meta-Analysis	13 prospective cohort studies (3,635 cases and 459,910 participants)	Association of dietary fat intake and colorectal cancer risk		colorectal cancer incidence	Combined RRs (95%CI) 0.99 (0.89,1.09) for total dietary fat	dietary fat may not be associated with an increased risk of CRC	2a

12.1.1.2.2.2. Wird das sporadische KRK-Risiko durch die Aufnahme von Acrylamid beeinflusst?

Suchstrategie

((("colorectal neoplasms"[MeSH Terms] OR ("colorectal"[All Fields] AND "neoplasms"[All Fields]) OR "colorectal neoplasms"[All Fields] OR ("colorectal"[All Fields] AND "cancer"[All Fields]) OR "colorectal cancer"[All Fields]) AND ("acrylamide"[MeSH Terms] OR "acrylamide"[All Fields])) AND ("humans"[MeSH Terms] AND (English[lang] OR German[lang]))

Evidenztabelle

Referenz	Studientyp	Teilnehmer FU	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[8]	Prospective Cohort study	N= 5000; 2190 cases of crc 13.3 years FU	Association of acylamide intake and GI-cancer risk		Colorectal cancer incidence	HR (95% CI) between highest vs. lowest quintile intake: 1.00 (0.96–1.06)	no association between dietary acrylamide intake and cololorectal cancer risk	2b
[9]	Prospective Cohort study	45,306 men; 676 cases of crc 9.3 years FU	Association of acylamide intake and CRC risk		Colorectal cancer incidence	RR (95% CI) between highest vs. lowest quartile intake 0.95 (0.74-1.20)	no significant association between acrylamide intake and risk of colorectal cancer in men	2b
[10]	Prospective Cohort study	61,467 women; 504 cc, 237 rc 15.1 years FU	Association of acylamide intake and CRC risk		Colorectal cancer incidence	multivariate-adjusted relative risk (95% CI; p for trend) comparison of highest vs. lowest quintile intake) 0.9 (0.7–1.3; p = 0.85)	acrylamide intake in the amounts taken in through diet do not increase the risk of colorectal cancer in women	2b

12.1.1.2.2.3. Wird das sporadische KRK-Risiko durch die Einnahme von Magnesium beeinflusst?

Suchstrategie

#1 colorectal

#2 colonic

#3 sigmoid

#4 rectal

#5 #1 or #2 or #3 or #4

#6 neoplasms

#7 tumor

#8 carcinoma

#9 #6 or #7 or #8

#10 #5 and #9

#11 prevention and control

#12 #10 and #11

#13 magnesium

#14 #12 and #13, Limits: Limits: Humans, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Comparative Study, Controlled Clinical Trial, English, German

Evidenztabelle

Referenz	Studientyp	Teilnehmer FU	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[11]	Prospective cohort study	38.345 women, 259 crc 11 years FU	Association of magnesium intake and CRC risk		Colorectal cancer incidence	Multivariate RR comparison of highest vs. lowest quintile intake: 0.97 (95% CI,0.63-1.49) (P for trend = 0.88)	little support for an inverse association between total magnesium intake and colorectal cancer incidence in women	2b

12.1.1.2.3. *Suchfrage: Wird das sporadische KRK-Risiko durch die Einnahme von Selen beeinflusst?*

Suchstrategie

#1	colorectal
#2	colonic
#3	sigmoid
#4	rectal
#5	#1 or #2 or #3 or #4
#6	neoplasms
#7	tumor
#8	carcinoma
#9	#6 or #7 or #8
#10	#5 and #9
#11	prevention and control
#12	#10 and #11

#13 selenium

#14 #12 and #13, Limits: Limits: Humans, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Comparative Study, Controlled Clinical Trial, English, German

Evidenztabelle

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[12]	Combined analysis of data from three randomized trials	1763 participants, with recently removed adenoma FU 3-4 years	Association of selenium blood concentration and risk of developing new adenoma		Adenoma recurrence	OR comparison of highest vs. lowest quartile 0.66 (95% CI 0.50 – 0.87); p for trend = 0.006	Higher selenium status may be related to decreased risk of colorectal cancer	2b
[13]	RCT	1312 participants with a history of basal cell or squamous cell carcinoma of the skin, Selenium group 653, Placebo group 659. FU: 7.4 years	200 µg selenized yeast	Placebo	Primary end points: skin BCC and SCC Secondary end points: total mortality and cancer mortality, as well as the incidences of lung, colorectal, and prostate cancers	Total cancer incidence HR = 0.75, 95% CI = 0.58–0.97, P = 0.03 Colorectal cancer incidence HR=0.46, 95% CI = 0.21–1.02, P = 0.057.	This trial supports the efficacy of selenium supplementation in reducing total cancer incidence, total cancer mortality, and the incidence of colorectal cancer.	2b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[14]	CCT	28 patients with polyp > 1 cm, 24 patients with cancer, 35 controls			relationship of serum selenium status with the presence of large size colorectal adenomas and colorectal cancer	serum selenium levels were significantly lower in patients with cancer than in healthy controls in subjects < and > 60 years (p < 0.0055). In subjects aged <60 yr, mean serum selenium levels were significantly lower in both patients groups than in controls (p = 0.0001), whereas in subjects aged > 60 yr, there were no differences among groups (p = 0.62).	High selenium status may decrease the risk of large size adenomas in a low selenium geographical area, this preventive effect seems to be exclusive to subjects <60 yr.	3b
[15]	RCT	35 533 men (Placebo 8696, Vitamin E 8737, Selenium 8752, Selenium + Vit. E 8703) Mean FU: 5.46 years	200 µg Selenium, 400 IU Vitamin E or combination of both	Placebo	Prostate cancer and prespecified secondary outcomes, including lung, colorectal, and overall primary cancer	no statistically significant differences in the rates of prostate cancer between the 4 groups Colorectal cancer: Placebo HR 1.00 (reference) Vitamin E HR 1.09 (0.69-1.73) Selenium HR 1.05 (0.66-1.67) Selenium + Vit. E HR 1.28 (0.82-2.00)	selenium, vitamin E, or selenium + vitamin E did not prevent prostate cancer in the generally healthy, heterogeneous population of men in SELECT. So significant differences in CRC incidence.	2b (only secondary outcome)
[16]	Case-control study	758 cases with advanced colorectal adenoma and 767 sex- and race-matched controls	Association of blood selenium concentration and advanced colorectal adenoma of the distal colon	Controls had a negative sigmoidoscopy	Advanced colorectal adenoma recurrence of the distal colon	OR comparison of highest vs. lowest quintile : 0.76 (95% CI 0.53-1.10; Ptrend = 0.01]	Selenium may reduce the risk of developing advanced colorectal adenoma .	3b
[17]	Secondary analysis of an RCT	1312 participants, 598 participants underwent sigmoidoscopy or colonoscopy	200 µg selenized yeast	Placebo	Incidence of prevalent and incident adenomas	prevalent adenomas: OR 0.67, 95% CI 0.43–1.05) incident adenomas: OR 0.98 (95% CI 5 0.57–1.68)	Selenium supplementation was associated with a significantly reduced risk of prevalent adenomas, but only among subjects with	3b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		7.6 years FU					either a low baseline selenium level or among current smokers.	
[18]	CCT	552 subjects, 276 cases and 276 conrols		Controls had a negative colonoscopy	To investigate the relation between prediagnostic serum selenium concentrations and colorectal adenomas	compared with the lowest quintile, the highest quintile of total serum selenium was associated with a modest reduction in risk of adenoma recurrence (OR, 0.76; 95% CI, 0.44–1.30), but there was no apparent trend in risk. When we analyzed total serum selenium as a continuous variable, the adjusted OR associated with a 25 ug/liter increase in serum selenium was 0.91 (95% CI, 0.73–1.16).	Our findings do not indicate a clear association between serum selenium concentrations and adenoma recurrence.	3b

12.1.1.2.3.1. Wird das sporadische KRK-Risiko durch die Einnahme von Folsäure beeinflusst?

Suchstrategie

#1 colorectal

#2 colonic

#3 sigmoid

#4 rectal

#5 #1 or #2 or #3 or #4

#6 neoplasms

#7 tumor

#8 carcinoma

#9 #7 or #8 or #9

#10 #6 and #10

#11 prevention and control

#12 #10 and #11

#13 folic acid (Title/ Abstract)

#14 folate (Title/ Abstract)

#15 #13 or #14

#16 #12 and #15 Limits: Humans, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Comparative Study, Controlled Clinical Trial, English, German

Evidenztabelle

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[19]	Meta-analysis	1. 3 RCTs with patients with history of adenomas (429 patients in folic acid group, 411 patients in placebo group) FU 3 years 2. 3 RCTs examined general population with no increased risk of colorectal cancer (5523 pat. in folic acid group, 5539 pat. in placebo group) FU 5-7 years	1. Folic acid supplementation (0,5 – 5 mg/day) 2. Folic acid supplementation (2,5 or 20 mg/day) +/- other vitamins	1. Placebo 2. Placebo in 2 studies, 1 study placebo + beta-carotene)	1. adenoma recurrence 2. colorectal cancer incidence	1. RR 0.93, 95% CI 0.61-1.41 2. RR 1.13 95% CI 0.77-1.64	No evidence that folic acid is effective in the chemoprevention of adenomas or CRC.	1a
[20]	Meta-analysis	Five prospective RCTs with patients with history of adenomas (805 patients in the folate and 775 in the placebo groups)	Folic acid supplementation (0,5 – 5 mg/day)	Placebo	Adenoma recurrence	OR = 1.08 95% CI;0.87,1.33; p =0.49	No potential benefit for folate supplementation.	1a
[21]	Pooled analysis of 13 prospective cohort studies	725.134 participants with 5.720 incident colon cancers follow-up 7-20 y	Association of folate intake and Colon cancer risk		Colon cancer incidence	RR of highest vs. lowest quintile intake: 0.92 95% CI 0.84-1.00 for dietary folate RR: 0.85 95% CI 0.77-0.95 for total folate	Higher folate intake is modestly associated with reduced risk of colon cancer	2a

12.1.1.2.3.2. Wird das sporadische KRK-Risiko durch die Einnahme von COX-2 Inhibitoren beeinflusst?

Suchstrategie

#1 colorectal

#2 colonic

#3 sigmoid

#4 rectal

#5 #1 or #2 or #3 or #4

#6 neoplasms

#7 tumor

#8 carcinoma

#9 #7 or #8 or #9

#10 #6 and #10

#11 prevention and control

#12 #10 and #11

#13 COX-2 inhibitor

#14 celecoxib [Supplementary Concept]

#15 rofecoxib [Supplementary Concept])

#16 #13 or #14 or #15

#17 #12 and #16, Limits: Limits: Humans, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Controlled Clinical Trial, English, German

Evidenztabelle

Referenz	Studientyp	Teilnehmer FOLLOW-UP	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[22]	RCT	N = 1561 of patients who had adenomas removed (933 in celecoxib group, 628 in the placebo group) FU 3 y	400 mg of celecoxib once daily	Placebo once daily	Detection of adenomas at either year 1 or 3	RR of cumulative adenoma recurrence: 0.64 CI: 0.56 to 0.75; P<0.001	Celexocib reduced the recurrence of colorectal adenomas	1b
[23]	RCT	N = 1277 subjects who had adenomas removed (1277 in rofecoxib group, 1293 in placebo group) FU 3 y	25 mg of rofecoxib once daily	Placebo once daily	Cumulative proportion of subjects with 1 or more adenomas detected during the 3 year treatment	RR of cumulative adenoma recurrence: 0.76 CI, 0.69 – 0.83, P < .001	Rofecoxib reduces the 3-year risk of colorectal. Given the toxicity associated with the use of rofecoxib, it is unlikely to be attractive for chemoprevention	1b
[24]	RCT	N = 2035 patients who had adenomas removed (Placebo: 679, celecoxib 200 mg: 685, celecoxib 400 mg: 671) FU 3 y	200 mg of celecoxib twice daily, 400 mg of celecoxib twice daily	Placebo twice daily	Detection of an adenoma during a post-randomisation colonoscopy	RR of cumulative adenoma recurrence 200-mg group 0.67 CI 0.59 - 0.77 400-mg group 0.55 CI 0.48 - 0.64)	This trial documented prevention of premalignant adenomas with celecoxib but was not designed to assess effectiveness of the drug for the prevention of colorectal cancer.	1b

12.1.2. Recherchestrategie Themenkomplex III

Für diesen Themenkomplex gab es keine systematische Literatursuche.

12.1.3. Recherchestrategie Themenkomplex V

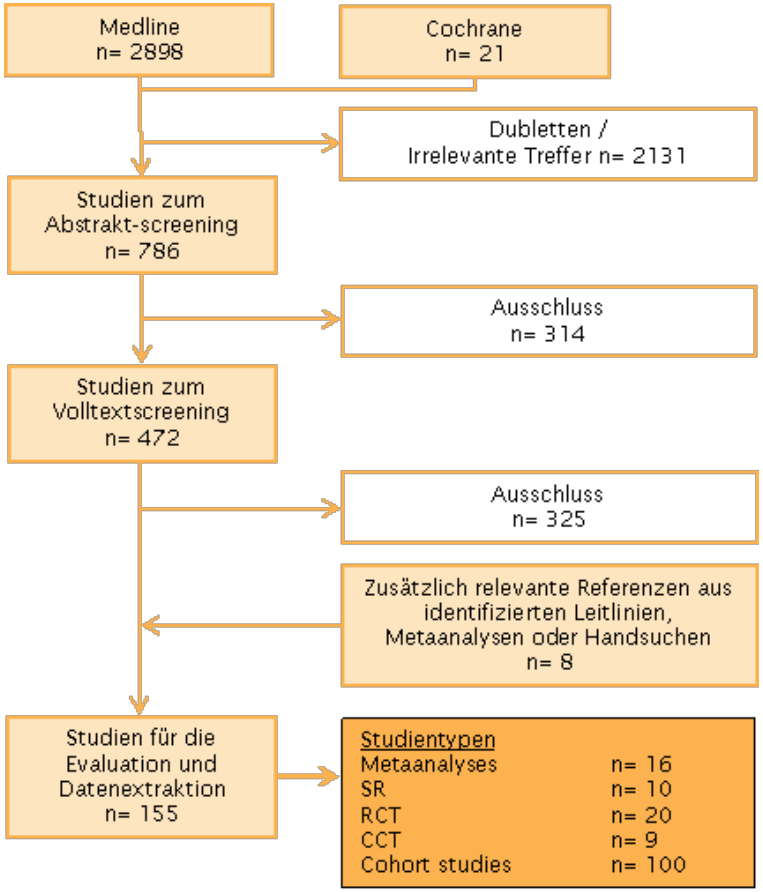

Abbildung 4: Rechercheergebnisse zum Themenkomplex V

12.1.3.1. Suchebene 2: Meta-Analysen

Im Themenkomplex V war die Suche nach Meta-Analysen bei den gezielten Suchen auf Suchebene 3 enthalten.

12.1.3.2. Suchebene 3: Primärliteratur

12.1.3.2.1. Ergebnisse der systematischen Literaturrecherchen

Suchfragen	Suchzeitraum	Suchdatum	Treffer	Identifizierte Abstracts (nach Dubletten-abgleich)	Aus-geschlossene Abstracts	Identifizierte Volltext-publikationen	Ein-geschlossene Volltext-publikationen	Zusätzlich berücksichtigte Volltext-publikationen (Handsuche, Referenzen-recherche)
Rekonstruktions-Verfahren bei der tiefen anterioren Rektumresektion	01.02.2006 (ab Ende des Literatursuche-Zeitraums des Cochrane Reviews von Brown) bis 05.11.2010	05.11.2010	15	9	3	6	6	0
Technik der abdominoperinealen Rektumexstirpation und Defektdeckung	Bis 07.20.2010	07.20.2010	157	8	2	6	6	0
... inklusive plastische Deckung	Bis 05.20.2010	05.02.2010	48	12	3	9	7	0
Exstirpation vs Kontinenzerhalt	bis 28.02.2011	28.02.2011	292	292	283	9	7	0
Laparoskopie beim Rektumkarzinom	01.01.2005 (ab Ende des	05.11.2010	109	32	3	29	14, davon 7	0

Suchfragen	Suchzeitraum	Suchdatum	Treffer	Identifizierte Abstracts (nach Dubletten-abgleich)	Aus-geschlossene Abstracts	Identifizierte Volltext-publikationen	Ein-geschlossene Volltext-publikationen	Zusätzlich berücksichtigte Volltext-publikationen (Handsuche, Referenzen-recherche)
	Literatursuche-Zeitraums des Cochrane Reviews von Kuhry) bis 05.11.2010						Rektumkarzinom 7 Kolorektales Karzinom (ident. Mit Lap Kolon)	
Laparoskopie beim Kolonkarzinom	01.01.2005 (ab Ende des Literatursuche-Zeitraums des Cochrane Reviews von Kuhry) bis 23.03.2011	23.03.2011	241	109	103	6	9, davon 2 Kolonkarzinom 7 Kolorektales Karzinom (ident. Mit Lap Rektum)	5
Resektion simultaner Lebermetastasen	2008 bis 21.03.2011	21.03.2011	225	7	0	7	7	0
Fernmetastasierung bei asymptomatischem Primärtumor	28.02.2001 bis 28.02.2011	28.02.2011	180	29	24	5	5	0
HIPEC und Peritonektomie	bis 16.02.2011	16.02.2011	180	18	1	17	17	0
Endosono/ CT/ MRT beim Staging des RektumCA	2003 bis 15.12.2011	15.12.2011	290	91	40	51	26	1
Bildgebende Verfahren nach Radiochemotherapie	2003 bis 15.12.2011	15.12.2011	290	45	22	23	23	1

Suchfragen	Suchzeitraum	Suchdatum	Treffer	Identifizierte Abstracts (nach Dubletten-abgleich)	Aus-geschlossene Abstracts	Identifizierte Volltext-publikationen	Ein-geschlossene Volltext-publikationen	Zusätzlich berücksichtigte Volltext-publikationen (Handsuche, Referenzen-recherche)
beim RektumCA								
PET/ PET-CT zur Primärdiagnostik	Bis 28.02.2011	28.02.2011	401	58	36	22	20	0
PET/ PET-CT bei Metastasen	Bis 01.07.2011	01.07.2011	432	76	68	8	7	1

12.1.3.2.2. **Suchstrategie und Evidenztabellen**

12.1.3.2.3. *Welche der folgenden Rekonstruktions-Verfahren sollten bei der tiefen anterioren Rektumresektion eingesetzt werden: Bildung eines J-Pouch/ Bildung einer transversen Coloplastik/ Seit-zu-End-Anastomose?*

Suchstrategie

((("Rectal Neoplasms"[Mesh] AND "Surgical Procedures, Operative"[Mesh]) AND ("surgery "[Subheading] OR "Colorectal Surgery"[Mesh])) AND ("J pouch"[All Fields] OR "transverse coloplasty"[All Fields] OR "side-to-end anastomosis"[All Fields]) AND ("humans"[MeSH Terms] AND (Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Randomized Controlled Trial[ptyp] OR Review[ptyp]) AND ("2006/02/01"[PDAT] : "2010/11/05"[PDAT]))

Evidenztabelle

Referenz	Studientyp	Teilnehmer Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[25]	Meta-analysis	4 RCTs (273 patients with rectal cancer and anterior resection: 138	CJP	STE	Functional outcome	No staticstical difference in overall morbidity and mortality, operative time, hospital stay and anastomotic stricture. resting pressures at 24 months postoperatively: CJP vs STE [random effects	CJP or STE are acceptable and safe options after AR for rectal cancer.	1a

Referenz	Studientyp	Teilnehmer Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		colonic J pouch (CJP), 135 side to end (STE))				model: SMD = −1.23, 95% CI (−2.47, −0.01), z = −1.94, P = 0.053]; volumetric parameters (volume at which the patient first experiences a sensation to defecate and maximal tolerable volume): no significant differences between groups Urgency at 6 months CJP vs. STE RR 0.61 (95%CI 0.39-0.96) p< 0.05 Urgency after 2 years RR 0.60 (95%CI 0.33-1.11) p=0.10 No statistical difference in other functional outcomes was found ie. use of enemas, bowel medications, use of pads, incomplete defecation and stool frequency		
[26]	Meta-analysis	10 RCTs with patients with rectal cancer and curative anterior resection: colonic J pouch (CJP) vs. straight coloanal anastomosis (SCA)	CJP	SCA	Functional outcome and complications	CJP vs. SCA: anastomotic leak RR 0.36 (95% CI 0.12-1.08) Anastomotic stricture RR 2.45 (95% CI 0.79-7.57) stool frequency weighted mean difference −1.21 (95% CI: −1.92- −0.49) fecal continence OR 0.23 (95% CI: 0.08–0.69)	There is minimal difference in the functional outcome between CJP and SCA at 1 year, although the data seems to favor CJP.	1a
[27]	Systematic review	9 RCTs (n=473): SCA vs. CJP 4 RCTs (n=215): STE vs. CJP 3 RCTs (n=158): TCP vs. CJP	Different rectal reconstructive techniques (straight coloanal astomosis (SCA), colonic J pouch (CJP), side-to-end anastomosis		functional outcome (bowel function defined by outcome measures such as bowel movements per day, urgency, fecal incontinence, incomplete evacuation…) of different rectal	SCA vs. CJP: up to 18 months postop, CJP was superior to SCA in most studies regarding bowel frequency, urgency, fecal incontinence, and use of antidiarrheal medication. There were too few patients with long-term bowel function outcomes to determine if this advantage continued after 18 months postop. STE vs. CJP: no difference in bowel function outcomes TCP vs. CJP: no differences in bowel function	After LAR for rectal cancer, reconstruction with CJP leads to better bowel function and similar rates of postoperative complications when compared to SCA. STE is a compelling alternative to CJP that has similar functional outcomes in 3	1a

Referenz	Studientyp	Teilnehmer Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
			(STE)		reconstructive techniques	outcomes	small RCTs.	
[28]	RCT	149 patients with RC undergoing LAR CJP: 73 pts (but 3 received a TCP); TCP: 76 pts	LAR+TME+CJP	LAR+TME+TCP..	rate of late evacuation problems after 2 years anastomotic leak rate, perioperative morbidity and mortality	Late functional outcome data were expected to be published in 2010 Mortality: 0% Surgical complications: CJP: 19%; TCP: 18% Overall anastomotic leak rate; 8%	This trial demonstrated a comparable early outcome for TCP and CJP. This contradicts previous reports suggesting a higher leak rate after TCP.	2b
[29]	RCT	364 patients with low RC (CP-1 group: 47 pts, SA group: 49 pts, JP group: 137 pts, CP-2 group: 131 pts)	JP feasible group: JP JP not feasible group: SCA	JP feasible group: CP2 JP not feasible group: CP1	functional outcome and QOL + complications	JP feasible group: JP vs. CP-2 Total daily bowel movements after 4 months 3 vs. 4 (p=.0.03), after 12 mo 3 vs. 3 (p=0.03), after 24 mo 2 vs. 3 (p=0.007) Fecal incontinence severity index (FISI) at 4 mo 39.5 vs. 51 (p=0.001), at 12 mo 35.9 vs. 40 (p=0.18), at 24 mo 31.1 vs. 36.8 (p=0.04). Pad usage at 24 mo 53.9 vs. 70.4% (p=0.02) Clutering at 24 mo JP < CP-2 (p<0.03) Other parameters without statistical significance. J-Pouch ineligible group: CP-1 vs. SA No statitistically significant differences in bowel function parameters. QOL scores at 24 months: similar for each of the 4 groups Complication rate overall 32% (no difference between groups).	In patients undergoing a restorative resection for low rectal cancer, CJP offers significant advantages in function over SCA or CP. In patients who cannot have CJP, CP seems not to improve the bowel function of patients over that with SCA	1b
[30]	RCT	48 patients with lower RC (24 in each group)	Laparoscopic assisted CJP	Laparoscopic SCA	anorectal functional outcomes (assessed by functional questionnaires, anorectal manometry and	CJP vs. SCA during the first 3 postoperative months: stool frequency (mean ± sd: 4.0 ± 2.0 vs. 7.0 ± 2.4 times/day, p<.001); use of antidiarrheal agents (29.2% [n=7] vs. 75.0% [n=18], p=.004); and perineal irritation (45.8%[n=11]	Laparoscopic-assisted creation of a CJP achieved better short-term functional results and did not increase surgical morbidity, as compared	2b

Referenz	Studientyp	Teilnehmer Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
					volumetric study)	vs. 79.2%[n=19], p=.037).	with laparoscopic SCA.	

12.1.3.2.4. *Technik der abdominoperinealen Rektumexstirpation und Defektdeckung bei Rektumkarzinomen inkl. plastischer Deckung*

Suchstrategien

(("Rectal Neoplasms"[Mesh] AND "Surgical Procedures, Operative"[Mesh]) AND "surgery "[Subheading]) AND ((extra[All Fields] AND levator[All Fields]) OR "cylindric"[All Fields] OR "abdominoperineal resection"[All Fields] OR "abdominoperineal excision"[All Fields]) AND ("humans"[MeSH Terms] AND (Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Randomized Controlled Trial[ptyp] OR Review[ptyp]) AND ("1"[PDAT] : "2011/02/07"[PDAT]))

Plastische Deckung nach APR:
(("Rectal Neoplasms"[Mesh] AND "Reconstructive Surgical Procedures"[Mesh]) AND "Surgical Flaps"[Mesh]) AND ("humans"[MeSH Terms] AND ("1"[PDAT] : "2011/02/05"[PDAT]))

Evidenztabelle (ab der 7. Referenz: Plastische Deckung nach APR)

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[31]	Case-control study	300 patients analysed (176 extralevator APE, 124 standard APE)	Standard APE	Extralevator APE (with or without flap)	Oncological quality/outcome of the APE	Extralevator vs. standard APE tissue removed from outside the smooth muscle layer per slice: median area 2120 vs. 1259 mm²; P < 0.001) CRM involvement: 49.6 vs. 20.3%; P < 0.001 IOP: 28.2 vs 8.2%; P < 0.001	Extralevator APE with perineal dissection in the prone jack-knife position can lead to substantial reductions in CRM involvement and IOP independent of other factors.	3b
[32]	Systematic review	36 studies with heterogenous patient groups mostly with rectal cancer patients (191/385 with rectus abdominus (RAM) and 58/83 with	Reconstruction of pelvic defects after abdominoperineal excision (APE) using myocutaneous flaps		Clinical outcome following myocutaeous flap reconstruction after APE.	5 controlled studies reported improved outcomes after APE and chemoradiotherapy with RAM reconstruction and 2 controlled studies reported improved outcomes with gracilis reconstruction. In 7/300 patients with RAM reconstruction there was total flap loss. In 8/83 patients with gracilis reconstruction there was total flap loss.	Data from controlled studies support the use of myocutaneous flaps for single-stage reconstruction after APE in the presence of chemoratiotherapy.	3a

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		gracilis reconstruction) FU 3 – 67 months						
[33]	Cohort study	11 patients	APR followed by reconstruction with a biological mesh.		Postoperative complications	1 mesh had to be removed due to perineal wound infection, 1 pt developed a seroma, 1 developed recurrence (the same pt who had the mesh removed), 6 suffered from perineal pain for several weeks (5-26), 1 pt developed a fistula	The use of biological mesh as reconstruction of the pelvic floor after APR is possible and seems to be associated with few complications.	4
[34]	Case control	1,219 patients with RC, 846 AR, 373 APR Median FU: 60 months	Abdominoperineal resection (APR)	Anterior resection (AR)	CRM involvement, quality of the resection plane, survival, perforation	APR vs. AR Survival 38.5% vs 57.6%, p = .008 Positive margins 30.4% vs. 10.7%, p=.002 Perforations 13.7% vs. 2.5%, p=.001 The plane of resection lies within the sphincteric muscle, the submucosa or lumen in >1/3 of the APR cases, and in the remainder lay on the sphincteric muscles	The poor prognosis of the patients with an APR is ascribed to the resection plane of the operation leading to a high frequency of margin involvement by tumor and perforation with this current surgical technique	3b
[35]	Case control	1036 patients with RC, AR 629, APR 306, Hartmann's procedur 101	AR	APR/Hartmann's procedure	CMI	average CMI: 12.5% (range 0–33.3% between hospitals); CMI for AR: 7.5% (n = 629) compared with a CMI of 16.7% for APR (n = 306) and a CMI of 31.7% for Hartmann's procedure (n = 101); P < 0.001; CMI for patients undergoing curative surgery was 7.1% (423 AR, CMI 3.8% (n = 16); 181 APR, CMI 13.3% (n = 24); 29 Hartmann's procedure, CMI 17.2%); multivariate analysis: CMI was significantly different between APR and AR (OR 3.3, 95%CI 2.0–5.4), but less so between Hartmann's procedure and AR (OR	APR is associated with a significantly higher CMI than AR. Attention to surgical technique, with a wide perineal dissection and the use of pre-operative adjuvant therapy, may reduce CMI in patients undergoing APR."	3b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
						2.2, 95%CI 1.1-4.2)		
[36]	Cohort study	148 patients with RC and APR	APR with TME	LAR	Overall survival Local recurrence, morbidity, mortality, distant metastasis, sexual and urinary function	Survival: APR vs. LAR 80.7% versus 60.2%; p < 0.0003 Sexual function: APR vs. LAR Engagement in sex. Intercourse for male patients: 57% vs. 86%; p<0.05 Achieve orgasm: 85% vs. 88% APR: Operative mortality: 3/148 (2%); local recurrence within 5 years: 11/148 (11%); L+ (p = 0.0241) and perineural invasion (p = 0.0020) = independent risk factors for local recurrence; distant metastasis: 25/148 pts;	Low rectal cancer requiring APR seems to be a disease with more locally advanced disease and adverse pathologic features than are seen with mid-rectal cancers treatable by LAR. APR when performed in accordance with the principles of TME and ANP ensures the greatest likelihood of resecting all regional disease while preserving both sexual and urinary functions.	4
[37]	Cohort study	19 patients with rectal or anal cancer mean FU: 26 months	EAPE with unilateral right-sided gluteus maximus flap reconstruction of the pelvic floor		Physical performance, QOL local recurrence, complications	Physical performance: The timed-stands test showed that 12/19 patients performed worse than the upper limit of reference values adjusted for age and gender; the Berg balance scale: mean score of 52.8, close to the maximum score (56) of the test; the ability to sit 10 minutes was reduced in 4 patients, and 8 patients used a cushion or ring; hip mobility was normal, but 6 patients had reduced flexion strength on the right side compared with the left side. QOL: the mean calculated EQ-5D quality-of-life index was 0.71; mean pain score was 20 (scale from 0 to 100) while sitting, and only 9/19 patients were pain free. Local recurrence: 4/36 patients (11%); deep perineal wound infections: 5/19; perineal	The oncological outcome of the operation was acceptable, but functional drawbacks must be considered preoperatively in counseling the patient	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
						wound cavity and delayed healing: 5/19; urinary retention: 5/19; erectile dysfunction: 3/19.		
[38]	Cohort study	6 patients with RC + neoadjuvant RCT	EAPE + immediate reconstruction with an islanded IGAM transposition flap		Flap success Oncological outcome, complications	No flap failures or partial flap losses clear histological margins in all cases; no major wound complications, with only one superficial breakdown associated with high BMI and adhesive tape allergy, treated with dressings alone; no donor site morbidity; no post-operative hernias	The IGAM flap is a reliable and useful technique for perineal reconstruction in patients following extensive APE in the setting of pre-operative chemo-radiotherapy.	4
[39]	Cohort study	51 patients with RC and APE, 21 primary closure , 30 myocutaneous flap closure mean FU: 38 months	APE with myocutaneous flap reconstruction (VRAM/gracilis)	APE with primary closure of the perineal wound	Perineal wound complications/flap failure	No major complications following primary closure of the unirradiated perineum; major perineal wound complications requiring reoperation or debridement: 3 (14%) patients following primary closure, 5 (17%) patients with flap closure; (p = 0.65); after radiotherapy, closure with a flap reduced the length of stay from 20 to 15 days (p = 0.36).	Primary closure is suetable for patients without RCT. The use of flap closure in irradiated patients is asscociated with fewer perineal complications and a shorter hospital stay	4
[40]	Cohort study	35 patients with RC + neoadjvuant RCT and APR (10 pat. with flaps, 25 patients with direct closure)	APR + Muscle flaps	APR + primary closure	Postoperative recovery assessed by haemoglobin levels, time being bedridden, body temperature,..., complications	- no significant differences were observed between the 2 groups with regard to: postoperative blood transfusions (p = 0.2294), patients' body temperature, WBC count, length of being bedridden (p = 0.2598), and length of hospitalization (p = 0.5743), initial hemoglobin levels, in the onset of mild and moderate complications between the 2 groups (p = 1.0000 and p = 0.6614, respectively) - major complications between the 2 groups: flap group 0 vs. 10 in the nonflap group (1 perineal abscesses,1 posterior vaginal wall collapse, 6 perineal infections with wound dehiscence, 2 bacterial sepsis) (p = 0.03339):	Following APR, pelvic reconstruction with gracilis muscle flaps determines faster postoperative recovery and improvement of quality of life in the short and long run	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
						- significant differences in the late hemoglobin levels (from POD 10): higher in the flap group		
[41]	Case-control study	19 patients with anorectal cancer, 59 controls	APR + either RAM flap	APR + primary perineal closure	perineal wound complications	Perineal wound complications: 3 (15.8%) of the RAM flap patients and 26 (44.1%) of the control patients (p = .03)	Perineal closure with a RAM flap significantly decreases the incidence of perineal wound complications in patients undergoing external beam pelvic radiation and APR for anorectal neoplasia.	3b
[42]	Cohort study	25 patients with sacrectomy and reconstruction incl. 4 patients with rectal carcinoma.	Perineal reconstruction using different flaps following total sacrectomy		functional outcome determined by comparing preoperative and postoperative gait, motor strength, and sensory function of the lower extremities	21/25 patients (84.0%) were ambulatory preoperatively vs. 23/25 patients (92.0%); postoperative motor strength (5/5 scale) was abnormal in 1/8 patients with bilateral gluteal advancement flaps (12.5%), 3/10 patients with transpelvic rectus myocutaneous flaps (30.0%), and 1/3 patients with combined gluteal and posterior thigh flaps (33.3%); sensation of light touch in the lower extremities was abnormal in 2/8 patients with bilateral gluteal advancement flaps (25.0%), 4/10 patients with transpelvic rectus myocutaneous flaps (40.0%), and all 3 patients with combined gluteal and posterior thigh flaps; all patients required rehabilitation therapy before discharge	There are three reliable options for the reconstruction of large sacral wound defects: bilateral gluteal advancement flaps, transpelvic rectus myocutaneous flaps, and free flaps.	4
[43]	Case-control study	111 patients with RC or anal cancer mean FU: 3.8 years	APR + VRAM flap	APR + primary closure	Perineal wound complications	Flap vs. primary closure: incidence of perineal abscess 9% vs. 37%, p = 0.002 major perineal wound dehiscence 9% vs. 30%, p = 0.014 drainage procedures required for	VRAM flap reconstruction of irradiated APR defects reduces major perineal wound complications without increasing early abdominal wall morbidity	3b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
						perineal/pelvic fluid collections 3% vs. 25%, p = 0.003) tha		

12.1.3.2.5. *Verfahrenswahl zur Exstirpation vs Kontinenzerhalt nach neoadjuvanter Therapie abhängig von der ursprünglichen Einschätzung oder einer Reevaluation?*

Suchstrategie

(("Rectal Neoplasms"[Mesh] AND "Neoadjuvant Therapy"[Mesh]) AND ("Neoplasm Staging"[Mesh] OR "restaging"[All Fields] OR "reevaluation"[All Fields])) AND ("surgery"[Subheading] OR "Surgical Procedures, Operative"[Mesh]) AND ("humans"[MeSH Terms] AND ("1"[PDAT] : "2011/02/28"[PDAT]))

Evidenztabelle

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[44]	Cohort study	90 patients with locally advanced mid/low rectal cancer	pelvic CT, MRI, ERUS, proctoscopy) before CRT and 6—8 weeks after completing CRT	Histology	performance of CT, MRI, and ERUS in restaging patients with rectal cancer after CRT and before surgery (potential impact of restaging on the subsequent operative approach)	accuracy ypT staging (% overstaging) CT 37% (32%), MRI 34% (18%), ERUS 27% (17%) Accuracy ypN staging CT 62%, MRI 68%, EUS 65%. Accuracy CRM-Involvement CT 71%, MRI 85%	Current imaging techniques are inaccurate in restaging rectal cancer after CRT but are useful in predicting T <3 tumors, cases with negative nodes and tumor-free CRM. These findings may be of clinical relevance for planning less invasive surgery.	3b
[45]	Cohort study	122 patients with advanced lower rectal cancer + preoperative	Preoperative CRT followed by: either APR or SPP(LAR+CRA or	Histology	CMI, postoperative morbidity, local and systemic recurrence, cancer-specific survival	CRM positive rate: APR 22%, SPP 8% (p=0.037) Postoperative morbidity: APR 28%, SPP 9% (p=0.032) 5-year local recurrence rate	Our study shows that APR following preoperative CRT exhibited more adverse oncologic outcomes compared with SPP.	3b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		CRT: 50 APR, 72 SPP (53 LAR+CRA, 19 ultraLAR+CAA) Median FU 47.7 months	ultraLAR+CAA)		after APR or SPP	APR 22%, SPP 11.5% (p=0.028) 5-year cancer-specific survival rate APR 52.9%, SPP 71.1% (p=0.03)		
[46]	Cohort study	92 patients with locally advanced rectal cancer cT4a	Pre-treatment MRI + post-treatment MRI	Histology	clinical ability of MRI taken before and after neo-adjuvant treatment in locally advanced rectal cancer to predict the necessity of extension TME (ETME) and the possibility to achieve a R0 resection	R0-resection 79%, R1-resection 18%, R2-resection 3% R0-resection after CRT 85%, after RT 64% (p<0.05) Accuracy MRT-staging yT 40%, yN 51% (13% understaged, 36% overstaged)	Post treatment MRI is a poor predictor of final histology and should not be relied upon to guide the extent of surgical resection.	3b
[47]	Cohort study	49 patients with rectal cancer	Pre- and post-treatment MRI	Histology	correlation between post-CRT MRI and pathological staging	MRI-staging accuracy: 43% (43% overstaging, 14% understaging) T-stage accuracy: 45% (33% overstaging, 22% understaging) N-stage accuracy: 71%	MRI staging following CRT is poor. Over-staging occurs three times more commonly than under-staging. Over-staging is due to poor PPV of nodal assessment.	4
[48]	Cohort study	46 patients with mid/low rectal cancer	TRUS, pelvic CT, MRI 4 weeks after completing CRT	Histology	Postchemoradiotherapy performance of TRUS, pelvic CT, MRI, and endoscopic biopsies for predicting the	The sensitivity, specificity, PPV, NPV, and accuracy in predicting T status (T0 vs. T >1) were: TRUS 77%, 33%, 74%, 36%, and 64% CT 100%, 0%, 74%, not assessable, and 74% MRI 100%, 0%, 77%, not assessable, and 77%.	Current rectal cancer staging modalities after chemoradiotherapy allow good prediction of node-negative cases, none of them is able to predict a	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
					pathologic complete response	N status (N-negative vs. N-positive) TRUS 37%, 67%, 21%, 81%, and 61% CT 78%, 58%, 32%, 91%, and 62% MRI 33%, 74%, 25%, 81%, and 65%	pathologic complete response.	
[49]	Cohort study	58 patients with rectal cancer	DRE, endoscopic biopsies, ERUS, CT after completion of CRT	Histology	predictive value of the clinical response to neoadjuvant therapy on the basis of pathological results	Complete response pathologically and clinically 8.6% Partial response: clinical 48.3%, pathological 44.8 Stable disease clinical 37.9%, pathological 34.5% Progressive disease clinical 5.2%, pathological 12.1% Clinical partial response and clinical stable disease PPVs 92.8% and 90.9%, Clinical progressive disease NPV 20%.	PPVs and NPVs, in particular for partial response and stable disease, of clinical evaluation of the response to CRT were not high enough to consider clinical evaluation accurate enough to make treatment decisions	4
[50]	Cohort study	50 patients with middle and lower rectal cancer	MRI after CRT	Histology	Correlation between pathologically verified tumor stages and clinical stages predicted by MRI after CRT	accuracy in T stage 52%, overstaging 38%, understaging 10%. Accuracy N stage 68%, overstaging 24%, understaging 8%	Poor agreement between post-CRT MRI and pathologic staging was observed in both T (k = 0.017) and N (k = 0.031) stages. Most of the inaccuracy in both T and N stages was caused by overstaging.	4

12.1.3.2.6. *Was ist die Rolle der laparoskopischen Chirurgie in der Behandlung des Rektumkarzinoms?*

Suchstrategie

((((("Rectal Neoplasms"[Mesh] AND "Surgical Procedures, Operative"[Mesh]) AND ("surgery "[Subheading] OR "Colorectal Surgery"[Mesh])) AND "Laparoscopy"[Mesh]) AND "Surgical Procedures, Minimally Invasive"[Mesh]) OR (("Colorectal Neoplasms"[Mesh] AND "Laparoscopy"[Mesh]) AND ("Cost-Benefit Analysis"[Mesh] OR "Postoperative Complications"[Mesh])) AND ("humans"[MeSH Terms] AND (Meta-Analysis[ptyp] OR Randomized Controlled Trial[ptyp] OR Review[ptyp]) AND ("2005/01/01"[PDAT] : "2010/11/05"[PDAT]))

Evidenztabelle

Siehe 14.1.3.2.2.5.

12.1.3.2.7. *Wie ist der Stellenwert der laparoskopischen Chirurgie in der Behandlung des Kolonkarzinoms?*

Suchstrategie

(laparoscopic OR laparoscopy OR minimal* invasive OR robot* OR key hole* OR notes OR SILS OR hand assist*) and (colonic OR colon OR colorectal OR colo-rectal OR intestin* OR bowel) and (cancer OR carcinoma OR neoplasm* OR malign*); Limits German, English, human, clinical trial, randomized controlled trial, metaanalysis, controlled clinical trial, review, multicenter study

Evidenztabelle

Die identifizierten Metaanalysen beider Suchen zur Laparoskopie enthalten überwiegend Angaben zum kolorektalen Karzinom, ohne Unterscheidung zwischen Kolon und Rektum. Dies war zum Teil auch bei den Primärstudien der Fall. Aus diesem Grund ist die Literatur in einer gemeinsamen Evidenztabelle dargestellt.

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[51]	Meta-Analysis	3 Studies (2147 patients with colon cancer)	Laparoscopic resection	Open resection	recurrence rates	Lap vs. open surgery: Recurrence rate 19.3% vs. 20.0%, p=0.71 overall mortality 24.9% vs. 26.4%	laparoscopic surgery was as efficacious and safe as open surgery for colon cancer.	1a
[52]	Systematic review	48 studies (4224 patients	Laparoscopic or laparoscopic-	Open TME	3-year and 5-year disease-free survival	As only one RCT described primary outcome, 3-year and 5-year disease-free survival rates,	Based on evidence mainly from non-randomized	1a

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		with rectal cancer)	assisted Total Mesorectal Excision		rates	no meta-analyses could be performed: Only one RCT described the long-term outcome of sigmoid cancer and upper rectal cancer and found a 5 years disease-free survival rate of 75.3 % in the laparoscopic group and 78.3 % in the open group (p=0.45). 17 studies reported on long-term survival data of LTME: Three papers showed a range of 67 -88% of overall survival rate of 5 years. Two level 2b studies reported a 5-year disease-free survival rate ranging 63-75 %. The only level 2b study containing data for APR and LAR separately, found a 2-year disease-free survival rate of 62.4 and 54.8 % respectively.	studies, LTME appears to have clinically measurable short-term advantages in patients with primary resectable rectal cancer. The long-term impact on oncological endpoints awaits the findings from large on-going randomized trials	
[53]	Meta-Analysis	10 RCTs (3830 patients with CRC)	Laparoscopic resection	Open resection	CRC-related survival and recurrence rates	Laparascopic vs. open resection: CRC-related deaths: RR 0.80 (0.62-1.04) Recurrences: RR 0.90 (0.73-1.10)	Laparoscopic surgery for CRC appears to be an oncologically sound option for treatment of CRC and may offer distinct advantages.over traditional approaches	1a
[54]	Systematic review	12 trials (3346 patients with CRC)	laparoscopically-assisted surgery	open surgery	Evaluation of long-term outcome	Rates of recurrence at the site of the primary tumor: colon cancer: 4 RCT, 938 pts, 5.2% vs 5.6%; OR (fixed) 0.84 (95% CI 0.47 to 1.52)(p= 0.57) rectal cancer: 4 RCT, 714 pts, 7.2% vs 7.7%; OR (fixed) 0.81 (95% CI 0.45 to 1.43) (p = 0.46). No differences in the occurrence of port-ite/wound recurrences were observed (P=0.16). Similar Cancer-related mortality after laparoscopic	Laparoscopic resection of colon carcinoma is associated with a long term outcome no different from, that of open colectomy. Laparoscopic suergy for cancer of the upper rectum is feasible, but more randomised trials need to be conducted to assess long term outcome	1a

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
						surgery compared to open surgery: colon cancer: 5 RCT, 1575 pts, 14.6% vs 16.4%; OR (fixed) 0.80 (95% CI 0.61 to 1.06) (p=0.15) rectal cancer: 3 RCT, 578 pts, 9.2% vs 10.0%; OR (fixed) 0.66 (95% CI 0.37 to 1.19) (p=0.16).		
[55]	Meta-Analysis	10 RCTs (2474 patients with CRC)	Laparoscopic resection	Open resection	Recurrence rates (overall, local, distant metastases, port- or wound-site)	Laparoscopic vs. open resection: Local recurrence (OR 0.80, 95% CI 0.50-1.29, P = 0.36) Distant metastases (OR 0.90, 95% CI 0.62-1.29, P = 0.56) Port or wound-site recurrence (OR 1.04, 95% CI 0.18-6.03, P=0.97)	Recurrence rates for patients with CRC treated by laparascopic surgery do not differ from those for open surgery.	1a
[56]	Meta-Analysis	3 RCTs (189 patients with CRC)	HALS	Conventional laparoscopic resection	duration of surgery, conversion rate	There was a trend towards decreased operative time -21.99 mins [95% CI: -46.39, 2.41] with hand-assisted surgery compared to conventional laparoscopic surgery Conversion: odds ratio 0.32 [95% CI: 0.11, 0.90]. Complication rates were comparable.	Despite the limited number of trials performed, meta-analysis demonstrated a statistically significant decrease in conversion rates among the hand assisted group.	1a
[57]	Meta-Analysis	Systematic review with 12 RCTs with CRC	LS or laparoscopically assisted surgery	Open surgery	To compare safety and efficacy of LS vs. OS	Time required to complete LS was significantly longer (0·5–1·0 h more). Compared with OS, LS reduced blood loss and pain, and resulted in a faster return of bowel function and earlier resumption of normal diet. Hospital stay was up to 2 days shorter after	LS takes longer than OS but offers several short-term benefits. However, complication rates are similar for both procedures and no differences were found in long-term outcomes	1a

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
						LS. No significant differences between the techniques were noted in the incidence of complications or postoperative mortality. No significant differences were found between the two procedures in terms of overall mortality, cancer-related mortality or disease recurrence.		
[58]	Meta-Analysis	25 RCTs with CRC	Laparoscopic resection	Open resection	Possible benefits of LAP in the short-term posteroperative period	Methodological quality of most trials was only moderate. Operative time was longer in LAP, but intraoperative blood loss was less. Intensity of postoperative pain and duration of postoperative ileus was shorter after LAP. Total morbidity and (local) morbidity was decreased in the LAP group. Postoperative hospital stay was less in LAP patients. General morbidity and mortality was not different.	Under traditional perioperative treatment, laparascopic colonic resections show clinically relevant advantages in selected patients.	1a
[59]	RCT	268 patients with planned left colonic resection (134 lap, 134 open) median FU: 73 months	Laparoscopic resection	Open resection	cost-benefit analysis, QoL, long term morbidity and 5 year survival	Open vs LAP: Long-term morbidity rate: 11.9% vs. 7.5% (p = 0·413). 5-year survival rate: 66% vs. 72% (p = 0·321). QoL was significantly improved in the laparoscopic group 6 months after surgery, but no difference was found subsequently. Cost-benefit analysis: additional cost of 351$ per patient randomly allocated to the laparoscopic group.	Laparoscopic left colonic resection resulted in an earlier recovery after surgery. As cost-benefit analysis and long-term follow-up showed similar results, the laparoscopic approach should be preferred to open surgery.	1b
[60]	RCT	1076 patients with colon cancer (534 lap,	Laparoscopic resection	Open resection	disease free survival at 3 years	Combined 3-year disease-free survival for all stages 74·2% (95% CI 70·4–78·0) in the laparoscopic group and 76·2% (72·6–79·8) in	The results justify implementation of laparoscopic surgery for	1b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		542 open) Median FU: 53 months				the open surgery group (p=0·70 by log-rank test); the difference in disease-free survival after 3 years was 2·0% (95% CI −3·2 to 7·2). The hazard ratio (HR) for disease-free survival (open vs laparoscopic surgery) was 0·92 (95% CI 0·74–1·15).	colon cancer into daily practice	
[61]	RCT	852 patients with colon cancer (435 lap, 328 open) Median FU: 7 years	Laparoscopic resection	Open resection	Recurrence rates Secondary overall survival and DFS	Lap vs. open surgery Recurrence rate 19.4 vs. 21.8% (p=0.25) OS 76.4 vs. 74.6% (p=0.93) DFS 69.2 vs. 68.4% (p=0.94)	Laparoscopic colectemy for curable colon cancer is not inferior to open surgery.	1b
[62]	RCT	794 patients (526 laparoscopic, 268 open), 413 colon cancer, 381 rectal cancer median FU: 56.3 months	Laparoscopic resection	Open resection	overall survival, disease-free survival local and distant recurrence	Open vs. laparoscopic surgery Overall survival Overall 58.1% vs. 57.9%, p=0.848 Colon cancer 62.7 vs. 55.7%, p= 0.253 Rectal cancer 52.9 vs. 60.3%, p=0.132 DFS Overall 58.6 vs. 55.3%, p=0.483 Colon cancer 64.0 vs. 57.6%, p=0.399 Rectal cancer 52.1 vs. 53.2%, p=0.953 Local recurrence rate Overall 8.7 vs. 10.8% p=0.594 Rectal cancer with anterior resection 7.6 vs. 9.4%, p=0.740 Distant recurrence rate 20.6 vs. 21.0%, p=0.820	The 5-year analyses confirm the oncological safety of laparoscopic surgery for both colonic and rectal cancer.	1b
[63]	RCT	340 patients with mid or low rectal cancer who had	Laparoscopic resection	open resection	Involvement of the circumferentional resection margin Macroscopic quality	Lap vs. open group Estimated blood loss 200ml vs 217.5 ml; p=0.006) surgery time 244.9 min vs 197.0 min;	Laparoscopic surgery after preoperative chemoradiotherapy for mid or low rectal cancer is safe	1b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		undergone preoperative neoadjuvant CRTX (170 lap, 170 open)			of the total mesorectal excision specimen Number of harvested lymph nodes Recovery of bowel function Preoperative morbidity Postoperative pain Quality of life	p<0.0001). No difference for: Involvement of the circumferential resection margin, macroscopic quality of the total mesorectal excision specimen, number of harvested lymph nodes, and preoperative morbidity. lap group showed earlier recovery of bowel function than in the open surgery group (median time to pass first flatus 38.5 h vs 60.0 h; p<0.0001). The total amount of morphine used was less in the lap group than in the open surgery group (median 107.2 mg vs 156.9 mg; p<0.0001).	and has short-term benefits compared with open surgery; the quality of oncological resection was equivalent.	
[64]	RCT	219 patients with colon cancer (111 lap, 108 open) Median FU: 95 months	Laparoscopic resection	Open resection	Cancer-related survival Secondary OS, recurrence rate	Lap vs. open resection Cancer related mortality 16 vs. 27% (p = 0.07, NS) Overall mortality 36% vs. 49% (p = 0.06, NS) Recurrence rate 18 vs. 28% (p=0.07)	laparoscopy-assited colectomy (LAC) is more effective than open colectomy in the treatment of colon cancer	1b
[65]	RCT	269 patients with stage II/III left sides colon cancer (135 lap, 134 open) Median FU: 40 months	Laparoscopic resection	Open resection	Oncological outcome	Lap vs. open surgery cumulative recurrence rate Stage II 13.2% versus 17.2% Stage III 20.9% vs. 25.7% Number of dissected lymph nodes 15.6 vs. 16.0, p=0.489	The estimated cumulative recurrence rate for the surgery of (...) leftsided colon cancers is the same between laparoscopic and open methods	1b
[66]*	RCT	186 patients with rectal cancer median FU: 16.3 months	Hand-assisted laparoscopic surgery (HALS)	Open resection	procedure time, blood loss, post-operative pain, time to oral intake, return of bowel function, length of	Open vs. HALS Procedure time 140 vs. 161 min (p< 0.001) Duration of patient-controlled post-surgical analgesia 3 vs. 2 days (p<0.001) Blood loss 380 vs. 310 ml (p<0.001) Time to first passing flatus 4 vs. 3 days	HALS was safe and effective and may offer several potential advantages to patients in their post-operative recovery	1b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
					hospital stay, morbidity and functional recovery	(p<0.001) Postoperative hospital stay 15 vs 12 days (p<0.001)		
[67]	RCT	204 patients with low and mid rectal cancer (101 lap, 103 open) median FU: over 30 months	Laparoscopic surgery	Open surgery	hospital stay Complication rates number of isolated lymph nodes CMI involvement Secondary endpoints: local recurrence and survival	Lap vs. open surgery: Blood loss 128 vs. 234 ml (<0.001) Operating time 194 vs. 173 min (p=0.020) Time to oral diet 2.8 vs. 3.6 days (p=198) Hospital stay 8.2 vs. 9.9 days (0.106) Complications 33.7 vs. 33% Isolated lymph nodes 13·63 vs 11·57 (p = 0·026) CRM involvement 4.0 vs. 2.9 (p=0.422) Local recurrence 4.8 vs. 5.3% DSF 84.8 vs. 81.0% OS 72.1 vs. 75.3%	Laparoscopic surgery for rectal cancer has a similar complication rate to open surgery, with less blood loss, rapid intestinal recovery, shorter hospital stay, and no compromise of oncological outcomes	1b
[68]	RCT	472 patients with colon or upper rectum (250 lap, 222 open) Median FU: 40 months (LS), 58 months (OS)	Laparoscopic surgery	Open surgery	overall, general and surgical morbidity; mortality	Laparascopic vs. open surgery morbidity 25.2 versus 23.9 % (p=ns) mortality 1.2 versus 0.9 % (p=ns) Postoperative hospital stay median (range) 10 (1–123) versus 12 (4–109) days; P = 0.032).	Laparoscopic resection of colorectal cancer is associated with increased operating time but does not decrease morbidity even in a moderate-risk population	1b
[69]*	RCT	99 patients with low rectal cancer (51 lap, 48 open) median FU: 90 months	Laparoscopic surgery	Open surgery	Postoperative recovery	Lap. vs. open surgery Operative time 214 vs. 164 min (p<0.001) Postoperative analgesic requirements 6.0 vs. 11.4 injections (p=0.007) Pain score on postop. Day 1 4.5 vs. 4.9 (p=0.41) Time first passing flatus 3.1 vs. 4.6 days (p<0.001) Time to first bowel motion 4.3 vs. 6.3 days	Laparoscopic-assisted APR improves postoperative recovery and seemingly does not jeopardize survival when compared with open surgery for low rectal cancer.	1b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
						(p<0.001) Direct cost 9588 vs. 7517 USD OS 75.2 vs. 76.5% DFS 78.1 vs. 73.6%		
[70]	RCT	153 patients with upper rectal cancer (76 lap, 77 open) median FU: 112.5 months (LS), 108.8 (OS)	Laparoscopic surgery	Open surgery	Long-term morbidity	Lap vs. open surgery Long-term morbidity 10.8 vs. 25.7% Total number op patients requiring operation for long term morbidity 8.1 vs. 9.5% Local recurrence after 10 y. 7.1 vs 4.9% (P=0.677) Distant recurrence rate after 10 y. 12.3 vs. 18.1% (P=0.366) DFS at 10 y. 82.9 vs. 80.4% (p=0.698) OS at 10 y. 63.9 vs. 55.1% (P=0.303)	Laparoscopic-assisted anterior resection for upper rectal cancer is associated with fewer long-term complications and similar ten-year oncologic outcomes when compared with open surgery	1b
[71]	RCT	74 patients with middle and low rectal cancer (34 lap. 39 open)	laparoscopic TME	open TME	number of lymph nodes retrieved	total number of retrieved lymph nodes: lap vs. open 19.2 (5–45) vs. 19.2 (8–41) (p = 0.2)	Laparoscopic resection of the rectum can achieve similar lymph node clearance to the open approach.	1b

12.1.3.2.8. *Sollen simultane Lebermetastasen synchron oder metachron reseziert werden?*

Suchstrategie

synchronous[All Fields] AND metachronous[All Fields] AND ("liver"[MeSH Terms] OR "liver"[All Fields]) AND ("neoplasm metastasis"[MeSH Terms] OR ("neoplasm"[All Fields] AND "metastasis"[All Fields]) OR "neoplasm metastasis"[All Fields] OR "metastases"[All Fields]) AND ("surgery"[Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "surgery"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields])

Evidenztabelle

Referenz	Studientyp	Teilnehme / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[72]	Systematic Review	21 studies of patients with CRC and synchronous or metachronus liver metastases 16 studies of patients with CRC and synchronous liver metastases	Resection of liver metastases Simultaneous vs. delayed resection of heaptic metastases with primary tumor		differences between the outcomes and management of metachronous and synchronous hepatic metastases	Most studies reported that synchronous lesions were associated with poorer survival rates (8% to 16% reduction over 5 years). Sixteen articles comparing combined vs staged resections for synchronous tumour showed comparable morbidity and mortality.	Combined resection of primary tumour and synchronous metastases is a viable option. However, the decision to offer such an operation is still not clear and depends on careful patient selection and institutional experience.	3a
[73]	Cohort study	108 patients with CRC and resection of hepatic metastases (67 synchronous (SH), 41 metachronous (MH)) mean FU 31 months	Synchronous or metachronous resection of synchronous heapatic metastases with primary CRC		Prognostic Factors in cases of synchronous liver metastases from CRC.	OS 1-, 3-, and 5- years Whole group: 85.5%, 51.4%, 41.6% Synchronous group 49.5%, 39%, 26.7% Metachronous group 58.1%, 49.1%, 39.2% Multivariate prognostic factor for SH: tumor-free margin (≥ 5mm vs. < 5mm): RR 5.033, p=0.0002 Sex, T-stage, LN0 vs. LN+ and Number of lesions (solitary vs. multiple) no significant prognostic factors. OS 1-, 3-, and 5- years of SH who had both primary tumor and metastases resected simultaneously: 81.8%, 37.8% and 37.8% who had metachronous resection of hepatic meatases: 71.4%, 57.1% and 57.1% (p=ns)	Patients with synchronous liver metastases from colorectal cancer should undergo radical resection of the primary lesion and simultaneous hepatectomy with an adequate tumor-free margin as a standard surgical course.	4
[74]	Cohort study	74 patients with CRC and synchronous hepatic metastases	Simultaneous resection with colorectal surgery	delayed resection of liver metastases	Disease-free and long-term survival rates, time to hepatic recurrence, hepatic disease free	Disease-free survival rate and overall survival rates of all patients were 38.7 and 67.8% at 3 years, 33.7 and 57.6% at 5 years, and 33.7 and 55.2% at 10 years, respectively In the delayed and simultaneous groups, the	Delayed resection of synchronous liver metastases may be useful to reduce the risk of rapid recurrence in the remnant	3b

Referenz	Studientyp	Teilnehme / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		Median FU: 31 months			survival rates	median time to hepatic recurrence after resection was 16.0 and 11.5 months, respectively. Hepatic disease free survival rates of the delayed, and simultaneous groups at 5 years, 59.5 vs 43.2% (p=0.0049)	liver.	
[75]	Cohort study	137 patients with CRC and synchronous hepatic metastases (116 simultaneous, 21 delayed)	Simultaneous resection with colorectal surgery	delayed resection of liver metastases	Hepatic recurrence within 12/ 24 months, hepatic disease-free survival, hepatic recurrence	Hepatic recurrence within 12 months and 24 months: 48% and 61 % of patients with simultaneous resection. Hepatic disease-free survival was higher for the delayed vs the simultaneous group (p=0.0028) Multivariate analysis of predictive factors for hepatic recurrence: synchronous vs. delayed 4.74 (1.72-13.1) p=0.003	Delayed hepatic resection may be a useful approach that allows the detection of occult metastases in synchronous CRLM and may reduce rapid remnant liver recurrence after hepatic resection for synchronous CRLM.	3b
[76]	Cohort study	42 patients with CRC and resection of hepatic metastases (Synchronous n=9, metachronous n=33) Median FU: 40±12.87 months	simultaneous or delayed resection of hepatic metastases with primary tumor		Early postoperative morbidity and mortality rates, survival rates	Early postoperative morbidity and mortality rates: 7.14% and 0%, respectively. Median survival: 56 months, 3-year survival rate: 71.30%. Recurrences after liver resection 11/42 patients (26%). Multivariate analysis of risk of death: liver metastases size: > 4cm HR: 5.89, p=0.001, >4 metastases HR: 2.18, p=.082.	Surgical resection if one of the most important treatments associated with long-term cure in patients with liver metastases from CRC.	4
[77]	Cohort study	3957 patients ≥ 65 years with CRC and liver resections (32% simultaneous,	Resection of liver metastases		survival after hepatic resection	Crude 30-day and 90-day mortality rates: 4% and 8.2%. 5-year survival rate 25.5%. Associated with worse 90-day mortality: advancing age (hazards ratio [HR], 1.83; 95% CI, 1.32-2.53 for age >80 years vs ages 65-69	Simultaneous approach is not generally recommended. Especially not for patients of advanced age, with co-	3b

Referenz	Studientyp	Teilnehme / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		68% metachronous)				years), comorbid disease (HR, 1.40; 95% CI, 1.06-1.85 for Charlson >5 vs Charlson 0), and synchronous colon/hepatic resection (HR, 2.46; 95% CI, 1.89-3.20 for synchronous vs metachronous resection). Long-term mortality was associated with age (HR, 1.36; 95% CI, 1.18-1.56), comorbid disease (HR, 1.51; 95% CI, 1.36-1.69), and synchronous colon/hepatic resection (HR, 1.37; 95% CI, 1.24-1.51 for synchronous vs metachronous resection).	morbidities and need for extended resection.	
[78]	Cohort study	35 patients with non-obstructing CRC and advanced synchronous liver metastases	Chemotherapy – liver resection – resection of primary – completion of chemotherapy courses		Feasibility and safety of the reversed approach. Long-term survival	overall actuarial survival rates were 91, 82, 54, 41 and 30% at 1, 2, 3, 4 and 5 years from start of the treatment. The median survival was 44 months	High-impact chemotherapy followed by resection of liver metastases before removal of the primary tumor is a feasible and safe approach with an appealing rationale.	4

12.1.3.2.9. *Wie ist das Vorgehen bei ausgedehnter Fernmetastasierung und asymptomatischem Primärtumor?*

Suchstrategie

#1 colorectal

#2 colonic

#3 sigmoid

#4 rectal

#5 #1 or #2 or #3 or #4

#6 neoplasms

#7 tumor

#8 carcinoma

#9 #6 or #7 or #8

#10 #5 and #9

#11 metastases

#12 metastatic* (Title/Abstract)

#13 #11 or #12

#14 primary

#15 primaries

#16 primary* (Title/Abstract)

#17 #14 or #15 or #16

#18 #9 and #17

#19 no surgery

#20 leave

#21 #19 or #20

#22 #18 and #21

#23 #10 and #13

#24 #22 and #23

#25 #24 Limits: Humans, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Controlled Clinical Trial, English, German, published in the last 10 years

Zusätzliche Einschlusskriterien: keine primäre Operation des Primärtumors, keine Obstruktion, Chemotherapie

Zusätzliche Ausschlusskriterien: symptomatische Patienten, Operation des Primärtumors, keine Chemotherapie

Evidenztabelle

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[79]	Meta-Analysis	8 retrospective non-randomised studies (1062 patients, 725 resection group (RG), 337 chemotherapy group (CG))	Chemotherapy	Resection of primary tumor	survival after diagnosis of stage IV colorectal cancer; response to chemotherapy resulting in shrinkage of metastatic disease amendable to curative surgery; postoperative morbidity and mortality; complications from the intact primary or recurrent disease	Median Survival: 14 - 23 months (RG), 6 - 22 months (CG); estimated standardized difference 0.55, 95% CI, 0.29, 0.82; p<0.001. Curative resection rate after CT 1.2 – 22%, Curative resection in RG 1.8 – 18.8% p=.0662 Postoperative morbidity after surgery: 23% (95% CI, 18.5%, 28.1%) of patients. complication from the primary tumor: CG was 7.3 times more likely to have a complication (95% CI, 1.7, 34.4; p = 0.008).	Asymptomatic or minimally symptomatic patients with stage IV colorectal cancer are likely to benefit from surgical resection of their primary tumor	3a
[80]	Cohort study	37 patients with stage IV CRC and asymptomatic primary tumor	Chemotherapy, urgent surgery if required.		Identify the percentage of patients requiring urgent operative interventions for symptoms related to the primary tumour	8% patients subsequently developed acute obstruction and thus needed urgent surgery whilst being treated	It is acceptable to treat such patients in an expectant manner. It is not possible to predict those patients, likely to require surgical intervention.	4
[81]	Cohort study	233 patients with stage IV CRC and asymptomatic primary tumor	Chemotherapy, urgent surgery, stenting, radiotherapy if required		incidence of primary tumor–related complications, which required operative or nonoperative intervention	217 (93%) never required surgical palliation of their primary tumor. 7% required emergent surgery for primary tumor obstruction or perforation, 4% required nonoperative intervention (ie, stent or radiotherapy), and 89% never required any direct symptomatic management for their intact primary tumor.	The finding supports (…) nonoperative initial management of the asymptomatic primary tumor in patients with synchronous stage IV colorectal cancer.	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[82]	Cohort study	24 patients with stage IV CRC and minimally symptomatic primary tumours	Chemotherapy with 5-FU, surgery, stenting		Rate of primary tumour-specific complications, survival	3 (12%) patients developed progressive incomplete colonic obstruction. One patient (4%) underwent sigmoid colectomy, two patients (8%) underwent stenting without surgery. For the whole cohort median survival was 10.3 (6-18) months	Administration of systemic chemotherapy and symptom-directed intervention for the primary tumour is a safe and effective approach.	4
[83]	Cohort study	227 patients (144 resection group (RG), 83 chemotherapy group (CG))	primary tumor resection plus chemotherapy	first-line chemotherapy	incidence of major intestinal complications in asymptomatic patients, survival	Incidence of major intestinal complications: 20.2% RG, 20.5% CG incidences of intestinal obstruction, peritonitis, fistula, and intestinal hemorrhage : CG: 14.6%, 0%, 0.7%, and 4.8% RG: 15.2%, 1.2%, 0%, and 3.5% OS: RG 22.0 mo, CG 14.0 mo (p=0.076).	In asymptomatic patients with unresectable stage IV CRC, first-line chemotherapy may be considered safe, with no increased risk of major intestinal complications compared with primary tumor resection plus chemotherapy.	4

12.1.3.2.9.1. Behandlung der Peritonealkarzinose → HIPEC und Peritonektomie: Indikation und Technik

Suchstrategie

((("Rectal Neoplasms"[Mesh] OR "Colorectal Neoplasms"[Mesh]) AND "Peritoneal Neoplasms"[Mesh]) AND ("Chemotherapy, Adjuvant"[Mesh] OR "hyperthermic intraperitoneal chemotherapy"[All Fields] OR "HIPEC"[All Fields] OR "cytoreductive surgery"[All Fields]) AND ("humans"[MeSH Terms] AND ("1"[PDAT] : "2011/02/16"[PDAT]))

Evidenztabelle

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[84]	Systematic review	25 studies (1 RCT and 24 observational case series)	CRS + PIC		Prognostic factors for survival; patient selection criteria (preoperative assessment etc.)	contrast-enhanced CT, MRI, PET, and laparoscopy can be utilized in the preoperative evaluation process to identify potential surgical candidates; patients with good performance status, low volume of peritoneal disease (assessed by PCI or other scores), and absence of extra-abdominal metastases are more likely to benefit from CRS + PIC	Quantitative assessment of the extent of disease is now possible and should be performed at the time of primary cancer operation. Careful selection of patients to identify surgical candidates with favorable prognostic indicators is important.	2a
[85]	Meta-Analysis	47 studies: 2 RCTs, 2 controlled observational studies, 3 multi-institutional studies, and 40 case-series	CRS + PIC (HIPEC or EPIC)	palliative approach (surgery and systemic chemotherapy)	overall survival, defined as time from the surgical procedure to the last follow-up or death	2 controlled studies: All cause of death within 3 years CRS + HIPEC vs. control Survival (95%CI) 0.47 (0.32-0.69) (p<0.00001)) CRS + EPEC vs. control survival (95%CI) 0.76 (0.43-1.34) (p=0.35)	The meta-analysis showed that combined therapy involving CRS and PIC had a statistically significant survival benefit over control groups.	2a
[84]	Systematic review	25 studies (1 RCT and 24 observational case series)	CRS + PIC		Prognostic factors for survival; patient selection criteria (preoperative assessment etc.)	contrast-enhanced CT, MRI, PET, and laparoscopy can be utilized in the preoperative evaluation process to identify potential surgical candidates; patients with good performance status, low volume of peritoneal disease (assessed by PCI or other scores), and absence of extra-abdominal metastases are more likely to benefit from CRS + PIC	Quantitative assessment of the extent of disease is now possible and should be performed at the time of primary cancer operation. Careful selection of patients to identify surgical candidates with favorable prognostic indicators is important.	2a
[86]	Systematic review	14 studies (1 complete and 1 incomplete RCT, 1 comparative study, 1 multi-	CRS + PIC (many variations)		survival	Median survival varied from 13 to 29 months, and 5-year survival rates ranged from 11% to 19%. Patients who received complete cytoreduction benefited most, with median survival varying from 28 to 60	The current literature suggests that CRS + PIC for patients with CRPC is associated with an improved survival when viewed against the prognosis	2a

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		institutional registry study, and 10 case-series studies)				months and 5-year survival ranging from 22% to 49%.	associated with treatment by systemic chemotherapy.	
[87]	Cohort study	368 patients with colon (341) or rectal (27) cancer and peritoneal carcinomatosis mean FU: 60.3 for colon cancer pts., 59.4 for rectal cancer pts	Surgery + HIPEC/EPIC		survival	5-year overall survival rates: colon (29.7%), rectum (37.9%) Multivariate survival analysis of prognostic factors: RR 95% CI Peritoneal index 1.049 (1.027-1.072) (p < 0.0001), Adjuvant chemotherapy 0.599 (0.434-0.828) (p=0.002) N+ 1.568 (1.13-2.28 (p = 0.001) Origin Colon 1.00, Rectum 1.147 (0.592-2.224)	CRS+HIPEC yields satisfying and similar survival results in the treatment of PC from colon and rectum. […] When feasible, this combined approach should become the gold standard treatment of PC	3b
[88]	RCT	35 patients with CRC and peritoneal carcinomatosis (16 in the EPIC group, 19 in the Standard group)	CRS + EPIC + adjuvant chemotherapy	CRS + adjuvant chemotherapy	survival	Overall survival rates at 2 years: 60% in both groups.	Complete surgical excision of CRPC (when feasible) associated with chemotherapy, whatever the administration route, resulted in a 60% 2-year survival rate	2b
[89]	Case-control study	48 patients with CRC and PC each group median f/u: 95.7 months in the standard group vs 63 months in the HIPEC group	neoadjuvant chemo, CRS and HIPEC	standard chemotherapy +/- palliative surgery	Long-term survival	2-year and 5-year overall survival rates: 81% and 51% for the HIPEC group, respectively, 65% and 13% for the standard group, respectively. Median survival: 23.9 months in the standard group versus 62.7 months in the HIPEC group (p < .05)	Patients with isolated, resectable PC have a median survival of 24 months with modern chemotherapies, but only CRS + HIPEC is able to prolong median survival to 63 months, with a 5-year survival rate of 51%.	3b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[90]	Cohort study	523 patients with CRC and PC Median FU 45 months	CRS + HIPEC (443 pts) or EPIC (84 pts) or both (9 pts)		Survival, Morbidity and mortality	overall 1-year, 3-year, and 5-year survival (95%CI): 81% (77-85%), 41% (36-47%), and 27% (21-33%). Disease-free survival (95%CI): 47% (43-52%), 15% (11-19%), and 10% (6-14%), respectively Median survival: 30.1 months. Multivariate analysis, Hazard ratio (95%CI): PCI 1.052 (1.029-1.076) Completeness of surgery 1.398 (0.970-2.014) N+ 1.534 (1.058-2.224) adjuvant chemotherapy 0.578 (0.407-0.820) Morbidity: 31% (11% underwent reoperation); mortality: 3.3%	This combined treatment approach against PC achieved low postoperative morbidity and mortality, and it provided good long-term survival in patients with PCI <20.	4
[91]	Case-control study	115 patients with CRC and peritoneal carcinomatosis (CRS+HIPEC group: 67; control group: 38)	systemic chemotherapy, CRS+HIPEC	systemic chemotherapy,	survival measured from the diagnosis of peritoneal carcinomatosis to the date of last follow-up or death	Median survival CRS+HIPEC vs. CTX (34.7 months vs 16.8 months; P<.001); Multivariate Cox proportional hazard regression model for survival HR (95%CI): CS-HIPEC vs. CTX 0.421 (0.195-0.907) p = 0.273 rectum vs. colon 2.237 (0.971-5.154) p=0.588 Liver lesion 2.133 (1.049-4.341) p = 0.0366 Biological agents 0.776 (0.392-1.536) p=0.4672 Oxaliplatin 0.945 (0.496-1.798) p= .8624 Age 1.008 (0.981-1035) p= 0.5825 Carcinomatosis at initial presentation 0.607 (0.314-1.174) p=0.1379	Cytoreductive surgery combined with HIPEC may be associated with survival benefit in selected patients with peritoneal carcinomatosis from CRC.	3b
[92]	Cohort study	1290 patients with peritoneal carcinomatosis from nonovarian	HIPEC after CRS or EPIC or both		Survival	Overall 3-year and 5-year survival rates: 41%, and 26%, respectively; median survival 30 months; prognostic factors of survival – Multivariate analysis of survival RR (95%CI)	A therapeutic approach that combined cytoreductive surgery with PIC was able to achieve long-term survival in a	3b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		origin incl. CRC 523				PCI (per point increase) 1.043 (1.027-1.058) p< 0.0001) Completeness of surgery 1.460 (1.192-1.787) p = 0.0003 Pos. lymph nodes 1.366 (1.060-1.761) p=0.0160	selected group of patients who had PC of nonovarian origin and had acceptable morbidity and mortality.	
[93]	Cohort study	506 patients with CRC and peritoneal carcinomatosis median follow-up 53 months	CRS + PIC (HIPEC and/or EPIC)		Survival	Morbidity rate: 22.9%, Mortality rate: 4% Overall median survival: 19.2 months. Median survival in patients with complete CRS vs.patients in whom complete CRS was not possible 32.4 months vs. 8.4 months (P < .001). Multivariate survival analysis Cox, p: complete cytoreduction 0.71, <0.0001 treatment with second procedure -1.10, <0.001 carcinomatosis extent 0.51, <0.001 LN involvement 0.23, 0.002 adjuvant CTX -0.26, 0.04 Treatment with IPCH -0.33, 0.07 treatment with EPIC -0.22, 0.17	The therapeutic approach combining CRS with PIC achieved long-term survival in a selected group of patients with CRPC with acceptable morbidity and mortality. The complete cytoreductive surgery was the most important prognostic indicator.	3b
[94]	Case-control study	36 patients with CRC and peritoneal metastases (18 in intervention group, 18 in control group)	CRS + EPIC	Chemotherapy	Survival	Median survival: EPIC vs. CTX 32 months (95%CI 22.2–62.6 months) vs. 14 months (95% CI 5.6–24.9 months) (p=0.01) 2 and 5 years survival: 60 and 28% vs. 10 and 5% Survival of patients who were considered macroscopically tumour free after CRS 34.5 months, 95% CI 28.7–75.7) vs. those who did not undergo macroscopically radical surgery 10 months, 95% CI -15.7 to 70.0, (p=0.02)	a survival benefit can be achieved with CRS followed by repeated courses of EPIC. A complete remission of the disease is possible for an extended period of time.	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[95]	Cohort study	121 patients	CRS + HIPEC		Survival	5 year overall survival and resection status: 36% for R0, 14% for R1, 5% for R2a, 0% for R2 b or c; independent prognostic factors of survival: resection status (the most important factor), bowel obstruction, malignant ascites	Outcomes for patients with CRPC optimally treated with CRS and HIPEC resulted in up to a quarter of patients achieving long-term survival	4
[96]	RCT	105 patients with CRC and peritoneal carcinomatosis (51 standard group, 54 experimental group) Median FU 21.6 months	CRS + HIPEC + systemic chemotherapy (same regimens as for the standard group)	5-FU + leucovorin weekly for 26 weeks or irinotecan if they had already been treated with 5-FU; palliative surgery if needed	survival, measured as time from randomization to death from any cause	Risk of dying CRS + HIPEC vs. control HR, 0.55; 95% CI, 0.32 to 0.95; log-rank (p = .032). Median survival HIPEC vs. control 22.4 months vs. 12.6 months (p = .032). Significant prognostic factors: number of involved abdominal regions (median survival patients with 0-5 regions involved vs. 6-7 regions > 29 vs. 5.4 months; p <.0001]); success of the surgical procedure:	CRS + HIPEC improves survival in patients with CRPC. However, patients with involvement of >6 abdominal regions, or grossly incomplete CRS, had still a grave prognosis.	2b
[97]	RCT	105 patients with CRC and peritoneal carcinomatosis (51 standard group, 54 experimental group) Median FU 8 years	CRS + HIPEC + SC (same regimens as for the standard group)	5-FU + leucovorin weekly for 26 weeks or irinotecan if they had already been treated with 5-FU; palliative surgery if needed	survival, measured as time from randomization to death from any cause	Median progression-free survival: 7.7 months in the control arm, 12.6 months in the HIPEC arm (P = 0.020); median disease-specific survival: 12.6 months in the control arm, 22.2 months in the HIPEC arm (p = 0.028); 5-year survival: 45% if R1 resection was achieved.	With 90% of all events having taken place up to this time, this randomized trial shows that CRS + HIPEC does significantly add survival time to patients affected by CRPC. For a selected group, there is a possibility of long-term survival.	2b
[98]	Cohort study	102 patients	laparotomy for CRS + HIPEC, followed by adjuvant systemic		factors associated with survival	Factors associated with short survival: Location of the primary tumour in rectum (HR 3.14 (95% CI 1.11 to 8.91); p = 0·069), poor differentiation (HR 1.73 (95% CI 1.04 to 2.88); p = 0·031) and signet cell	The survival of patients with CRPC is dominated by the extent of disease and the amount of residual tumour after cytoreduction.	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
			chemotherapy			histological type (HR 2.24 (95% CI 1.21 to 4.16); p = 0·008) Important factors predicting survival were the number of affected regions (HR 1·38 (95% CI 1.20 to 1.59); p<0·001), the simplified peritoneal cancer score (HR 1·19 (95% CI 1.12 to 1.26); p<0·001) and completeness of cytoreduction (HR 8.54 (95% 4.01 to 18.18); p<0·001)		
[99]	Cohort study	102 patients	laparotomy for CRS + HIPEC, followed by adjuvant systemic chemotherapy		Toxicity (NCI CTC classification)	Grade 3, 4, or 5 toxicity: 66 patients (65%); 8 patients died of treatment-related causes (8%); surgical complications: 36 patients (35%); fistulae: 18 patients (18%) Higher risk of a complicated recovery in PC: recurrent CRC (P=0.009), > 5 regions affected (P=0.044), with an incomplete initial cytoreduction (p=0.035); Patients with blood loss exceeding 6 L (P=0.028) and those with > 3 anastomoses also had an increased postoperative complication rate (P=0.018)	Toxicity of CRS + HIPEC was 65% (Grade 3–5 NCI CTC), with a surgical complication rate of 35%. Patients with six or seven regions involved and those in whom complete cytoreduction cannot be reached are probably better off without this treatment	4

12.1.3.2.10. *Wie ist der Stellenwert von Endosonographie, CT und MRT beim prätherapeutischen lokalen Staging des Rektumkarzinoms ?*

Suchstrategie (Weiterführende Suche der Meta-Analyse von Bipat S., et al. Radiology.2004 Sep;232(3):773-83)

("administration, rectal"[MeSH Terms] OR ("administration"[All Fields] AND "rectal"[All Fields]) OR "rectal administration"[All Fields] OR "rectal"[All Fields]) AND (("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields]) OR ("tumour"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "tumor"[All Fields]) OR ("carcinoma"[MeSH Terms] OR "carcinoma"[All Fields])) AND (("endosonography"[MeSH Terms] OR "endosonography"[All Fields]) OR (endosonic[All Fields] AND ("ultrasonography"[Subheading] OR "ultrasonography"[All Fields] OR "ultrasound"[All Fields] OR "ultrasonography"[MeSH Terms] OR "ultrasound"[All Fields] OR "ultrasonics"[MeSH Terms] OR

"ultrasonics"[All Fields])) OR ("contraindications"[Subheading] OR "contraindications"[All Fields] OR "ct"[All Fields]) OR ("tomography, x-ray computed"[MeSH Terms] OR ("tomography"[All Fields] AND "x-ray"[All Fields] AND "computed"[All Fields]) OR "x-ray computed tomography"[All Fields] OR ("computed"[All Fields] AND "tomography"[All Fields]) OR "computed tomography"[All Fields]) OR ("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields] OR "mri"[All Fields]) OR "magnetic resonance imaging"[All Fields]) AND ((("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "sensitivity"[All Fields]) OR ("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "specificity"[All Fields])) AND MeshTerms[All Fields] OR (("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "sensitivity"[All Fields]) OR ("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "specificity"[All Fields]) OR accuracy[All Fields])) AND staging[All Fields] AND ("humans"[MeSH Terms] AND (English[lang] OR German[lang]) AND ("2003/01/01"[PDAT] : "3000"[PDAT]))

Zusätzliche Einschlusskriterien: 20 Patienten, Referenzstandard operatives Präparat, keine neoadjuvante Radiochemotherapie (Kurzzeitbestrahlung erlaubt), Daten, die Berechnung einer 2 x 2 Tabelle erlaubten oder Angabe Sensitivität/Spezifität, Sensitivität T-Stadium u./o. N-Stadium u./o. zirkumferentieller Rand

Evidenztabelle

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[100]	Meta-Analysis	90 articles with patients with RC	EUS, CT and MR imaging	histology	Sensitivity and specificity of muscularis propria invasion, perirectal tissue invasion, adjacent organ invasion and lymph node involvment	For muscularis propria invasion, US and MR imaging had similar sensitivities; specificity of US (86% [95% CI: 80, 90]) was significantly higher than that of MR imaging (69% [95% CI: 52, 82]) (p = .02). For perirectal tissue invasion, sensitivity of US (90% [95% CI: 88, 92]) was significantly higher than that of CT (79% [95% CI: 74, 84]) (p< .001) and MR imaging (82% [95% CI: 74, 87]) (p = .003); specificities were comparable. For adjacent organ invasion and lymph node involvement, estimates for US, CT, and MR imaging were comparable. Summary ROC curve for US of perirectal tissue invasion showed better diagnostic accuracy than that of	For local invasion, endoluminal US was most accurate and can be helpful in screening patients for available therapeutic strategies.	3a

						CT and MR imaging. Summary ROC curves for lymph node involvement showed no differences in accuracy.		
[101]	Meta-Analysis	91 articles (7 CRM, 84 lymph node)	EUS, CT and MRI	histology	Sensitivity, Accuracy, OR of predicting the circumferential resection margin (CRM) and N-status.	CRM: The summary ROC curve shows that for MRI a sensitivity of about 80% for the prediction of CRM is associated with a false positive rate of about 20%. Lymph node involvement: The diagnostic odds ratio of EUS is 8.83. For CT and MRI the diagnostic odds ratios are 5.86 and 6.53, respectively.	MRI is the only modality that predicts the CRM with good accuracy, making it a good tool to identify high and low risk patients. The results show that EUS is slightly but not significantly better than MRI or CT for identification of nodal disease.	3a
[102]	Meta-Analysis	35 studies (2732 patients with RC)	EUS	histology	Sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio for N-staging	N+ of EUS: Pooled sensitivity 73.2% (95% CI 70.6–75.6). EUS Pooled specificity 75.8% (95% CI 73.5–78.0). Positive likelihood ratio 2.84 (95% CI 2.16–3.72), Negative likelihood ratio 0.42 (95% CI 0.33–0.52). Diagnostic odds ratio of having nodal metastasis in positive compared with negative EUS studies, was 7.9 (95% CI 5.3–11.7).	EUS is an important and accurate diagnostic tool for evaluating nodal metastasis of rectal cancers. This meta-analysis shows that the sensitivity and specificity of EUS is moderate.	3a
[103]	Meta-Analysis	42 studies (5039 patients with RC)	EUS	histology	Sensitivity, specificity for T1-T4	Pooled sensitivity and specificity: T1 87.8% (95% CI 85.3–90.0%) and 98.3% (95% CI 97.8–98.7%), respectively T2 80.5% (95% CI 77.9–82.9%) and 95.6% (95% CI 94.9–96.3%), respectively. T3 96.4% (95% CI 95.4–97.2%) and 90.6% (95% CI 89.5–91.7%), respectively. T4 95.4% (95% CI 92.4–97.5%) and 98.3% (95% CI 97.8–98.7%).	EUS should be the investigation of choice to T stage rectal cancers.	3a
[104]	Meta-Analysis	10 studies with RC	MRI	histology	Sensitivity, specificity for Circumferential margin involvement (CMI)	The overall sensitivity and specificity for MRI detecting CMI preoperatively: 94% and 85%, respectively, with an overall weighted AUC of 0.92 (DOR 57.21, 95% CI 18.21–179.77), without significant heterogeneity between the studies (Q-value 14.66, P = 0.06).	MRI can accurately predict CMI preoperatively for rectal cancer in single units and this is reproducible across different centres.	3a
[105]	Cohort	37 patients	MDCT	histology	Sens., Spec., PPV,	Sens., Spec., PPV, NPV, Accuracy:	MDCT with multiplanar	4

	study				NPV, Accuracy	<T2: 83%, 88, 77%, 91%, 86 respectively T3: 87%, 86%, 91%, 80%, 86 respectively T4: 100%, 100%, 100%, 100%, 100% respectively N+: 100%, 68%, 75%, 100%, 84% respectively MRF status: 86%, 97%, 86%, 97%, 94,5% respectively	reconstruction is an accurate technique in the preoperative local staging of rectal tumor.	
[106]	Cohort study	53 patients with lower RC	1,5T MRI	spiral CT	Accuracy by prediction of the lateral pelvic lymph node involvement	Accuracy in T staging: MRI 68% (36/53); Accuracy in regional N staging: MRI 64% (34/53) and CT 51% (27/53) (p=.05) Accuracy in detecting lateral pelvic lymph node involvement: MRI 83%, CT 77%; (p<0.05).	With MRI the lateral pelvic lymph node involvement can be predicted with high accuracy.	
[107]	Cohort study	74 patients with RC	Radial TRUS (R-TRUS),	Frontal TRUS (F-TRUS)	Sens., spec., PPV, NPV	R-TRUS Sens., Spez., PPV, NPV T1 100%, 90%, 67%, 100%, T2 75%, 70%, 56%, 89% T3 53%, 94%, 90%, 68% N 25%, 93%, 33%, 91% F-TRUS Sens., Spez., PPV, NPV T1 100%, 96%, 70%, 100% T2 82%, 97%, 87%, 98% T3 85%, 96%, 89%, 89% N 86%, 92%, 67%, 97%	Compared with radial transrectal ultrasound, frontal transrectal ultrasound has a better accuracy for T staging of rectal cancer.	4
[108]	Cohort study	49 patients with RC	EUS	body coil MRI (BC-MRI), phased array MRI (PA-MRI	Accuracy, Sens., Spec., PPV, NPV	T staging: Accuracy, Sens., Spec., PPV, NPV: EUS: 0,70, 0,80, 0,67, 0,85, 0,64 BC-MRI: 0,43, 0,55, 0,63, 0,79, 0,36 PA-MRI: 0,71, 0,75, 067, 0,79, 0,57 N Staging: Accuracy, Sens., Spec., PPV, NPV: EUS: 0,63, 0,47, 0,80, 0,67, 0,64 BC-MRI: 0,64, 0,62, 0,80, 0,73, 0,71 PA-MRI: 0,76, 0,63, 0,80, 0,75, 0,77	Although none of the results differed significantly, phased-array coil MRI seems to be the best single method for the preoperative staging of rectal cancer.	4
[109]	Cohort study	24 patients with RC	EUS	3T MRI	Sens., Spec., Diagnostic Accuracy,	Sens., Spec., Acc.: Muscularis Propria Invasion : MRI: 100%, 66,7%, 0,971	In our preliminary study, despite use of a newly developed 3-T system, MRI was less accurate than	4

						EUS: 100%, 61,1%, 0,978 Perirectal Tissue Invasion: MRI: 91,1%, 92,6%, 0,938 EUS: 100%, 81,5%, 0,996 P Accuracy: 0,028 Lymph Node Involvment MRI: 63,6%, 92,3%, 0,778 EUS: 57,6%, 82,1%, 0,721	endorectal sonography in the detection of perirectal tissue invasion.	
[110]	Cohort study	231 patients with local rectal tumour	ERUS	histology	Sens., Spec., PPV, NPV	Sens., spec., PPV, NPV TVA 89%, 86% T1 73%, 96%, 55%, 96% T2 54%, 97%, 54%, 97% In 21 tumors, ERUS was not conclusive, mainly in tumors being recurrent or after recent endoscopic manipulation (P<0.001). With ERUS the rate of preoperative missed carcinomas could be reduced from 21% to 3% (P<0.01.	ERUS is technically feasible in almost all presumed rectal adenomas, referred for local excision. Proper ERUS interpretation is possible in 78 percent of all presumed rectal adenomas. ERUS is very reliable in diagnosing tubulovillous adenomas, and therapeutic decision-making regarding local excision vs. radical surgery based on ERUS is valid.	4
[111]	Cohort study	34 patients with RC	MRI	EUS	Sens., Spec., Accuracy, PPV, NPV	MRI Sens., Spec., Accuracy, PPV, NPV T-Stadium 79%, 93%, 90% T1/2 96%, 60%, 85% 85%, 63% N+ 62%, 81%, 74% EUS T-Stadium 71%, 90%, 85% T1/2 87%, 50%, 76%, 81%, 86% N+ 53%, 84%, 76%	Phased-array MRI is slightly superior in determining the depth of transmural tumor invasion (T stage) and has same value in detecting lymph node metastases (N stage) as compared to ERUS.	4
[112]	Cohort study	78 patients with RC	EUS	spiral CT	Sens., Spec., Accuracy, PPV, NPV	Sens., Spec., PPV, NPV, Accuracy ERUS: T1 100%, 97%, 78%, 100% T2 84%, 94%, 87%, 93% T3 82%, 91%, 81%, 87% T4 85%, 95%, 79%, 97% N+ 54%, 71%, 58%, 68%, 64% T gesamt Accuracy 84%	EUS is superior to SCT in judgment for tumor infiltrate depth, but neither method could provide satisfactory assessment of lymph node metastases for rectal cancer.	4

						CT: T1/2 72%, 85%, 77%, 82% T3 67%, 74%, 65%, 76% T4 77%, 94%, 71%, 95% N+ 61%, 62%, 54%, 68%, 61% T gesamt Accuracy 71% P accuracy (EUS – CT; T staging) <0,05 P accuracy (EUS – CT; N staging) > 0,05		
[113]	Cohort study	83 patients with RC	EUS	histology	Accuracy	Accuracy in T stage assessment: 76% (63/83); 14% overstaging, 10% understaging. Accuracy N+ 63%.	EUS examination of RC determines T stage with high accuracy.	3b
[114]	Cohort study	31 patients with RC	3T MRI	MDCT	Sensitivity, Specificity, accuracy	Sensitivity, specificity, and accuracy between MRI and MDCT for < T2: 93% and 79%, 88% and 76%, and 91% and 77%, respectively p=0.01 T3: 92% and 73%, 93% and 83%, and 92% and 78%, respectively; p=0.001 Accuracy for MRI and CT in N staging: 88% and 77%, respectively (P > 0.05).	For local staging of rectal cancer, 3-T MRI is more accurate than MDCT for determining the depth of tumor invasion and the extent of lymph node metastasis.	4
[115]	Cohort study	35 patients with RC	3T MRI	histology	Sensitivity, specificity and accuracy (T1-T3, invasion, nodal involvement)	T1: sens. 88%, spec. 100%, acc. 97% T2: sens 86%, spec.89%, acc. 89% T3: sens. 90%, spec. 96%, acc. 91% N: sens. 80%, spe. 98%, acc. 95%	Preoperative 3-T MRI using a phase array coil accurately indicates the depth of tumor invasion for rectal cancer with a low variability.	4
[116]	Cohort study	57 patients with RC	1,5T MRI	histology	Sens., Spec., PPV, NPV, Accuracy	Sens., Spec., PPV, NPV, Accuracy: CRM 41%, 89%, 69%, 70%, 70% respectively N 50%, 96%, 94%, 60%, 70% respectively Accuracy T 81%	MRI provides an accurate prediction of preoperative CRM. There exist differences in diagnostic accuracy according to each different scan plane of MRI and tumor location within the rectum.	4
[117]	Cohort study	66 patients with RC	1,5T MRI	histology	Sens., Spec., PPV, NPV, Accuracy	Sens., Spec., PPV, NPV, Accuracy : T2: 76%, 85%, 58%, 94%, n.a. respectively T3: 95%, 82%, 91%, 90%, n.a. respectively N+: 69%, 93%, 97%, 47%, 74% respectively T1/T2: 82%, 95%, 90%, 91%, 91% respectively	MRI provides accurate preoperative local staging with regard to T and N stages and CRM and EMI status.	4

						CRM: 94%, 57%, 90%, 73%, 86% respectively		
[118]	Cohort study	552 patients with RC	clinical staging (CS), biopsies, EUS	histology	Accuracy	Preoperative histological diagnosis of the rectal carcinoma depended on tumor size (52% in cancers <3 cm,25% in cancers >3 cm; p=0.001) and was correct in 56% of cases. Transanal US (uT0/1) had superior sensitivity (95% vs 78%) and a higher PPV (93% vs 85%) than clinical staging (CS I) in detecting adenoma or T1 rectal carcinoma, whereas specificity was similar in both (62% vs 58%).In patients in whom preoperative histological analysis revealed adenomas, transanal US was accurate (uT0/1) for the postoperatively assessed adenoma pT1 in 97%, whereas diagnosis (uT0/1) was correct in only 71% of cases in which preoperative histological analyses showed rectal carcinomas.	In patients with rectal tumors, preoperative staging with transanal US and biopsy is essential for the indication and allows selection of patients for transanal local excision	4
[119]	Cohort study	134 patients with RC	EUS	histology	Accuracy and specificity in N staging	Overall accuracy of EUS for N-staging: 70%, a 16% false positive rate and 14% false-negative rate.	Early RC are more likely to have small LN metastases that are not easily identified by ERUS.	4
[120]	Cohort study	61 patients with RC	EUS	CT	Accuracy	Accuracy of EUS and CT in T staging: 75% and 48%; understaging in 10% and 41% and overstaging in 15% and 11%, respectively. Accuracy of EUS and CT in N staging: 75% and 57%, understaging in 8% and 30% and overstaging in 17% and 13%, respectively. In cases in which both methods resulted in identical T- (uT+ctT) or N-staging (uN+ctN), the accuracy increased to 82% and 80%, respectively.	The staging of pretherapeutic, locoregional T- and N status by EUS is superior to that by CT (T-status: p=0.0164, N-status: p=0.0035).	4
[121]	Cohort study	129 patients with RC	EUS	histology	Accuracy in T staging, Accuracy, Sensitivity and Specificity in N staging	Accuracy of overall T: 86,5%; T1 (86,7%), T2 (94,0%), T3 (86,2%), T4 (65,5%). Acc, sens. and spec. of N staging: 77,8%, 85,6%, 74,2%, respectively.	EUS is safe and effective for preoperative staging of rectal cancer and should be a routine examination before surgery.	4
[122]	Cohort study	7096 patients with	EUS	histology	Accuracy, influence of	T-stage accuracy: 64,7%, understaging in 18%, overstaging in 17,3%.	Only in the hands of diagnosticians with a large case volume of rectal	4

		RC			hospital volume upon accuracy	T-stage accuracy < 10 EUS/year: 63,2%; 11-30 EUS/year: 64,6%; >30 EUS/year: 73,1%	carcinoma patients can EUS lead to therapy-relevant decisions.	
[123]	Cohort study	51 patients with middle or lower RC	1,5T MRI	histology	optimal criterion for preoperative diagnosis of lymph node metastasis by high resolution MRI	For 6 mm cut-off Sens. 77.8%, Spec. 78.3%, Accuracy 78.0%	A 6-mm longitudinal diameter criterion is thought to be optimal in the MRI evaluation of mesorectal lymph node metastasis in patients with middle or lower rectal carcinoma.	3b
[124]	Cohort study	134 patients with RC	1,5 T MRI GI-radiologist	TRUS General radiologist	Effect of experience on accuracy (Reader 1 vs. Reader2)	TRUS sensitivity in rectal tumour T-staging was 93% for R1 and 75% for R2 (p<0. 01); specificity was 83% for R1 and 46% for R2 (p<0.05). The MRI sensitivity in rectal tumour T-staging was 96% for R1 and 77% for R2 (p<0.05); the specificity was 74% for R1 and 40% for R2 (p<0.05). There was no difference in the results of N-staging between R1 and R2 for either TRUS or MRI.	To obtain high-quality preoperative prediction of rectal cancer T-stage, it is suggested that preoperative TRUS and MRI staging should be supervised by an expert in the colorectal cancer team.	3b
[125]	Cohort study	126 patients with rectal tumors	EUS (3D)	histology	Accuracy	Overall kappa for accuracy of EUS 0.81 (95% CI 0.72– 0.89). No invasive carcinomas remained undetected. The depth of invasion was correctly determined in 87.2% of both pT1-slight and pT1-massive lesions. The accuracy of EUS in selecting appropriate management was 95.2% (kappa, 0.84; 95% CI 0.71– 0.96). Adequate surgery was performed in 87.5% of pT1 tumors.	3D EUS is useful for assessing the depth of submucosal invasion in early rectal cancer and for selecting therapeutic options.	4
[126]	Cohort study	44 patients	EUS (colonoscopic US)	histology	predictability CUS in preoperative staging of rectal cancer during the learning curve,	Accuracy of T-stage 52%, overstaging 23%, understaging 25%. N-staging PPV 61%, NPV 73%, sensitivity 61%, and specificity 73%.	At least in the learning phase of CUS, it would be beneficial to compliment US staging of rectal tumors with other modalities such as MRI or CT.	4

12.1.3.2.11. *Wie ist der Stellenwert bildgebender Verfahren (CT, MRT, Endosonographie, PET, andere) beim Rektumkarzinom zum Restaging nach erfolgter Radiochemotherapie bzw. Radiotherapie?*

Suchstrategie (Weiterführende Suche der Meta-Analyse von Bipat S., et al. Radiology.2004 Sep;232(3):773-83)

("administration, rectal"[MeSH Terms] OR ("administration"[All Fields] AND "rectal"[All Fields]) OR "rectal administration"[All Fields] OR "rectal"[All Fields]) AND (("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields]) OR ("tumour"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "tumor"[All Fields]) OR ("carcinoma"[MeSH Terms] OR "carcinoma"[All Fields])) AND (("endosonography"[MeSH Terms] OR "endosonography"[All Fields]) OR (endosonic[All Fields] AND ("ultrasonography"[Subheading] OR "ultrasonography"[All Fields] OR "ultrasound"[All Fields] OR "ultrasonography"[MeSH Terms] OR "ultrasound"[All Fields] OR "ultrasonics"[MeSH Terms] OR "ultrasonics"[All Fields])) OR ("contraindications"[Subheading] OR "contraindications"[All Fields] OR "ct"[All Fields]) OR ("tomography, x-ray computed"[MeSH Terms] OR ("tomography"[All Fields] AND "x-ray"[All Fields] AND "computed"[All Fields]) OR "x-ray computed tomography"[All Fields] OR ("computed"[All Fields] AND "tomography"[All Fields]) OR "computed tomography"[All Fields]) OR ("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields] OR "mri"[All Fields]) OR "magnetic resonance imaging"[All Fields]) AND ((("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "sensitivity"[All Fields]) OR ("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "specificity"[All Fields])) AND MeshTerms[All Fields] OR (("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "sensitivity"[All Fields]) OR ("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "specificity"[All Fields]) OR accuracy[All Fields])) AND staging[All Fields] AND ("humans"[MeSH Terms] AND (English[lang] OR German[lang]) AND ("2003/01/01"[PDAT] : "3000"[PDAT]))

Zusätzliche Einschlusskriterien: 20 Patienten, Referenzstandard operatives Präparat, keine neoadjuvante Radiochemotherapie (Kurzzeitbestrahlung erlaubt), Daten, die Berechnung einer 2 x 2 Tabelle erlaubten oder Angabe Sensitivität/Spezifität, Sensitivität T-Stadium u./o. N-Stadium u./o. zirkumferentieller Rand

Evidenztabelle

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[127]	Cohort study	51 patients with RC after neoadjvant CRT	EUS	Histology	Accuracy of EUS	42 pats (45%) with major pathological response; sens, spec., NPV and PPV (T-stage): 77,8%, 37,5%, 60% and 58% sens, spec., NPV and PPV (N-stage): 44%, 88%, 88% and 44%	EUS has a limited ability to predict primary tumour response after preoperative CRT, but it is useful for accurately determining LN status.	4
[50]	Cohort study	50 patients	Pelvic MRT	Histology	accuracy of MRI	Overall predictive accuracy in T stage: 52%,	Poor agreement between post-	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		with RC and neoadjuvant CRT				(38% overstaging, 10% understaging) Overall predictive accuracy in N stage 68% (24% overstaging, 8% understaging)	combined chemoradiotherapy MRI and pathologic staging was observed in both T (k = 0.017) and N (k = 0.031) stages.	
[128]	Cohort study	30 patients with RC and neoadjuvant CRT	MRI, FDG-PET/CT	Histology	Accuracy of MRI and PET/CT	MRI Overall accuracy in T stage was 67% (k= 0.422, P = 0.003), (30% overstaging, 3% understaging) Accuracy in N stage 75% (k = 0.410, P = 0.030), (14% overstaging, 11% understaging). FDG-PET/CT The overall accuracy rates for the T and N categories 60% (k = 0.372, P = 0.004) and 71% (k = 0.097, P = 0.549), respectively. Prediction of complete response: MRI 0/4, PET/CT 3/4 PET/CT identified distant metastases with an accuracy rate of 97%.	For restaging patients with rectal cancer after preoperative CCRT, MRI is a useful diagnostic modality to predict both the T and N categories. FDG-PET/CT is helpful in predicting a pathologic complete response and in finding metastasis after preoperative CCRT.	4
[129]	Cohort study	67 patients with RC and neoadjvunat CRT	MRI	Histology	Accuracy of MRI	Accuracy for prediction of ypT0-2: 78%, 72% and 73% for expert abdominal radiologist, surgeon, and general radiologist, respectively. Overstaging in 14 pat, 18 pat. And 17 patients respectively	Downsizing to ypT0–2 tumors can be accurately predicted by combining morphologic tumor staging predictions with results from volumetric analyses.	4
[130]	Cohort study	79 patients with RC and CRT	MRI	Histology	Accuracy of MRI	yT3/4: University/general setting Sens. 95/88%, spec. 46/41%, PPV 64/40%, NPV 90/76% N+: University/general setting Sens 67/64%, spec. 84/69%, PPV 63/45%, NPV 86/83%	With a dedicated MRI ypT0 to 2N0 RC after CRT can be accurately identified with a reasonably low risk of understaging.	4
[131]	Cohort study	29 patients	EUS	Histology	Accuracy of EUS	EUS postradiotherapy:	Postradiation endorectal ultrasound is	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		with RC and CRT				Accuracy for T-stage : 72.4%, overstaging in 27.6%. Accuracy for N-stage : 70.3% ; overstaging in 11%, understaging in 19.7%	a valid toot, because the extent of fibrosis in the rectal wall is a direct indication of the depth of residual cancer.	
[132]	Cohort study	35 patients with RC and CRT	MRI	Histology	Accuracy of MRI	Overall predictive accuracy in T stage was 45% (19/35), (9/20 overstaging, 7/15 understaging) Accuracy in N stage was 54% (19/35), (6 pats overstaging, 10 pats understaging).	MRI proved independent of the response status as not suitable to restage locally advanced rectal carcinoma after preoperative radiochemotherapy..	4
[133]	Cohort study	32 patients with RC and RT	EUS	Histology	Accuracy of EUS	uT3/4: Accuracy: 77,4%, Sens: 76,5%, Spec: 78,6%, PPV.81%, NPV:73%	EUS after radiotherapy makes morphologic evaluation of tumor regression possible, but its interpretation is less reliable.	4
[134]	Cohort study	83 patients with RC and RCT (60 ERUS, 80 CT)	ERUS, CT	Histology	Accuracy of ERUS and of CT	Accuracy in T stage ERUS 38,3%,CT 70,4%. Accuracy in N stage ERUS 72.6%, CT 70.4% Complete remission was not predicted by neither modality.	ERUS and CT may allow good prediction of node-negative rectal cancers, although they are inaccurate modalities for predicting treatment response on the rectal wall.	4
[135]	Cohort study	65 patients with RC and RCT	MRI	Histology	Accuracy of MRI in regard to CRM, mesorectal fascia (MRF) invasion and tumor response to CRT	The measured CRM was not significantly different from the reference standard (mean difference, -1.4 mm; 95% limits of agreement, -8.3–5.4 mm; interclass correlation coefficient, 0.82). The diagnostic accuracy (Az) for determining MRF invasion was 0.890 for reviewer 1 (95% confidence interval [CI], 0.788–0.954) and 0.829 for reviewer 2 (95% CI, 0.715–0.911). The Az for predicting complete or near-complete regression was 0.791 for reviewer 1 (95% CI, 0.672–0.882) and 0.735 for reviewer 2 (95% CI, 0.611–0.837).	MRI provides accurate information regarding the CRM of locally advanced rectal cancer after neoadjuvant CRT; it also shows relatively high accuracy for predicting MRF invasion and moderate accuracy for assessing tumor response.	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[136]	Cohort study	80 patients with RC and RCT	MRI	Histology	Accuracy of MRI in regard to CRM and tumor stage	CRM: Accuracy 81%, sens 54%, spec 87% , PPV 44%, NPV 91%. T-staging: Accuracy 43%, (38% overstaging, 20% understaging) N-staging: Accuracy 78%, (4% overstaging, 19% understaging).	Magnetic resonance imaging has good specificity and NPV for predicting an uninvolved CRM post downstaging CRT in locally advanced rectal cancer although sensitivity and PPV for an involved CRM were unsatisfactory.	4
[137]	Cohort study	28 patients with RC and RCT	EUS	Histology	Accuracy of EUS in regard to tumor stage and nodal stage	Accuracy for T status and N status: 75%. No understaging for T- and N status. Overstaging. T stage (7/28); N stage (7/28)	Die EUS nach präoperativer Radio-(Chemo)therapie erlaubt eine exakte Einschätzung von Infiltrationstiefe und Lymphknotenbefall und gibt damit wichtige Hinweise für die Operationsplanung, um die Resektabilität und das Ausmaß der resektion nicht zu unterschätzen.	4
[138]	Cohort study	36 patients with RC and RCT	MRI	Histology	Accuracy of MRI in regard to CRM and tumor stage	T-stage: accuracy 47% Overstaging 47% understaging 6% N-stage: accuracy 64% Overstaging 28% understaging 8%	MRI is commonly used in staging of pelvic malignancies because of its fine resolution, but CRT may decrease its accuracy.	4
[120]	Cohort study	41 patients with RC and RCT	ERUS, CT	Histology	Accuracy of EUS and CT	T-stage Accuracy of EUS and CT: 66% and 51%, respectively. Understaging EUS and CT 2% and 22%. Overstaging EUS and CT: 32% and 27%. N-stage	After RCT, the predictive efficacy of the EUS for the downsizing/-staging of rectal cancer must be evaluated on greater numbers of patients receiving standardized diagnostic procedures	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
						Accuracy of EUS and CT: 68% and 76%, respectively. Understaging EUS and CT: 20% and 17%. Overstaging EUS and CT: 12% and 7%, respectively.	and therapy.	
[48]	Cohort study	45 patients with mid to low RC and RCT	TRUS, CT, MRI	Histology	sensitivity, specificity, PPV, NPV and accuracy of TRUS, MRI and CT	sens., spec., PPV, NPV, and accuracy in predicting T status (T0 vs. T >1): TRUS: 77%, 33%, 74%, 36%, and 64% CT: 100%, 0%, 74%, not assessable, and 74% MRI: 100%, 0%, 77%, not assessable, and 77% sens., spec., PPV, NPV, and accuracy in predicting N status (N- vs. N+): TRUS: 37%, 67%, 21%, 81%, and 61% CT: 78%, 58%, 32%, 91%, and 62% MRI: 33%, 74%, 25%, 81%, and 65%	Current rectal cancer staging modalities after chemoradiotherapy allow good prediction of node-negative cases, although none of them is able to predict the pathologic complete response on the rectal wall.	4
[139]	Cohort study	39 patients with distal RC and RCT	EUS, MRI	Histology	Accuracy of EUS and MRI in regard to tumor stage and nodal stage	Accuracy in T staging EUS 46% (18/39), MRI 44% (17/39) Accuracy in N staging EUS 69% (27/39), MRI 62% (24/39) Accuracy of EUS and MRI: T0-T2 (44% vs. 33%; P>0,05; N0 (87% vs. 52%; P=0,013)	EUS and MRI are accurate imaging techniques for staging rectal cancer. However, after neoadjuvant RT-CT, the role of both methods in the assessment of residual rectal tumors remains uncertain.	4
[140]	Cohort study	235 patients with RC and neoadjuvant therapy	EUS	Histology	Accuracy of EUS in regard to tumor stage and nodal stage	Accuracy in T staging: 54%, in N staging 75%. Sens., spec., PPV and NPV to predict nodal involvement were 39%, 91%, 67%, and 76%, respectively. Overstaging: 88/235 (37%), understaging 21/235 (9%)	EUS allows prediction of involved lymph nodes in 75% of the cases; however, 1 in 5 patients are missclassified as uN0 after neoadjuvant treatment.	3b
[44]	Cohort study	90 patients with RC and CRT (68 MRI, 79 CT, 83	ERUS, CT, MRI	Histology	accuracy of ERUS, MRI and CT in predicting T stages, N stages and CRM	Accuracy T staging: CT 37%, MRI 34%, ERUS 27% N staging: CT 62%, MRI 68%, ERUS 65% CRM: CT 71%, MRI 85%	Current imaging techniques are inaccurate in restaging rectal cancer after CRT but are useful in predicting T<3 tumors, cases with negative	3b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		EUS)					nodes and tumor-free CRM.	
[141]	Cohort study	44 patients with RC and CRT	EUS	Histology	Accuracy of EUS in regard to tumor stage and nodal stage	Accuracy: T stage : 75% (33/44) with overstaging 18% (8/44), understaging 7% (3/44); N stage: 68% (30/44). overstaging 20% (9/44), understaging 11% (5/44).	ERUS provides a good accuracy rate for staging rectal cancer after neoadjuvant chemoradiation. However, it is insuficient in detection of complete pathological response.	4
[142]	Cohort study	84 patients with RC and RCT	EUS	Histology	Accuracy of EUS in regard to tumor stage and nodal stage	accuracy for T stage: 29% in responders and 82% in nonresponders. accuracy for N stage: 57% accuracy for wall invasion 50%, underestimation 13%, overestimation 37%.	After RCT EUS does not provide a satisfactory accuracy for preoperative staging of rectal cancer.	4
[143]	Cohort study	30 patients with RC and RCT	EUS, MRI	Histology	Accuracy of EUS and MRI in regard to tumor stage and nodal stage	accuracy for T stage: MRI 47%, EUS 53%;	Both imaging modalities provide useful information for operation planning despite limited accuracy after CRT.	4
[47]	Cohort study	49 patients with RC and RCT	MRI	Histology	Accuracy of MRI in regard to tumor stage and nodal stage	Accuracy 43% (21/49) with over- and understaging in 43% (21/49) and 14% (7/49) respectively. T-stage accuracy 45% (22/49) with overstaging in 33% (16/49) and understaging in 22% (11/49). N-stage accuracy 71% (35/49), with 82% (9/11) sensitivity, 68% (26/38) specificity and of 43% (9/21) and NPV of 93% (26/28). Complete radiological response: 4% (2/49). Complete pathological response: 10% (5/49)	MRI staging following chemoradiation is poor. Overstaging occurs three times more commonly than under-staging. Overstaging is due to poor PPV of nodal assessment.	4
[144]	Cohort study	24 patients with RC and RCT	MRI	Histology	Accuracy of MRI in regard to tumor size, CRM and tumor stage	Accuracy yT-stage 60% Distance to CRM: no significant correlation	The value of a second MRI after radiotherapy for assessment of distance to CRM and ypT-staging is, not apparent.	4
[145]	Cohort study	82 patients	EUS	Histology	Accuracy in regard	Accuracy overall T-Stage: 48% (23/56	EUS staging of rectal cancer after	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		withRC and RCT			to tumor stage and nodal stage	responders (41%), 16/24 nonresponders (97%); understaging 14%, overstaging 38%; T0-stage: 63% (10/16) N-stage: 77%	chemorsdiation is inaccurate, especially in the group of patients with visual and EUS evidence of response.	

12.1.3.2.12. *Wie ist der Stellenwert des PET-CT zur Primärdiagnostik des kolorektalen Karzinoms?*

Suchstrategie

#1	colorectal
#2	colonic
#3	sigmoid
#4	rectal
#5	#1 or #2 or #3 or #4
#6	neoplasms
#7	tumor
#8	carcinoma
#9	#6 or #7 or #8
#10	#5 and #9
#11	primary diagnostic
#12	staging
#13	#11 or #12
#14	PET
#15	PET-CT
#16	PET CT
#17	#14 or #15 or #16
#18	#10 and #13 and #17

#19 Limits: English, German; Humans

Evidenztabelle

Referenz	Studien-typ	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[146]	Cohort study	48 male patients with known CRC	FDG-PET	CT, surgery and histopathological findings	Sensitivity, Specificity, PPV, NPV	Sensitivity: 100% Specificity: 43% PPV: 90% NPV: 100%	FDG PET is superior to CT staging of primary crc.	3b
[147]	Cohort study	65 patients with CRC	FDG PET	MDCT	Sensitivity, Specificity, Accuracy	Tumour detection rate PET 98%, MDCT 100% LN Sensitivity PET 43%, MDCT 89% Specificity PET 95%, MDCT 52% Liver metastases Accuracy PET 97%, MDCT 98% PET affected treatment in 15% of patients.	Preoperative FDG-PET is not superior to MDCT for detection of primary tumour, lymph node involvement or liver metastases. It may have potential clinical value in patients with advanced colorectal cancer by detecting extrahepatic distant meatastes.	3b
[148]	Cohort study	25 patients with rectal cancer, candidates for radiotherapy	FDG-PET/CT	CT	Gross tumor volume (GTV) Clinical stage volume (CTV)	PET/CT-GTV > CT-GTV (25.4%) PET/CT-CTV > CT-CTV (4.1%) PET/CT affected tumour staging or treatment purpose in 24%	Imaging with PET/CT for preoperative radiotherapy of rc may lead to a change in staging and target volume delineation.	4
[149]	Cohort study	83 patients with rectal cancer FU at least 12 months	PET-CT	Conventional imaging e.g. abdominal and pelvic CT-scan, chest-x-ray or chest CT scan, pelvic MRI scan,	Change in T-staging, change in N-staging, change in management intent	PET-CT -> stage change in 26 patients (31%). 12 (14 %) were upstaged (7 change in N stage; 4 change in M stage; 1 change in N and M stage), and 14 (17%) were downstaged (10 change in N stage; 3 change in M stage; 1 change in N and M stage). PET-CT scan altered management in 10 patients (12%).	PET-CT scan impacts the management of patients with primary rectal cancer and influences staging/therapy in a third of patients and should be a component of rectal cancer workup.	3b

Referenz	Studien-typ	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
				endoanal US scan				
[150]	Cohort study	44 patients with CRC	FDG PET-CT	MDCT	detectability of the primary tumor, lymph node involvement	Tumour detection rate: 95% for MDCT, 100% for FDG-PET. N-status: accuracy 62% for MDCT, 59% for FDG-PET. FDG-PET findings resulted in treatment changes in only one (2%) patient.	FDG-PET is not superior to routine MDCT in the initial staging of primary CRC.	3b
[151]	Cohort study	37 patients with rectal cancer	FDG-PET/CT	TRUS/ MRI, CT, Histology	Utility of PET/CT in evaluation of rectal cancer	discordant findings: 14 patients (38%), upstaging of 7 patients (50%), downstaging of 3 patients (21%)). N+: no statistically significant discordance Discordant PET/CT findings in patients with a low rectal cancer vs. mid or high rectal cancer: 13 vs. 1; P = .0027. Lymph node metastasis (n = 7; 50%). Discordant PET/CT findings resulted in an altered treatment plan in 27% of patients (n = 10).	FDG-PET/CT frequently yields additional staging information in patients with low rectal cancer. Improved accuracy of pretreatment imaging with FDG-PET/CT will allow more appropriate stage-specific therapy.	3b
[152]	Cohort study	23 patients with rectal cancer	MRI-PET additionally MRI, CT and EUS		Role of MRI-PET in staging of rectal cancer	T-stage: MRI correctly staged 14 of 22 T2/T3 tumours. N-stage: MRI-PET fusion had a sensitivity of 44 %, with a specificity and positive predictive value of 100 %. No additional information was acquired from MRI-PET fusion over MRI plus abdominal CT and chest radiography.	MRI-PET fusion adds little to conventional investigations for staging rectal carcinoma.	4
[153]	Cohort study	38 patients with CRC	FDG PET Additionally chest x-ray, ultrasound, CT		Clinical benefit by FDG PET	Detection of primary tumor: FDG PET – 95%, CT – 49%, Sono – 14% Lymph node involvement: Sensitivity, specificity, and accuracy of FDG PET 29%, 88%, and 75%. CT and sonography did not reveal any lymph node involvement. Liver metastases: FDG PET, CT, and sonography sensitivity of	FDG PET is the best method for the staging of CRC in all localities, despite the high rate of false-negative PET findings in patients with lymph node involvement. PET should be performed as a first examination after verification	4

Referenz	Studien-typ	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
						78%, 67%, and 25%; specificity of 96%, 100%, and 100%; accuracy of 91%, 91%, and 81%. FDG PET revealed further lesions in 11 patients. FDG PET changed the method of treatment for 16% of patients.	of CRC. We propose a PET/CT hybrid system as optimal in the staging of CRC.	
[154]	Cohort study	50 patients with CRC	PET/CT-colonography Additionally colonoscopy	CT-colongraphy	Evaluation of PET/CT-colonography	Accuracy PET vs. CT TNM-staging: 74% vs. 44% (p<0.05) T-stage 84% vs. 70% N-stage 82% vs. 68% No significant difference was found for M-staging	Staging patients with whole-body PET/CT-colonography is technically feasible and accurate.	4
[155]	Cohort study	104 patients with CRC	FDG-PET	CT	Evaluation of PET and impact on therapeutic management	N staging: Sensitivity, Specificity, accuracy, PPV, NPV PET 21%, 95%, 56%, 83%, 51% CT 25%, 100%, 60%, 100%, 54% M assessment: Sensitivity, Specificity, accuracy, PPV, NPV PET 89%, 93%, 92%, 73%, 98% CT 44%, 95%, 87%, 67%, 89% FDG-PET results revealed unknown disease in 19.2%, changed the staging in 13.5% and modified the scope of surgery in 11.54%.	FDGPET appears to be useful in pre-surgical staging of CC, revealing unsuspected disease and impacting on the treatment approach.	3b
[156]	Cohort study	24 patients with CRC	Whole body PET		Comparison of preoperative PET findings and postoperative histopathological findings	Sensitivity: primary tumor: 95,8% (23/24) lymph node metastases: 22,2% (2/9) distant metastases: 75% (3/4)	Preoperative PET is useful for the diagnosis of primary colorectal cancer, but it is of limited value for detecting metastases of regional lymph nodes.	4
[157]	Cohort study	13 patients with obstructive	PET-CT-colonography		Evaluation of PET colonography for patients with	Sensitivity: primary CRC 13/13 synchronous CRC 2/2	In patients with obstructive colorectal cancers, preoperative PET/CT colonography provided	4

Referenz	Studien-typ	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		CRC median FU: 7.7 months			obstructive CRC	PET/CT colonography changed the method of treatment for 23% (3/13)	valuable anatomic and functional information of the entire colon to properly address surgery of colorectal cancer.	
[158]	Cohort study	93 patients with locally advanced rectal cancer median FU: 34 months	PET Additionally CT-pelvis/abdomen + chest		Accuracy of PET in distant disease	Distant disease Accuracy 99.7%, sensitivity 77.8%, specificity 98.7%. Liver metastases (n=8) accuracy 99.9%, sensitivity 100%, specificity 98.8% Lung metastases (n=4) accuracy 99.9%, sensitivity 80%, specificity 100%) disease	Although the role of PET in pretherapeutic management of locally advanced rectal cancer remains to be fully defined, our data demonstrate the ability of PET to accurately detect malignant disease in liver and lung.	3b
[159]	Cohort study	25 patients with CRC	PET	MRI	Detection of primary tumor, lymph node metastases	Detection of primary tumor: PET 93% (25/27), MRT 85% (23/27) Detection of metastatic lymph nodes: Sens. PET 30% (3/10), MRT 80% (8/10) Spez. PET 100% (13/13), MRT 77% (10/13) Accuracy: PET 78.3% (18/23), MRT 69.6% (16/23)	DW-MRI is inferior to FDG-PET for the detection of primary lesions, but superior for the detection of lymph node metastases.	4
[160]	Cohort study	100 patients with CTC and risk of metastases median FU: 18 months	PET-CT	Conventional staging with CT + chest x-ray/CT-Thorax	Accuracy of PET in the staging of CRC	PET/CT detected 15 intra-abdominal metastatic lesions more than abdomino-pelvic CT scan. PET/CT showed true negative findings in 13 patients and false positive or negative findings in 10. Due to PET/CT results, management plans were altered in 27 patients.	PET/CT altered management plan in 24% of patients with primary colorectal carcinoma in correct direction. These findings suggest that PET/CT should be considered a part of standard work up for preoperative evaluation in a subset of patients with crc.	4
[161]	Cohort study	36 Patienten mit lokal	PET-CT		Einfluss des PET auf die Bestrahlungsplanun	Die PET/CT-GTVs waren signifikant kleiner als die CT-GTVs ($p < 0,05$). Vorgehen geändert durch PET-CT in 8% (3/36), Änderung der	Das FDG-PET/CT hatte einen signifikanten Einfluss auf die Bestrahlungsplanung und das	4

Referenz	Studien-typ	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		fortgeschrittenem Rektumkarzinom			g	Bestrahlungszielvolumina (CT-PTV) bei 46% (16/35)	therapeutische Gesamtkonzept der Patienten mit lokal fortgeschrittenem Rektumkarzinom.	
[162]	Cohort study	53 patients with rectal cancer	PET-CT	MRCT	diagnostic accuracy of PET for preoperative nodal staging	Sens. PET/CT 85%, CT 85% Spec. PET/CT 68%, CT 42% Accuracy PET/CT 79% (42/53), CT 70% (37/53) p=0.063 Sens. PET prox. LN 51% (21/41), distant LN 63% Spec. PET prox. LN 85%, distant LN 93%	Contrast-enhanced PET/CT is superior to nonenhanced PET/CT for precise definition of regional nodal status in rectal cancer.	3b
[163]	Cohort study	88 patients with CRC	FDG-PET/CT		Diagnostic value of PET/CT for lymph node metastases in CRC	Sens. PET prox. LN 51% (21/41), distal LN 63% Spec. PET prox. LN 85%, distal LN 93%	FDG-PET/CT is useful for preoperative diagnosis of distant LN metastases of colorectal cancers.	4
[164]	Cohort study	14 patients with suspected CRC	PET-CT-Colonography		T-staging, N-staging	Accuracy T-Stadium 73% (8/11) LN: Sens. 50% (2/4), Spez. 100% (10/10) M1: Sens. 100% (3/3)	Whole body PET/CT with integrated colonography is technically feasible.	4
[165]	Cohort study	47 patients with CRC median clinical FU: 447 days	PET-CT-Colonography	Abdominal /chest CT	staging accuracy, effect on therapy planning	Accuracy in TNM-Staging: PET-CT 74% (37/50), CT 52% (26/50) LN: Sens. PET/CT 80% (15/20), CT 60% (12/20), Spez. PET/CT 97%, CT 93% M1: Sens. PET/CT 100% (6/6), CT 100% (6/6), Spez. PET/CT 100%, CT 98% Altered Therapy plan in 9% (4 pats.)	PET/CT colonography is at least equivalent to CT-PET for tumor staging in patients with colorectal cancer.	3b

12.1.3.2.13. *Wie ist der Stellenwert des PET/ PET-CT vor einer Metastasenresektion?*

Suchstrategie

#1	colorectal
#2	colonic
#3	sigmoid
#4	rectal
#5	#1 or #2 or #3 or #4
#6	neoplasms
#7	tumor
#8	carcinoma
#9	#6 or #7 or #8
#10	#5 and #9
#11	PET
#12	PET-CT
#13	#11 or #12
#14	metastases
#15	advanced disease
#16	resection surgery
#17	#14 or #15 or #16
#18	#10 and #13 and #17

#19 Limits: English, German; Humans

Evidenztabelle

Das in der Langversion erwähnte Abstrakt von Moulton, welches auf dem ASCO 2011 vorgestellt wurde, ist nicht enthalten, da die Studie bislang nicht als Volltext publiziert wurde.

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[166]	Metaanalysis		comparison of PET, CT scan and MRT	All modalities were compared to eachother, no standard diagnostic group	number of futile laparotomies	sensitivity for patient based analysis higher than lesion based analysis for all diagnostic modalities. Patient based results: Sensitivity PET: 94,1%, CT: 83,6%; MRT 88,2% Lesion based: 81,4%, 74,4%, 80,3%	Authors recommend MRT dscanning for the detection of liver lesions	2a
[167]	Systematic Review	Studien (1 RCT zu patientenrelevantem Nutzen; 21 zur diagnostischen Güte (6 Übersichten und 15 Einzelstudien),eine Metaanalyse zur Rezidivdiagnostik, 1 zur prognostischen	PET, PET-CT	konventionelle Bildgebung, V.a. CT, auch MRT	Bewertung des patientenrelevanten Nutzens und Schadens der PET/ PET-CT (krankheitsfreies Überleben, Gesamtüberleben, Reduktion der Rate überflüssiger Laparotomien) der diagnostischen (Rezidivdiagnostik)und prognostischen Güte der PET/ PET-CT	krankheitsfreies Überleben, Gesamtüberleben: kein statistisch signifikanter Effekt Reduktion der Rate überflüssiger Laparotomien: statistisch signifikanter Vorteil der PET Rezidivdiagnostik: Die Sensitivität und Spezifität [95 %-CI] betrugen für die PET-PET/CT-Gruppe 94,0 % [89,6; 96,1] und 81,2 % [66,4; 90,4] und für die CT-Gruppe 75,4 % [67,4; 81,9] und 69,0 % [49,9; 83,2]	Trotz einer nahezu durchgehend gefundenen höheren Testgüte der PET bzw. PET/CT blieb für die vorliegende Frage nach der Wertigkeit der PET-Technologie unbeantwortet, wie sich eine höhere Testgüte auf patientenrelevante Endpunkte auswirkt. Wegen methodischer Schwächen stufte der Bericht die RCT von Ruers et al von 1b auf 2 herab (Siehe Text)	2a

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		Güte)						
[168]	Systemativ Review	6 Studien mit 440 Patienten,	PET-CT	konventionelle Bildgebung, v.a. CT	diagnostic accuracy of PET-CT for colorectal liver metastases	For extra-hepatic lesions (3 studies; 178 patients), PET-CT was more sensitive than CT, but specificities were similar (PET-CT sensitivity [SN] = 75%–89% and specificity [SP] = 95%–96% vs. CT SN = 58%–64% and SP = 87%–97%). For hepatic lesions (5 studies; 316 patients), PET-CT had higher SN and SP than CT (PET-CT SN = 91%–100% and SP = 75%–100%; CT SN = 78%–94% and SP = 25%–98%). For local recurrence (3 studies; 206 patients), PET-CT also had better accuracy than CT with SN = 93% to 100% and SP = 97% to 98% versus SN = 0 %–100% and SP = 97%–98%.	PET-CT has a higher accuracy for detection of extra-hepatic and hepatic colorectal metastatic disease than CT alone.	2a
[169]	Case-control study	138 patients (120 hepatic resection, 2 RFA, 7 resection + RFA, 9 inoperable disease found intraoperatively)	PET, PET-CT	conventional imaging (CT, MRT, ultrasound)	Accuracy of PET scans to detect residual viable colorectal cancer liver metastases after a significant response to systemic chemotherapy	Negative predictive value of 13.3% and a positive predictive value of 94.3%. The sensitivity was 89.9%, the specificity was 22.2%, and the accuracy was 85.5%.	Positron emission tomography within 4 weeks of chemotherapy is not a useful test for evaluation of colorectal hepatic metastases. The high rate of falsenegative results is likely due to metabolic inhibition caused by chemotherapeutic drugs. We recommend that physicians not use PET in patients recently completing chemotherapy; they should undergo the appropriate oncologic hepatic operation based on the high probability of	2b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
							viable malignant disease	
[170]	Cohort study	Group 1: 27 (33 lesions) underwent immediate hepatic resection Group 2: 48 patients (122 lesions) received preoperative neoadjuvant chemotherapy (group 2).	Chemotherapy followed by PET, PET-CT	PET, PET-CT without previous chemotherapy	influence of chemotherapy on the sensitivity of FDG-PET and CT in detecting liver metastases	Sensitivity of FDG-PET and CT in detecting colorectal (CR) metastases was significantly higher in group 1 than in group 2 (FDG-PET: 93.3 vs 49%, P<0.0001; CT: 87.5 vs 65.3, P=0.038). CT had a higher sensitivity than FDG-PET in detecting CR metastases following neoadjuvant therapy (65.3 vs 49%, P<0.0001).	FDG-PET/CT sensitivity is lowered by neoadjuvant chemotherapy. CT is more sensitive than FDG-PET in detecting CR metastases following neoadjuvant therapy. Baseline FDG-PET and CT before neoadjuvant therapy are mandatory.	4
[171]	Cohort study	34 patients, 17 with neoadjuvant chemotherapy	PET, PET-CT, CT/MRI, IUS Preoperative chemotherapy	No preoperative chemotherapy	to evaluate the effects of neoadjuvant chemotherapy on the efficacy of PET, PET-CT, CT and intraoperative ultrasound (IUS) in the detection of liver metastasis.	For patients without systemic chemotherapy, sensitivities for PET, CT/MRI and IUS were 92%, 64% and 100% respectively as compared with 63%, 65% and 94% for patients after neoadjuvant chemotherapy in a segment based analysis.	Staging accuracy of colorectal liver metastasis is influenced by neoadjuvant chemotherapy. For PET, decreased tumour metabolism rather than downsizing may account for a drop in sensitivity after neoadjuvant chemotherapy. IUS is critical to avoid incomplete resections.	4
[172]	RCT	150 patients (75 CT only, 75 CT plus (18)F-FDG PET)	(18)F-FDG PET + CT, CT	histology	number of futile laparotomies	futile laparotomies (CT-arm): 34 (45%), (PET-arm): 21 (28%) relative risk reduction: 38% (95% CI, 4%-60%, P =	The number of futile laparotomies was reduced, thus, the addition of (18)F-FDG PET to the work-up for surgical resection of colorectal liver	2b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		FU: at least 3 y				0.042)	metastases prevents unnecessary surgery in 1 of 6 patients.	
[173]	Cohort study	74 patients, 21 with preoperative chemotherapy, 53 without preoperative chemotherapy	PET, PET-CT, CT/MRI, IUS after preoperative chemotherapy	PET, PET-CT, CT/MRI, IUS without preoperative chemotherapy. Analysis per patient and per lesion. Histology, intraoperative ultrasound and intraoperative exam as gold standard	to investigate FDG-PET/CT as a preoperative planning tool for detecting liver lesions in patients with and without preoperative chemotherapy	Accurate tests were six (29%) for the chemotherapy group versus 28 (53%) for the non-chemotherapy group (P = 0.06). 11 (52%) underestimations in the chemotherapy group versus 18 (34%) in the non-chemotherapy group. A total of 1.7 lesions were missed per patient in the chemotherapy group versus 0.7 in those who did not receive chemotherapy.	Preoperative assessment with FDG-PET/CT is not useful for hepatic colorectal metastases, particularly when preoperative chemotherapy is used, with a trend towards underestimation of lesions.	3a

12.1.4. Recherchestrategie Themenkomplex VIII

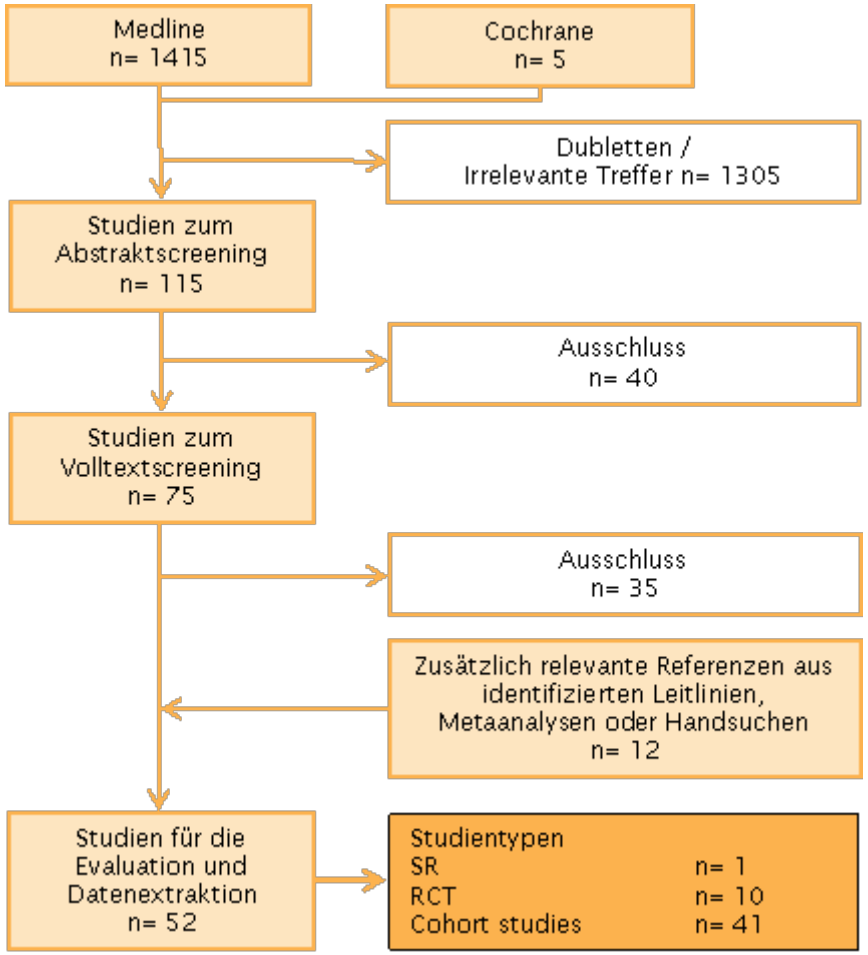

Abbildung 5: Rechercheergebnisse zum Themenkomplex VIII

12.1.4.1. Suchebene 2: Meta-Analysen

Database	Suche	Datum	Treffer	Identifizierte abstracts	Eingeschlossene Volltexte
Cochrane Database of Systematic Reviews	“colorectal neoplasms” in Title, Abstract or Keywords and follow-up in Title, Abstract or Keywords, from 2003 to 2010	08.10.2010	5	1	1
MEDLINE via Pubmed	("colorectal neoplasms"[MeSH Terms] AND ("surveillance"[All Fields] OR "follow up"[All Fields]) AND "Meta-Analysis "[Publication Type] AND ("humans"[MeSH Terms] AND (English[lang] OR German[lang]) AND ("2003/06"[PDAT] : "3000"[PDAT]))	08.10.2010	51	3	3

12.1.4.2. Suchebene 3: Primärliteratur

12.1.4.2.1. *Ergebnisse der systematischen Literaturrecherchen*

Suchfragen	Suchzeitraum	Suchdatum	Treffer	Identifizierte Abstracts (nach Dubletten-abgleich)	Aus-geschlossene Abstracts	Identifizierte Volltext-publikationen	Ein-geschlossene Volltext-publikationen	Zusätzlich ein-geschlossene Volltext-publikationen aus Meta-analysen-suche	Zusätzlich berück-sichtigte Volltext-publikationen (Handsuche, Referenzen-recherche)
1 Effektivität von Nachsorge und Nachsorgemetho den	2006 bis 18.02.2011	18.02.2011	123	5	1	4	0	1	0
2. Bildgebung der Lunge	Bis 23.04.2011	23.04.2011	270	19	3	16	13	0	5
3. Koloskopie	bis 13.02.2011	13.02.2011	457	39	6	33	21	0	7
4. PET/ PET-CT	bis 23.02.2011	23.02.2011	244	34	26	8	2	0	0
5. Reha	bis 21.03.2011	21.03.2011	270	17	4	13	3	0	0

Tabelle 2.8: Ergebnisse der systematischen Literaturrecherchen (MEDLINE via Pubmed)

12.1.4.2.2. *Wie hoch ist die Effektivität einer Nachsorge und der Nachsorgemethoden?*

Suchstrategie

#1 colorectal neoplasms/

#2 randomized controlled trial[Publication Type]

#3 randomization/

#4 randomized controlled trials

#5 double blind method/

#6 single blind method/

#7 random*

#8 #2 or #3 or #4 or #5 or #6 or #7

#9 (recur[MeSH Subheading]) OR recur[Title/Abstract]

#10 recurrence/

#11 neoplasms recurrence, local/

#12 neoplasm metastasis/

#13 #9 or #10 or #11 or #12

#14 follow up studies/

#15 (follow-up[MeSH Subheading]) OR follow-up[Title/Abstract]

#16 longitudinal studies/

#17 survival analysis/

#18	mortality/
#19	prognosis/
#20	office visits/
#21	episode of care/
#22	population surveillance/
#23	physician's practice patterns/
#24	treatment outcome/
#25	"outcome assessment (health care)"/
#26	quality of life/
#27	#14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
#28	#1 and #8 and #13
#29	#1 and #8 and #27
#30	#28 or #29
#31	#30 Limits: Humans
#32	#31 Limits: Publication Date from 2006 to 3000
#33	controlled clinical trials/
#34	controlled clinical trial[Publication Type]

Evidenztabelle

Referenz	Studientyp	Teilnehmer	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE (Level of Evidence)
[174]	Systematic review	8 studies (2141 patients)	Intensive follow-up	Minimalistic or no follow-up	mortality.	OR: 0.73 (95% CI 0.59 to 0.91); RD: 0.06 (95% CI -0.11 to -0.02).	There is a survival benefit for intensifying the FU of patients after curative surgery for crc	1a

12.1.4.2.3. *Hat die Bildgebung der Lunge eine Bedeutung bei der Nachsorge?*

Suchstrategie

#1	colorectal
#2	colonic
#3	sigmoid
#4	rectal
#5	#1 or #2 or #3 or #4
#6	neoplasms
#7	tumor
#8	carcinoma
#9	#6 or #7 or #8
#10	#5 and #9

#11 follow up

#12 follow-up

#13 surveillance

#14 #11 or #12 or #13

#15 #10 and #14

#16 lung imaging

#17 chest imaging

#18 chest x-ray

#19 #16 or #17 or #18

#20 #15 and #19

#21 #20 Limits: English, German; Humans

Evidenztabelle

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[175]	Cohort study	619 pats. With CRC stages II or III who had undergone curative surgery and received adjuvant	chest X-ray annually for 5 years (additionally CEA, colonoscopy, abdominal US; Abdominope	n.a.	relapse detected by chest X-ray	208 patients (33.6%) developed a recurrence. Detection of lung metastases by chest x-ray: 10/208, resection performed: 6/10	Imaging techniques in the survaillence of resected crc contribute to earlier detection of relapse with a high proportion of operable metastatic disease.	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		chemotherapy median FU 66.9 months	lvic CT (in cases with rectal cancer)					
[176]	Cohort study	505 pats with CRC Dukes A-C who had undergone curative surgery FU for at least 4 years	chest x-ray annually for 5 years (additionally CEA, ultrasound and colonoscopy)		relapse detected by Chest X-ray, further surgery	141 patients (27.9%) developed recurrence Detection of lung metastases by chest x-ray =10/141, PPV 0,71 Cured by surgery: 1/10	Follow-up programs should be tailored according to the stage and site of the primary to reduce costs.	4
[177]	Cohort study	496 pat. with colon cancer stage III who had undergone curative surgery and adjuvant chemotherapy median FU 43 months	Chest x-ray after 6 and 12 months and every 12 months for 5 years (additionally CEA, liver ultrasound or CT and colonoscopy)		Detection of recurrence, Resection of lung metastases, Costs per patient	213 patients (42.9%) developed recurrence 1025 chest X-rays were performed Detection of lung mestastase by chest x-ray= 7/213 pats, PPV 0,86 Curative resection: 2/7 Costs (Chest x-ray): US$19 850	The yield of CEA measurement, chest radiography and physical examination was relatively low; such methods were expensive and should not be recommended in the routine follow-up of these patients.	4
[178]	Cohort study	231 pat. with CRC stage I-III who had undergone	Chest x-ray annually for 5 years (additionally abdominal	CEA + ultrasound	Detection of recurrence, Resection of lung metastases,	59 recurrences (26%) 302 chest X-rays performed, cost 9074 Euros Detection of lung mestastase by chest x-ray= 2/59, Resection 0/2	The follow-up tests should only include CEA monitoring and abdominal ultrasonography for the diagnosis of recurrence.	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		curative surgery, 69 pat. With standard FU, 162 pat. Minimal FU FU 5 years	ultrasound, colonoscopy,		total costs			
[179]	Cohort study	239 patients with CRC stage I-III, FU at least 2 years	Chest x-ray at mo. 9, 18, 30, 42 and 60 Visits, lab incl. CEA, liver ultrasonography, endoscopy and/or barium enema		Detection of recurrence, Resection of lung metastases	Recurrences 74 (31%) Detection by chest x-ray: 5/74, PPV 0,56 Resection: 2/5 patients.	Chest x-ray was found to be fairly effective in detecting lung metastases.	4
[180]	Cohort study	190 patients with CRC Dukes A-C median FU 26 months	Chest x-ray after 12, 36 and 0 months (additionally physical examination, rectoscopy, DCE and CEA		Detection of recurrence, Resection of lung metastases,	47 recurrences Detection by chest x-ray: 3/47 recurrences, surgery: 0/3 PPV: 0,75.	Follow-up should include one postoperative colonoscopy and therafter only CEA, chest x-ray, and endoscopic investigations of the anastomotic region.	4
[181]	Cohort study	1356	Chest x-ray		Detection of	421 recurrences (31%)	CEA measurement was the most	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		patients with colon cancer Dukes B2 and C mean FU: 43.6 months	every 3-6 months in the first year, after that every 6-12 months for 4 years, (additionally colonscopy, CEA)		recurrence, Resection of lung metastases, Total costs/ cost per recurrence (chest x-ray)	Detection by chest x-ray: 28/421 recurrences, PPV 0,72 Surgery : 12/28 Costs: US$120,934/ US$10,078	cost-effective test in detecting potentially curable recurrent disease.	
[182]	Cohort study	108 patients with CRC stage I-III Median FU 73 months	Chest x-ray every 6 months for 3 years followed by annually for the next 2 years (additonally clinical examination, CEA, abdominal ultrasound, colonoscopy)		detection and resectability of recurrence	Recurrences 24 patients (22%) Detection by chest x-ray: 4/24, PPV 0,67 resection: 1/4	These data support routine imaging during follow-up	4
[183]	RCT	597 patients with CRC Dukes A-C Mean FU 4.2 years	Program 1: Chest x-ray every 6 months for 3 years, at 48, 60, 90, 120, 150 and 180		detection and resectability of recurrence, PPV	Recurrences 156 patients (26%) Lung metastases (n = 25) Chest x-ray group 1: Sensitivity 100%, Specificity 100% Chest x-ray group 2: Sensitivity 94%, Specificity 100% (96 – 100) Overall:	The present results indicate that clinical examination, digital rectal examination, proctoscopy, colonoscopy and chest x-ray should be included in such a programme	2b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
			months Program 2: Chest x-ray at Months 60, 120 and 180 months Additionally clinical examination, digital rectal examination, proctoscopy, colonoscopy , blood haemoglobin , faecal occult blood test, double contrast braium enema, serum alanine minotransfer ase, and serum bilirubin			Detection: 22/25, PPV 0,88 Resection: 2/22		
[184]	Cohort study	5230 patients with CRC stage I-III. Median FU	Chest x-ray every 6 months for 5-10 years. Additionally		detection and resectability of recurrence,	Recurrences 906 (17%) Detection of recurrence by chest x-ray: 121/906, PPV 0,48 Resection: 95/121 5-year survival after resection of lung	It is useful to take these characteristics of recurrence into account in the management of patients after curative resection for colorectal cancer and in the setting	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		6.6 +/- 3.1 years	colonoscopy, ultrasonography (US) and/or computed tomography (CT) of the liver, and CEA		PPV 5-year survival	metastases 48%	of clinical trial for follow-up after curative resection for colorectal cancer.	
[185]	Cohort study	194 patients with CRC Dukes A-C and regular follow up median FU: 66	Chest x-ray every 6 months for 5 years Additionally CEA, liver ultrasound and colonoscopy		detection and resectability of recurrence, PPV costs	Recurences 78 (40%) Detection of recurrences by chest x-ray: 9/78 Resection: 4/9 912 tests, 7177 US$	Whether the continuing implementation of such program and cost are justified should be debated.	4
[186]	RCT	106 patients with CRC Dukes A-C FU for at least 5 years or until death;	Chest x-ray every 3 months for 2 years, every 6 months for 3 years, addionally CEA, sigmo/colonoscopy, ultrasound, CT		detection and resectability of recurrence, PPV	Recurrences 43 (41%) Detection of recurrences by chest x-ray: 3/43, PPV 0,75 Resection: 0/3	Earlier detection of recurrent crc by intensified FU does not lead to either significantly increased reresectability or improved 5-year-survival	2b
[187]	RCT	107 patients	Chest x-ray		detection	Recurrences 35 (33%)	Intense follow-up did not prolong	2b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		with CRC Dukes A-C, 53 with intense and 52 without follow-up FU 5.5 - 8.8 years	every 3 months for 2 y., every 6 months for 2 y. and after 5 y. Additonally clinical examination, rigid proctosigmoidoscopy, colonoscopy, pelvic CT, liver function test, CEA, FOBT		and resectability of recurrence, PPV	Detection of recurrences by chest x-ray: 3/35, PPV 0,6 Resection: 0/3	survival in this study	
[188]	Cohort study	98 patients with colon cancer and recurrence enrolled in prospective adjuvant trial with Astler-Coller stages B2, B3, C FU up to 5 years	Chest x-ray every 3-4 months in year 1 and every 6-12 mo. Year 2-5, History and physical exam, Liver function test, CEA		detection and resectability of recurrence, PPV	Detection of recurrences by chest x-ray: 18/74, PPV 0,95 Resection: 6/18	The majority of tumor recurrences were detected by symptoms, physical examinations and chest x-rays. Testing for asymptomatic tumor recurrences during the 1st FU year is likely to be much less fruitful for detecting resectable recurrences than testing patients in the 2nd through 4th FU years.	4
[189]	Cohort study	65 patients	Chest x-ray		Detection	Recurrences 17 (26%)	We recommend the the following	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		with CRC Dukes A-C and follow-up mean FU 44.9 months	every 3 mo year 1+2, every 6 mo afterwards Clinical exam, liver function test, CEA level, colonoscopy or barium enema, proctoscopy		rate	Detection of recurrences by chest x-ray: 5/17 Costs: US$ 360 per patients per years	postoperative follow-up schedule: CEA level and chest x-ray every 3 months and colonoscopy every 6 months for the initial 4 years, and CEA level and chest x-ray every 6 months and annual colonoscopy thereafter	
[190]	RCT	259 patients with CRC stage 2 + 3 (132 simple strategy, 127 intensive strategy) median FU 48 months	In intense strategy: Chest x-ray annually Additionally clinical evaluation, CEA, abdominal CT or US, colonoscopy	clinical evaluation and CEA	Survival and recurrence resectability	Recurrences 41% vs. 44% OS: HR = 0.87; 95% CI, 0.49 to 1.54; P = .62 OS stage II tumours: HR = 0.35; 95%CI 0.12-0.98; p= 0.045 Detection of recurrences by chest x-ray: 3/35 Resection: 2/3	A more intensive surveillance strategy improves the prognosis of patients with stage II colorectal cancer or those with rectal tumors. Inclusion of regular performance of colonoscopy seems justified up to the fifth year of follow-up, at least.	2b
[191]	RCT	325 patients with CRC Dukes A-C (158 standard group, 167 intensive group)	Intense group (IG) Chest x-ray annually Colonoscopy , Liver CT	Standard group (SG), clinical review (including complete blood profile, LFTs,	Detection rate, recurrence rate, resection rate survival	Recurrence rate: 120/325 (33%) overall (64 SG, 56 IG) chest x-rays performed: 114 SG, 633 IG; 18/326 patients developed lung metastases (10/159 SG, 8/168 in IG). 4 patients underwent resection (1 SG, 3 IG). 1 patient remains disease free after > 4 years. 1 patient died 48 months after surgery, 1	Yearly colonoscopy, liver CT and chest x-ray will not improve survival from colorectal cancer when added to symptom and simple screening review.	2b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		FU 5 years or until death		CEA, FOBT)		patient died 31 months after surgery.		
[192]	Cohort study	791 patients with CRC stage I-III FU: 5 years	Chest x-ray every 6 mo. for 2 y., then annually History, physical exam, CEA, Colonoscopy		detection and resectability of recurrence, PPV	Recurrences 146 (18%) Detection of recurrences by chest x-ray: 15/146 Resection: 10/15	Patients with early-stage colon cancer have similar sites of recurrence, and receive similar benefit from postrecurrence therapy as late-stage patients; implementation of surveillance guidelines for early-stage patients is appropriate. We would recommend that patients under some manner chest imaging as part of their postoperative surveillance.	4

12.1.4.2.4. *Wie oft sollten Koloskopien im Rahmen der Nachsorge durchgeführt werden?*

Suchstrategie

#1 colorectal neoplasms

#2 follow up studies

#3 follow-up

#4 recur

#5 recurrence

#6 neoplasm recurrence, local

#7 surveillance

#8 colonoscopy

#9 #2 or #3 or #5

#10 #4 or #5 or #6

#11 #9 and #10

#12 #1 and #8 and #9

#13 #12; Limits: Clinical Trial, Randomized Controlled Trial, Comparative Study, Controlled Clinical Trial,Guideline, Multicenter Study, English, German

Evidenztabelle

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[193]	Cohort study	355 patients with CRC stage I-IV FU: 2 years	Colonoscopy between the 1st and 2nd year		presence of adenomas, crc	Presence of adenomas in 89 (25%) patients and crc in 14 (3.9%) patients	Patients with previous or synchronous colorectal adenoma have an increased risk of developing metachronous colorectal neoplasms. Accordingly, this subgroup of patients may benefit from specific surveillance strategies.	4
[194]	Cohort study	481 patients, mean FU 62 months	colonoscopy	Clinical visits, CEA levels	effectiveness of routine colonoscopy and marker evaluation in diagnosis of intraluminal recurrent cance	Number of recurrences 46 (About 10% of patients developed intraluminal recurrences, > 25% adenomatous polyps). >1/2 of the metachronous lesions arise within the first 24 months. The median time to diagnosis was 25 months for intraluminal recurrences and 22 months for adenomatous polyps.	Colonoscopy must be performed within the first 12-15 months after operation, whereas an interval of 24 months between examinations seem sufficient to guarantee early detection of metachronous lesions	4
[195]	Cohort study	175 patients with CRC Astler-Coller A-C2 and at least one follow-up colonoscopy	Colonoscopy after 1 y, and then every 2 years		assess the usefulness of routine colonoscopy in the management of colorectal cancer patients	341 postoperative colonoscopies performed. 11 anastomotic recurrences detected in pat. with rectosigmoid cancer at a mean follow-up of 14 months. Reoperation 8/14 patients underwent re-operation. 3 colon cancers detected (7, 8, 11 months), Curative operation 3/3. Adenomas detected at 12 m. 44 (6 > 10 mm), at 30 m. 20 (0 > 10 mm), at 54 m. 12 (0 > 10 mm)	(1) All colorectal cancer patients should have a total colonoscopy either before (whenever possible) or soon after operation; (2) Based on results of the perioperative colonoscopy, patients: should undergo their first follow-up colonoscopy only 3 yearly (presence of synchronous adenomatous polyps) or 5 yearly (absence of synchronous adenomatous polyps) after resection; (3) In patients with stage B or C primary rectosigmoid cancer, a surveillance of the suture line by	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
							rigid proctosigmoidoscopy should be added during the first 2 postoperative years: 6, 15 and 24 months after the operation	
[177]	Cohort study	496 pat. with colon cancer stage III who had undergone curative surgery and adjuvant chemotherapy median FU 43 months	Colonoscopy after 2 and 5 years liver US or CT, CEA, chest x-ray		clinical value and costs of different diagnostic tools used to identify potentially curable recurrent disease	Recurrences 213 (43%) 13/213 recurrences detected by colonoscopy 8/13 curative resection Cost per curative recurrence 14.952 $	Potentially curable recurrences were detected primarily by liver imaging and colonoscopy.	4
[196]	Cohort study	10801 patients with CRC 61879 personyears of FU			Calculation of the risk of metachronous colorectal cancers Specification of their chracteristics and potential risk factors	The cumulative rate of metachronous crc was 1.8% at 5 years, 3.4% at 10 years and 7.2% at 20 years. The incidence of metachronous crc following a first crc was higher than expected (SIR: 1.5; p<0.001). As compared to solitary cancers, metachronous cancers were diagnosed at earlier stages (23.5% versus 40.9% were stage I; p<0.001).	Patients with crc are at greater risk of developing a metachronous crc. Among them, no predictive factors for the development of metachronous tumors were found. Thus lifelong colonoscopic surveillance is needed.	2b
[197]	Cohort study	220 patients with CRC stages 0-II	Calcium carbonate Colonoscopy at year 1, 3		adenoma recurrence rates	The overall cumulative adenoma recurrence rate was 31% (19% in the first year, 29% for 2 years, and 35% for 3 years).	The substantial adenoma recurrence rate in patients resected of CRC justifies colonoscopic surveillance on a periodic basis.	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
			and 5					
[198]	Cohort study	5716 patients with CRC stages I-III ≥ 65 years FU 36 months	Colonoscopy, sigmoidoscopy		Determination of use of endoscopic follow-up	One or more colonoscopies were performed in 51%, with an average of 2.9 procedures performed among those tested; sigmoidoscopy was performed in 17%. Polypectomy was performed in 21% of all patients, and primary colorectal tumors were diagnosed in 1.3%. Sigmoidoscopy was more common in relation to rectal cancers.	Follow-up colonoscopy may be a worthwhile strategy. The 3-year follow-up suggested by most professional societies appears to be justified.	4
[199]	Cohort study	157 patients (group 1: 42 patients with cancers who underwent preoperative colonoscopy; group 2: 64 patients with benign polyps; group 3: 51 patients who were examined only postoperatively FU 28 -31 months	colonoscopy		Validation of endoscopy (preoperative and follow-up)	Group 1: 7% synchronous CRC, 26% synchronous polyps 7% metachronous CRC, 7% anastomotic recurrences, 12% polyps median interval for noting metachronous lesions was approximately 18 months. Group 3: 4% metachronous CRC, 2% anastomotic recurrences, polyps 45% Median interval for noting metachronous lesions was approximately 8 months	The findings endorsed preoperative colonoscopy and aggressive follow-up in patients with colorectal tumors.	4
[200]	Cohort study	65 patients with CRC	Colonoscopy every 6		Validation of the usefulness of	No recurrence was found solely due to colonoscopy.	As a routine follow-up test, CEA determination is preferable to CT	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		Dukes A-C FU: 6 to 60 months	months for first 2 y., annually afterwards Additionally history, LFT, FOBT, chest x-ry, CEA, CT-abdomen/pelvis, DCE		surveillance		scanning. There was no benefit to the routine use of liver function tests or chest x-rays during follow-up. The most beneficial aspect of the follow-up of these patients is probably the elimination of future metachronous lesions by removal of small, benign polyps by colonoscopy.	
[201]	Cohort study	212 patients with CRC Dukes A-C (Compliant patients: n=88, mean FU 90.7 months; noncompliant patients: n=124, mean FU 94 months)	Partial colonoscopy at month 3,6,9, 18 Colonoscopy at month 12, 24, 36, 48, 60		Evaluation of the effectiveness of a postoperative surveillance program	Tumor recurrence occurred in 10% of compliant and 14% of noncompliant patients. Endoscopy detected all of them. The OS rate was significantly higher (p<0.0002) in compliant patients (5-year actuarial survival: 80%) than in noncompliant patients (5-year actuarial survival: 59%). Noncompliance increased the risk of early death by a factor of 2.5 (95% CI = 1.5; 4.2).	Postoperative endoscopic surveillance leads to early tumor detection, and is associated with an improvement in survival in patients with crc.	4
[202]	Cohort study	3278 patients with resected stage II (650) and stage III (2628) colon cancer Median FU 7.1 y.	colonoscopy or barium enema and flexible sigmoidoscopy after 6, 12 and 18 months and then annually.		To determine the incidence of second primary colorectal cancer after treatment for localized colon cancer.	42 cases of second primary invasive colon cancer were found over 15 345 person-years of follow-up (including 24 in the first two years), yielding an incidence rate of 274 per 100 000 person-years (95% CI, 196 to 369 per 100 000 person-years) and a cumulative incidence of 1.5% (CI, 1.1% to 2.0%) at 5 years. This rate was compared with rates of first colon cancer in two reference groups: the general population and patients who had undergone	The incidence of second primary colorectal cancer remains high despite intensive surveillance strategies.	3b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
						frequent colonoscopy and polypectomy because of a history of adenomatous polyps; standardized incidence ratios were 1.6 (CI, 1.2 to 2.2) and 6.8 (CI, 2.7 to 22.0), respectively.		
[203]	Cohort study	318 patients with CRC without metastases 108 (34%, group A) with a synchronous lesion, 210 (group B) without it. FU unknown	Colonoscopy at 1,3 and 5 y.		Incidence of neoplastic lesions at a scheduled endoscopic follow-up and identification the patients at higher risk of recurrence.	A cumulative neoplastic incidence of 20.1, 32.4 and 44% was observed at 1, 3, and 5 years of FU, respectively (cancers 1.3, 2.9 and 3.3%). The cumulative incidence of all the lesions was 70% in group A and 30.2% in group B at 5-year FU. A neoplastic lesion was detected more frequently in group A at 1 year (30.5% versus 14.7%; p=0.0013), 3 years (21.4% versus 7.6%; p=0.0008) and at 5 years (18.1% versus 7.8%; p=0.02).	The incidence of adenomas in patients operated for crc is fairly high. Crc patients with synchronous lesions are at higher risk of neoplastic recurrence at follow-up as compared to those without them.	4
[204]	Cohort study	432 patients with CRC and a colonoscopy preoperatively and after 1 y. FU 1 year	Colonoscopy after 1 y.		Determination of the diagnostic yield of colonoscopy 1 year after crc resection based on whether the index colonoscopy was performed by the operating surgeon.	The index colonoscopy was performed for in 27.1% by one of the two study surgeons. Overall, 10 patients (2.3%) had a “new” cancer diagnosed at 1 year, and 1 patient (0.2%) had a local recurrence. Patients whose index colonoscopy was performed by their operating surgeon appeared less likely to have an advanced lesion found at 1 year (5.1% vs. 11.4%; p=0.06). The index colonoscopy for 9 of the 10 of cancers found at 1 year was not performed by the operating surgeon.	Colonoscopy 1 year after CRC resection is clearly justified. An index colonoscopy by the operating surgeon eliminates a “handoff” and may diminish the incidence of high-risk lesions at 1 year.	4
[205]	Cohort study	174 patients with CRC Dukes A-C	Colonoscopy annually, additonally		Assessment of the value of a surveillance	CRC recurred in 57 patients, ¾ within the first 24 months. 9 anastomotic recurrences were detected in the 12-30 months interval; none was reoperated	We recommend that patients undergo colonoscopy annually at least for the first 6 years	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		and regular follow-up FU 6 years	history and physical exam, Liver function test, CEA, Chest x-ray		program based on yearly colonoscopy	for cure. 4 metachronous colon cancers were found and resected for cure (3 after 18-24 months, 1 after 36-48 months). 30 polyps larger than 1 cm in size and 7 villous adenomas were removed in 30 patients. Combined, these findings represent an interval yield of 3-5% per year.	postresection of colorectal cancer.	
[185]	Cohort study	314 patients with CRC Dukes A-C; (194 FU group, median FU 66 month; 120 no FU group)	Colonoscopy after 1 and 5 y. additionally CEA, US of the liver, chest x-ray		asymptomatic curable recurrence, compliance with the program	Recurrences 78/194 (40%) 5 recurrences were detected by colonoscopy (3 at colonoscopy after 1 year, 2 after 5 years) All patients had curable disease. No of tests needed to detect one patient with treatable disases: Colonoscopy at 1 y. 36 (costs 5658$) Colonoscopy at 5 y. 27 (costs 4.685$)	The total diagnosis yield with regard to disease-free survival after surgery for recurrence was 9%. Whether the continuing implementation of such program and cost are justified should be debated.	4
[206].	Cohort study	142 patients with resected CRC FU unknown	Colonoscopy or double-contrast examinations within 3 months of surgery, after that every 6 months.		Effectiveness of repeated examinations after radical surgery for cancer.	1 metachronous cancer was detected after 12 months and underwent curative surgery. Within 3 months of radical surgery for colorectal cancer 35 of 142 patients had polypectomy. Repeated examinations every 6 months resulted in recurrence rates for adenomas of 11 of 85, 3 of 46. and 1 of 34. 5 uncomplicated laparotomies were performed after the 629 colonoscopies because of perforation or bleeding	A large number of patients with cancer also have polyps.	4
[207]	Cohort study	3846 patients with CRC Stage I-III FU: at least 5 y. or until death	Colonoscopy after 1 year and depending on result of this 1 or 2-3 years later.		Evaluation of post-operative colonoscopic surveillance	43 cases of metachronous cancer (annual incidence 0.18%). Mean duration of occurrence after primary operation: 71 +/- 46.6 months	Lifelong regular post-operative colonoscopic surveillance is essential for CRC patients.	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[186]	RCT	106 patients with CRC, (54 conventional FU group (cFUG), 52 intensified FU group (iFUG))	cFUG: rigid sigmo for rectal cancers, barium enema every 12 months iFUG: colonoscopyan nually additionally CEA, US, CT, FOBT, chest x-ray, clinical symptoms		Time of detection of recurrence, recurrence rates, first method showing recurrence, mode of recurrencs, and survival	Recurrence: intensified FUG vs. conventional FU g = 10 +5 months vs. 15 +10 months; Recurrence rate: 41% (42% iFUG vs. 39% cFUG) Endoscopy (1/3 recurrences with radical resection) was beneficial in iFUG Cumulative 5-year-survival: 59% iFiUG, 54% cFUG	Endoscopy was beneficial in the intensified follow-up group.	2b
[208]	Cohort study	105 patients with CRC Dukes A-C	Colonoscopy after 2 and 5 years		number of recurrences, number of metachronous tumours, size and number of polyps and their biopsy results	Overall 2 metachronous tumours, 3 recurrences, 24 patients with adenomas (9 multiple/advanced) Number of Colonoscopies: 140 At 2 years: 3 recurrences, 1 metachronous tumour, 4 advanced adenomas , 2 multiple adenomas At 5 years: 1 metachronous tumour, 1 advanced adenoma, 2 multiple adenomas	The risk of development of colonic pathology following curative resection for colorectal cancer is low. More intensive follow-up should be reserved for patients with additional risk of developing further cancers	4
[209]	Cohort study	798 patients with CRC Dukes A-C. 226 pats had 352 colos FU: 1437 patient years	colonoscopy		number and type of metachronous neoplastic lesions, development of new neoplasms, predictive factors of further	9 metachronous cancers in 8 patients, 5 of which were asymptomatic diagnosed by colonoscopy at a mean of 63 months. 3 asymptomatic recurrences were diagnosed but all were inoperable. 70 (31%) patients had adenomatous polyps diagnosed after a mean time from operation of 34 months for simple adenomatous polyps and 21 months for those with advanced features. Patients with multiple polyps or advanced polyps at the initial colonoscopy were more likely to form subsequent	Colonoscopic surveillance intervals need not be less than five years unless the patient has multiple adenomas or advanced adenomas at the first colonoscopy. Three yearly surveillance intervals are most probably adequate in these individuals.	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
					development of polyps or cancer	polyps. Only 5.8% of patients with a single adenoma or a normal colon formed an advanced adenoma over the next 36 months of surveillance.		
[210]	Cohort study	240 patients with CRC and curative surgery,	Colonoscopy annually (n=304)		accuracy and usefulness of FU-methods	11 patients (4.6%) with metachronous CRC, 17 (7.1%) with reucurrences, 42 with tubular adenomas and 9 with villous adenomas (=21.3%). Median time of detection after surgery: metachronous CRC 40 mo, recurrence 26 mo, tubular adenoma 32 mo, villous adenoma 41 mo	Colonoscopy is not only accurate but also easily performed.	4
[211]	Cohort study	41 patients with CRC Dukes A-D and follow-up	Colonoscopy at 6, 12 months and then annually. Additionally CEA, CT-abdomen and chest-x-ray		Evaluation of CT scan, colonoscopy and tumour markers	2/41 with recurrence (1 and 2 years after surgery) -> resection	The systematic postoperative follow-up of the patients with colorectal cancer through CT, colonoscopy and the use of tumour markers contributes decisively to the early diagnosis and treatment of any possible recurrence of the cancer or a metachronous cancer or misdiagnosed concomitant cancer.	4
[187]	RCT	107 patients with CRC Dukes A-C, 53 with intense and 52 without follow-up FU 5.5 - 8.8 years	Colonoscopy at 3, 15, 30 and 60 mo. Additonally clinical examination, rigid proctosigmoid oscopy, pelvic CT, chest x-ray, liver function test, CEA, FOBT		survival	Recurrence: CG 18 pats (33%), FUG 17 (32%) Colonoscopy: Sensitivity: 0 Specificity:100 Predictive Value of a negative test: 96 Accuracy: 96	Intense follow-up did not prolong survival in this study	2b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[212]	Cohort study	100 patients with CRC Stage I-III	Colonoscopy median interval 3 years		tumour location, stage (TNM) and screening intervals	Metachronous advanced adenoma/carcinoma in patients with no synchronous neoplasm at surgery: after 3 years 4.8%, after 5 years 3.9% In patients with synchronous neoplasm at surgery: after 3 years 22.6%, at 5 years 24.4%	Patients who undergo curative resection of a colorectal cancer and have no synchronous neoplasms are at lower risk of developing metachronous neoplasms. A less intensive colonoscopic surveillance programme may be more appropriate.	4
[213]	Cohort study	1002 pat. with CRC stage I-III median FU 3.6 years	Colonoscopy, sigmoidoscopy and barium enema		survival	97% of all follow-up exams were colonoscopies. 20 patients (3.1%) with second cancer (9 within 18 months). Advanced neoplasia 7.3%. 5-year survival for patients who had at least one follow-up exam 76.8%, no follow-up 52.2% (P < .0001) Multivariate analysis of colon examination and survival hazard ratio, 0.58; 95% confidence interval, 0.44–0.75.	After colorectal cancer resection, patients have a high risk of interval cancers. Therefore, surveillance colonoscopy within 1 year of initial diagnosis is warranted. After adjusting for key variables, endoscopic surveillance is associated with improved survival.	3b
[191]	RCT	325 patients with CRC Dukes A-C (158 standard group, 167 intensive group) FU 5 years or until death	Intense group (IG) annual Colonoscopy, Liver CT and Chest x-ray	Standard group (SG), clinical review (including complete blood profile, LFTs, CEA, FOBT)	Detection rate, recurrence rate, resection rate survival	Recurrence rate: 120/325 (33%) overall (64 SG, 56 IG) Colonoscopies SG 154, IG 577 Metachronous and locally recurrent carcinomas: 13 (SG), 10 (IG); all but one (IG) were found in assiciacion with symptoms, signs or screening test abnormalties; Deaths: 98 (55 SG, 43 IG); No significant difference in survival (p=0.1986)	Yearly colonoscopy, liver CT and chest x-ray will not improve survival from colorectal cancer when added to symptom and simple screening review	2b
[214]	Cohort study	341 patients with CRC and curative	Colonoscopy (in 91% 1st exam within 3		Identification of the high-risk groups for	22 metacronous colorectal carcinomas in 19 patients were detected and 14 (64%) of 22 were detected within 5 years of surgery. Cumulative	We recommend that patients with the above predictive factors receive surveillance colonoscopy	4

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
		resetion and surveillance colonoscopy Mean FU 6.2 (range, 3-17) years	y.)		metachronous colorectal carcinoma	incidence of developing colorectal carcinomas during a 5-year period was 5.3%. Significant Predictive factors: extracolonic malignancy, coexistence of adenoma, and synchronous multiple colorectal carcinoma possible predictive factor: family history of colorectal carcinoma	meticulously and regularly.	
[215]	RCT	326 patients (165 intensive colonosc. Surv. group=ICS; 161 routine cs=RCS)	Colonoscopy ICS at mo 3, 6, 9, 12, 18, 24, 30, 36 and annually after this RCS at mo 6, 30 and 60		Survival, recurrence resectability	5-year survival rate; ICS 77%, RCS 73% (p > 0.05). Postoperative CRC detected: ICS 13 patients (8.1%), RCS 18 patients (11.4%). Asymptomatic postoperative CRC: ICS vs. RCS 10 vs. 7 (p=0.04) Reoperation with curative intent: ICS vs. RCS 9 vs. 6 (p=0.048) survival after postoperative CRC ICS vs. RCS 69 mo vs. 24 (p=0.03).	Although the patients in the ICS group had more curative operations for postoperative CRC and survived significantly longer, ICS itself did not improve overall survival.	2b

12.1.4.2.5. *Hat das PET/PET-CT eine Bedeutung bei der Nachsorge*

Suchstrategie

#1	colorectal
#2	colonic
#3	sigmoid
#4	rectal
#5	anus
#6	#1 or #2 or #3 or #4 or #5
#7	neoplasms
#8	tumor
#9	carcinoma
#10	#7 or #8 or #9
#11	#6 and #10
#12	follow up
#13	follow-up
#14	surveillance
#15	#12 or #13 or #14
#16	#11 and #15
#17	PET
#18	#16 and #17

#19 #18 Limits: Humans

#20 #19 Limits: English, German

Evidenztabelle

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[216]	RCT	130 patients with CRC and curative R0-resections (65 conventional, 65 PET), FU. 2 years or until death	FDG-PET after 9 and 15 mo. Addtionally PE, CEA, ultrasound, chest x-ray and CT-abdomen after 9 and 15 mo.	CT-abdomen after 9 and 15 mo. Addtionally PE, CEA, ultrasound, chest x-ray	To detect recurrences after 9 + 15 mo	Recurrences 44 (34%) (23 in the PET group and 21 the Con group; P=0,6). Detection of recurrence: PET 12.1 vs. 15.4 mo in the Con group (p=0.01) Curative surgical resection PET 10/23 (44%), Con 2/21 (10%). Overall rates of sensitivity, specificity, positive predictive value, negative predictive values for detecting recurrence were 91, 93, 88.6 and 95% respectively in the conventional arm, and 96, 92.1, 89.2 and 97.2%, respectively in the PET arm.	Using this new follow-up strategy increased the rate of curative resection (R0) in patients by allowing us to detect CRC recurrences at an earlier stage. We would therefore expect improved patient survival if such a follow-up programme was undertaken.	2b
[217]	Cohort study	31 patients with CRC Dukes B+C	FDG-PET after 2 y., addtionally CT + MRI at 6 + 12 mo., CEA, colonoscopy		To assess the role FDG-PET imaging	The sensitivity was 100% and specificity 83.3%. Clinical management was altered in two cases (6.4%). 2 of 3 patients with a FDG-PET true-positive result who underwent surgery had a macroscopically curative resection that was not shown on CT.	For this reason FDG-PET should be considered in the routine postoperative assessment at 12 months	4

12.1.4.2.6. *Nachsorge – Reha (Physical activity)*

Suchstrategie

#1	colorectal
#2	colonic
#3	sigmoid
#4	rectal
#5	#1 or #2 or #3 or #4
#6	neoplasms
#7	tumor
#8	carcinoma
#9	#6 or #7 or #8
#10	#5 and #9
#11	physical activity
#12	life style
#13	#11 or #12
#14	survival
#15	recurrence
#16	recur
#17	#14 or #15 or #16

#18 #10 and #13 and #17

#19 #18 Limits: Humans, English, German

Evidenztabelle

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
[218]	Cohort study	573 women with CRC stage I-III Mean FU 9,6 years	leisure-time physical activity in metabolic equivalent task (MET) - hours per week		CRC and overall mortality	Comparison of patients who reported less than 3 total MET-hours per week of activity and those reporting 18 or more MET-hours per week: Adjusted HR for cancer-specific mortality 0.39 (95% CI, 0.18 to 0.82; P= .008). Adjusted HR for overall mortality 0.43 (95% CI, 0.25 to 0.74; P=.003).	Recreational physical activity after the diagnosis of stages I to III colorectal cancer may reduce the risk of colorectal cancer-specific and overall mortality.	2b
[219]	Cohort study	668 men with CRC stage I-III Mean FU 8.6 year	leisure-time physical activity in metabolic equivalent task (MET) - hours per week		CRC and overall mortality	Comparison of patients who reported 3 or less MET hours per week of physical activity (15.4% of the cohort) and those reporting more than 27 MET hours per week of physical activity (38.1% of the cohort): Adjusted HR for colorectal cancer-specific mortality 0.47 (95% CI, 0.24-0.92; P=.002 for trend) Adjusted HR for overall mortality 0.59 (95% CI, 0.41-0.86; P=.001 for trend).	In a large cohort of men with a history of nonmetastatic colorectal cancer, more physical activity was associated with a lower risk of colorectal cancer-specific and overall mortality.	2b
[220]	Cohort study	832 patients with Colon cancer stage III Mean FU 3.8 years	leisure-time physical activity in metabolic equivalent task (MET) - hours per week		time to cancer recurrence or death as a result of any cause	Comparison of patients who reported < 3 total MET-hours per week of activity and those reporting 18 to 26.9 total MET-hours per week: multivariate HR for disease-free survival 0.51 (95% CI, 0.26 to 0.97) Comparison of patients < 3 total MET-hours per week of activity with greater than 27 total	For patients who survive and are recurrence free approximately 6 months after adjuvant chemotherapy, physical activity appears to reduce the risk of cancer recurrence and mortality.	2b

Referenz	Studientyp	Teilnehmer / Follow-up	Intervention	Kontrolle	Zielgrößen	Hauptergebnis	Bewertung der Autoren	LoE
						MET-hours per week: HR for disease-free survival 0.55 (95% CI, 0.33 to 0.91; P=.01).		

13. Anhänge

13.1. Schema der Evidenzgraduierung nach Oxford: Oxford Centre for Evidence-based Medicine Levels of Evidence (2009)

Level	Therapy / Prevention, Aetiology / Harm	Prognosis	Diagnosis	Differential diagnosis / symptom prevalence study	Economic and decision analyses
1a	SR (with homogeneity) of RCTs	SR (with homogeneity) inception cohort studies; CDR validated in different populations	SR (with homogeneity) of Level 1 diagnostic studies; CDR with 1b studies from different clinical centres	SR (with homogeneity) of prospective cohort studies	SR (with homogeneity) of Level 1economic studies
1b	Individual RCT (with narrow Confidence Interval)	Individual inception cohort study with > 80% follow-up; CDR validated in a single population	Validating cohort study with good reference standards; or CDR tested within one clinical centre	Prospective cohort study with good follow-up	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
2a	SR (with homogeneity) of cohort studies	SR (with homogeneity) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity) of Level >2 diagnostic studies	SR (with homogeneity) of Level 2b and better studies	SR (with homogeneity) of Level >2 economic studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of CDR or validated on split-sample only	Exploratory cohort study with good reference standards; CDR after derivation, or validated only on split-sample or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses

Oxford Centre for Evidence-based Medicine Levels of Evidence (2009)

Level	Therapy / Prevention, Aetiology / Harm	Prognosis	Diagnosis	Differential diagnosis / symptom prevalence study	Economic and decision analyses
2c	"Outcomes" Research; Ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research
3a	SR (with homogeneity) of case-control studies		SR (with homogeneity) of 3b and better studies	SR (with homogeneity) of 3b and better studies	SR (with homogeneity) of 3b and better studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study; or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations
4	Case-series (and poor quality cohort and case-control studies)	Case-series (and poor quality prognostic cohort studies)	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

Tabelle 5.2: Schema der Evidenzgraduierung nach Oxford

13.2. Interessenkonflikterklärungen

AWMF-Formular zur Erklärung von Interessenkonflikten im Rahmen von Leitlinienvorhaben (http://www.dggg.de/fileadmin/public_docs/Leitlinien/Interessenkonflikterklaerung_Leitlinien.pdf; Stand 08.02.2010) sieht die Darlegung zu folgenden Punkten vor:

1. Berater- bzw. Gutachtertätigkeit oder bezahlte Mitarbeit in einem wissenschaftlichen Beirat eines Unternehmens der Gesundheitswirtschaft (z.B. Arzneimittelindustrie, Medizinproduktindustrie), eines kommerziell orientierten Auftragsinstituts oder einer Versicherung

2. Honorare für Vortrags- und Schulungstätigkeiten oder bezahlte Autoren- oder Co-Autorenschaften im Auftrag eines Unternehmens der Gesundheitswirtschaft, eines kommerziell orientierten Auftragsinstituts oder einer Versicherung

3. Finanzielle Zuwendungen (Drittmittel) für Forschungsvorhaben oder direkte Finanzierung von Mitarbeitern der Einrichtung von Seiten eines Unternehmens der Gesundheitswirtschaft, eines kommerziell orientierten Auftragsinstituts oder einer Versicherung

4. Eigentümerinteresse an Arzneimitteln/Medizinprodukten (z. B. Patent, Urheberrecht, Verkaufslizenz)

5. Besitz von Geschäftsanteilen, Aktien, Fonds mit Beteiligung von Unternehmen der Gesundheitswirtschaft

6. Persönliche Beziehungen zu einem Vertretungsberechtigten eines Unternehmens Gesundheitswirtschaft

7. Mitglied von in Zusammenhang mit der Leitlinienentwicklung relevanten Fachgesellschaften/Berufsverbänden, Mandatsträger im Rahmen der Leitlinienentwicklung

8. Politische, akademische (z.B. Zugehörigkeit zu bestimmten „Schulen"), wissenschaftliche oder persönliche Interessen, die mögliche Konflikte begründen könnten

9. Gegenwärtiger Arbeitgeber, relevante frühere Arbeitgeber der letzten 3 Jahre

Bewertung

Ergeben sich aus allen oben angeführten Punkten nach Ihrer Meinung für Sie oder die ganze Leitliniengruppe bedeutsame Interessenkonflikte?

Tabelle 11: Interessenkonflikterklärungen der Leitliniengruppe

Name	Berater- bzw. Gutachtertätigkeit	Vortrags- und Schulungstätig-keiten	Drittmittel für Forschungs-vorhaben	Patente	Besitz von Geschäfts-anteilen	Persönliche Beziehungen	Mitglied von Fachgesell-schaften	persönliche Interessen
Bischoff, Stephan C.	Danone	Falk, Yakult, Danone, Nestlé, u.a.	Merck	/	ZKES	/	DGEM, DGMIM	/
Bokemeyer, Bernd	Abbott, MSD, Ferring, Movetis	/	/	/	/	/	Bng	/
Brambs, Hans-Jürgen	/	/	/	/	Bayer, Pfizer, Novartis, Roche	/	DRG	/
Brenner, Hermann	/	/	Eiker Chemicals	/	/	/	DKG, DGEpi, gmds	/
Engeser, Peter	/	/	/	/	/	/	DGAM, HÄV	/
Epplen, Jörg T.	/	/	/	/	/	/	DfH, BVDH	/
Fischbach, Wolfgang	Pfizer, Norgine, Fresenius	Falk, Abbott, Pfizer, Norgine	/	/	/	/	DGVS	/
Graeven, Ullrich	Amgen, Roche, AstraZeneca, Sanofi	Amgen, Roche, AstraZeneca, Sanofi, Merck	/	/	/	/	DKG, DGHO, DGVS, AIO	/

Name	Berater- bzw. Gutachtertätigkeit	Vortrags- und Schulungstätig-keiten	Drittmittel für Forschungs-vorhaben	Patente	Besitz von Geschäfts-anteilen	Persönliche Beziehungen	Mitglied von Fachgesell-schaften	persönliche Interessen
Haß, Maria	/	/	/	/	/	/	/	/
Heike, Michael	Ganymed	/	/	/	/	/	DGVS, DGHO, DGIM	/
Heußner, Pia	Roche, Onko Inform, Glaxo Smith Kline, 4 Sigma	Roche, Onko Inform, 4 Sigma	/	/	/	/	DKG (AIO, PSO), DGHO	/
Höhler, Thomas	/	Roche, Merck	/	/	/	/	DGVS, DGHO	/
Hohenberger, Werner	/	Roche, Siemens, BMBF, Hollister, Lilly	6 Studien	/	/	/	DKG, DGCH, DGAV	/
Holstege, Axel	/	Roche, Falk	/	/	/	/	DGVS, AIO	/
Hübner, Jutta	/	Roche, Glaxo Smith Kline, Pfizer, Pierre Fabre	/	/	/	/	DKG (PRIO), DGP, DGHO	/
Jauch, Karl-Walter	/	Pfizer, Falk	Fresenius, Pfizer, Novartis, Roche	/	/	/	S3-LL Ernährungsmedizin	/
Kirchner, Thomas	Amgen, Merck-Serono, AstroZeneca	Amgen, Merck-Serono, Roche, Epigenomics	Roche, Deliniens	/	Roche, Merck, Rhönklinikum	/	DGP, BGP	/

Name	Berater- bzw. Gutachtertätigkeit	Vortrags- und Schulungstätig-keiten	Drittmittel für Forschungs-vorhaben	Patente	Besitz von Geschäfts-anteilen	Persönliche Beziehungen	Mitglied von Fachgesell-schaften	persönliche Interessen
		AG			, Novartis			
Körber, Jürgen	/	/	/	/	/	/	DKG (ASORS), GRVS	/
Kolligs, Frank	HCC, Bayer	Falk	/	/	/	/	DKG, DGVS	/
Kopp, Ina	/	/	/	/	/	/	AWMF, DNEbM, DGCH	/
Kreis, Martin	/	Nycomed	Steigerwald	/	/	/	DGCH, DGAV, CACP	/
Landenberger, Margarete	/	/	/	/	/	/	DKG (KOK)	/
Lang, Hauke	Nycomed	Nycomed	/	/	/	/	DKG, DGAV (CAO-V)	/
Layer, Peter	Abbott, Ardey, Axcan, Olympus, BerlinChemie, Boehringer Ingelheim, Falk, Fischer, Given Imaging, Norgine, Novartis, Shire, Nycomed, Lilly, Steigerwald	Abbott, Ardey, Axcan, BerlinChemie, Boehringer Ingelheim, Falk, Fischer, Given Imaging, Lilly, Norgine, Novartis, Nycomed, Olympus, Shire, Steigerwald	Abbott, Ardey, Axcan, BerlinChemie, Boehringer Ingelheim, Falk, Fischer, Given Imaging, Lilly, Norgine, Novartis, Nycomed, Olympus, Shire, Steigerwald	/	/	/	DGVS, LL Reizdarm	/

Name	Berater- bzw. Gutachtertätigkeit	Vortrags- und Schulungstätig-keiten	Drittmittel für Forschungs-vorhaben	Patente	Besitz von Geschäfts-anteilen	Persönliche Beziehungen	Mitglied von Fachgesell-schaften	persönliche Interessen
Link, Hartmut	Amgen, Johnson & Johnson, Ratiopharm, Sandoz, Vifor	Amgen, Ortho Biotech, Ratiopharm, Vifor	Amgen, Lilly, Roche	/	/	/	DKG, DGHO, DGIM, EORTC, PEG	/
Link, Karl-Heinrich	/	/	/	/	/	/	DGAV (CAO-V)	/
Lippert, Hans	/	Nycomed (2009)	/	1 Patent	/	/	DGAV	/
Ludt, Sabine	/	/	/	/	/	/	DGEM, AQUA	/
Lux, Philipp	/	ECMT	/	/	/	/	/	/
Maar, Christa	/	/	/	/	/	/	DGVS	/
Melle, Ulrike	/	/	/	/	/	/	DKG, AIO	/
Ockenga, Johann	Abbott	Fresenius, Kabi, Braun Melsungen, Roche, Pfrimmer, Nutricia, Baxter	/	/	/	/	DGVS, DGEM	/
Pereira, Philippe	/	Siemens, Celon-Olympus, Celonova, Bayer	Celon-Olympus, Siemens, Bracco	/	/	/	DGIM, DRG	/

Name	Berater- bzw. Gutachtertätigkeit	Vortrags- und Schulungstätig-keiten	Drittmittel für Forschungs-vorhaben	Patente	Besitz von Geschäfts-anteilen	Persönliche Beziehungen	Mitglied von Fachgesell-schaften	persönliche Interessen
Porschen, Rainer	/	Sanofi, Pfizer	/	/	/	/	DGVS	/
Post, Stefan	/	Johnson & Johnson, Roche, Merck, Siemens, Merck	Abraxis, Agennic, Amgen, Apogenix, Ariad, Arqule, Astra-Zeneca, Bayer, Böhringer Ingelheim, Celgene, Daiichi, EISAI, Erbe, Ethicon / J&J, Falk Foundation, GlaxoSmithKline, GSK, Imclone, ImClone, Infinity, Lilly, Merck, MSD, Novartis, Pfizer, PharmaMar, Roche, Transgene, Ziopharm	/	/	/	DGAV	/
Pox, Christian	Abbott, AQUA	AstraZeneca, Falk, Hitachi, Roche,	/	/	/	/	DKG, DGVS, AIO	/
Propping, Peter	DKH, Bundesärztekammer, Hallesche Lebensversicherung, Alte Leipziger Lebensversicherung	/	DKH	/	/	/	DfH	/

Name	Berater- bzw. Gutachtertätigkeit	Vortrags- und Schulungstätig-keiten	Drittmittel für Forschungs-vorhaben	Patente	Besitz von Geschäfts-anteilen	Persönliche Beziehungen	Mitglied von Fachgesell-schaften	persönliche Interessen
Raab, Hans-Rudolph	ACQUIN, AQUA, Fehling	Merck-Serano	/	Fehling	/	Fehling (Guido Fehling)	DKG, DGAV, BDC	/
Rahner, Nils	/	/	DKH	/	/	/	DfH	/
Reinacher-Schick, Anke	Amgen, Pfizer, Sanofi, Roche	Amgen, Pfizer, Sanofi, Roche	Sanofi, Roche	/	/	/	DGVS, AIO	/
Riemann, Jürgen	BMG, BKK24, DAK, Barmer, GEK, Given Imaging, Epigenomica, Bayer Vital, Eiai, Shire, BDI, DGVS, Schlichtungsstellen der Ärztekammern, div. Zeitschriften	Falk, Bayer Vital, Given Imaging, ABDA, Recordati Pharma	BMG (FAMKOL-Studie)	/	/	/	DGVS, DGIM, Stiftung Lebensblicke	/
Rödel, Claus	/	Roche	/	/	/	/	DEGRO	/
Sauer, Rolf	/	/	/	/	/	/	DEGRO	/
Sauerbruch, Tilman	Falk	/	/	/	/	/	DGVS, DGIM	/
Scheidhauer, Klemens	Gutachtertätogkeit (Verlage, Gerichte)	Vorträge (<2000 EUR/Jahr)	Drittmittel für Forschungs-projekte	/	<10.000 EUR	/	DGN, Bayr., Europ., US-amerikan. Fachgesell-schaft für Nuklearmedizin	/

Name	Berater- bzw. Gutachtertätigkeit	Vortrags- und Schulungstätig-keiten	Drittmittel für Forschungs-vorhaben	Patente	Besitz von Geschäfts-anteilen	Persönliche Beziehungen	Mitglied von Fachgesell-schaften	persönliche Interessen
Scheppach, Wolfgang	/	/	/	/	/	/	DGVS	/
Schmiegel, Wolff	Apceth, Amgen, AstraZeneca, Merck, Roche	Abbott, Falk Foundation, GSB GmbH, Lilly Deutschland GmbH, MCI, MedCongress, Merck Serono, Pfizer, Roche, Siemens Healthcare, Honorare für Publikationen von: Deutschland-funk (DLF), Deutsches Ärzteblatt, Elsevier Verlag, Springer Verlag, Westdeutscher Rundfunk (WDR), Zweites Deutsches Fernsehen (ZDF)	Sponsoren von Studien an der Medizinischen Klinik der Ruhr-Universität Bochum: Abbot, Amgen, Astra Zeneca, Bayer,Chugai Pharma, Clovis, Essex Pharma, GlaxoSmithKline, Ganymed, Merck, Novartis, Roche Pharma, Sanofi, Schwarz Pharma, AIO, Deutsche Krebshilfe (DKH), Deutsche Krebsgesellschaft (DKG), German Hodgkin Study Group (GSHG), Deutsche Studiengruppe Hochmaligne Non-Hodgkin-Lymphome (DSHNHL)	8 Patent-anmeldungen*	Medmotive GmbH: Bisher keinerlei Geschäfts-betrieb Bis 2010 Anteile am West-deutsches Darm-Centrum GmbH Mitgesell-schafter der Firma HeparDiag Biotech GmbH, (Dez. 2012 gegründet) Bisher keinerlei Geschäfts´-betrieb, kein Bezug zu Darmkrebs	/	DGVS, DKG, AIO	/

Name	Berater- bzw. Gutachtertätigkeit	Vortrags- und Schulungstätig-keiten	Drittmittel für Forschungs-vorhaben	Patente	Besitz von Geschäfts-anteilen	Persönliche Beziehungen	Mitglied von Fachgesell-schaften	persönliche Interessen
Schulmann, Karsten	/	/	/	/	/	/	DKG, DGVS, AIO	/
Sieg, Andreas	Capso Vision	/	Capso Vision (Studie zur Dünndarm-Kapselendoskopie)	/	/	/	DGVS, bng	/
Stemmler, Susanne	/	/	/	/	/	/	DfH	/
Tannapfel, Andrea	Berufsgenossen-schaften, Sozialgerichte	Amgen, Pfizer, Merck, Astrazeneca, Med. Update, Roche, Falk, Recordati	/	/	/	/	DGP, DGAV, DGE-BV	/
Theilmeier, Arno	/	/	/	/	/	/	DGVS, bng	/
Vogl, Thomas J.	carestream	/	Siemens	/	/	/	DRG	/
Wagener, Christoph	/	/	/	/	/	/	DGKL	/
Walz, Martin K.	Covidien	Covidien, Storz	Covidien	/	/	/	DGCH, DGAV	/
Weber, Klaus	/	/	/	/	/	/	DGCH, BDC	/

Name	Berater- bzw. Gutachtertätigkeit	Vortrags- und Schulungstätig-keiten	Drittmittel für Forschungs-vorhaben	Patente	Besitz von Geschäfts-anteilen	Persönliche Beziehungen	Mitglied von Fachgesell-schaften	persönliche Interessen
Weitz, Jürgen	Covidien, Astella	Ethicon, Covidien, Aesculap	Ethicon	/	/	/	DGAV	/
Witte, Christine	/	/	/	/	/	/	DCCV	/
Wittekind, Christian	/	/	/	/	/	/	DGP, BDP	/

Legende:

* Alle Patentanmeldungen wurden bisher nicht lizensiert, daher bisher kein Einkommen oder Wertschöpfung. Folgende Patentanmeldungen werden angezeigt:

1. Lösliches Cadherin 17 für die Diagnose und Risikostratifizierung von Darmtumor und Darmkrebs Internationale Patentanmeldung: PCT/DE2008/001220
2. Buproprion – Verwendung von Bupropion in Arzneimittel zur Behandlung von Hepatitis C Patentanmeldung Deutschland: DE 10 2004 063 132.8-41
3. Biomarker für hepatische Fibrose Patentanmeldung Deutschland: DE 10 2006 048249.2., Internationale Patentanmeldung PCT/DE 2007001427
4. Statine/HMG-CoA Reduktase Hemmer zur Herstellung von Mitteln, die sich zur Primär- und Sekundärprävention sowie zur Behandlung von hyperplastischen oder dysplastischen Dickdarmpolypen eignen. Patentanmeldung Deutschland DE 10 2004 036 907.0-41
5. Biomarker für die Diagnose von Pankreaskrebs Internationale Patentanmeldung PCT/DE2007/002174
6. Immunoscreening of the Extracellular Proteome of Colorectal Cancer Cells Patentanmeldung USA US 61/176,353
7. Diagnoseverfahrung und Verwendung von MicroRNA Patentanmeldung Deutschland 10 2010 046 866.5
8. Pantumormarker Patentanmeldung Deutschland 10 2011 108 254.2

14. Abbildungsverzeichnis

15. Tabellenverzeichnis

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