食欲不振，嘔気，下痢などがおもな有害事象である．これ以外では肝機能障害（総ビリルビン上昇，AST/ALT 上昇）が認められることがある．したがって，治療開始前には，これらの全身状態や臨床検査値が一定範囲内に改善していることが必要である．

2. 開始時期

術後補助療法の開始時期に関しては，全身状態の回復状況と切除組織の病理診断，とくにリンパ節転移の有無が判明してからになるため，一般には術後4週から12週頃までに開始されている．厳密には早期開始の意義や開始時期の高度遅延の再発抑制効果に関するデータは少ないので，上記期間は目安となる．臨床的にも術後退院し，初回外来時に全身状態や臨床検査値，および病理診断などを基に患者に説明することで大きな問題は生じていない．

3. 投与量

術後補助療法の抗癌剤投与量は，従来とは異なり，十分量の投与量が使用されるのが最近の傾向である．標準治療の5FUとアイソボリン併用療法は，5FU 500 mg/m^{2}とアイソボリン250 mg/m^{2}を週1回，6週間連続，2週休薬を1コースとして，3コース/6カ月を行う治療である．海外投与量と同様であり，切除不能転移・再発大腸癌に対する投与量とは5FUが600 mg/m^{2}から500 mg/m^{2}に減量されただけである．国内での経験でも，上記の条件を満たす患者であれば多くの患者で継続投与可能である．有害事象を恐れて早期に減量を行い，再発抑制効果を失うことは避けなければならない．

4. 経口抗癌剤

術後補助療法の治療レジメンに関しては，5FUとアイソボリン併用療法が標準であるが，毎週の外来受診と外来治療のための2時間以上の拘束が問題である．さらに，5FU急速静注に伴う，白血球減少や下痢，脱水など，時に緊急入院を必要とする有害事象も認められる．これらは術後早期に社会復帰を目指す患者にとって重要な問題である．

そのため，静注治療からフッ化ピリミジン系経口抗癌剤に移行することが試みられている．あくまでも5FUとロイコボリン併用療法を対照としたRCTにより，経口剤が無再発生存や生存期間で劣らないことと，有害事象を含めたなんらかの臨床的な利益を検証することが必要である．この結果，UFT/LVおよびカペシタビンの2種類が術後補助療法として静注群に置き換え可能と考えられている．この基になったRCTはNSABP C-06試験とX-Act試験であり，いずれも海外でのRCTである．また，前者はStage IIとIIIが半々を占める対象群である．このような試験の背景を考慮して，海外臨床試験成績をどのように評価し判断するかは慎重にすべきと考えられている．

国内臨床試験成績としてTAC-CRおよびNSAS-CCの直腸癌の成績が報告されている．いずれも手術単独群を対照としたUFT単独療法の評価である．直腸癌においてはいずれの試験でもUFT群の治療成績が良く，かつ手術単独群の無再発生存期間や生存期間もきわめて良好である成績が示されている．国内外の手術成績の優劣は一言で判断することは難しいが，大規模試験での多施設治療成績を継続的に集積することで判明すると考えられる．

5. オキサリプラチンの併用

最近報告されたオキサリプラチンの術後補助療法での有用性に関する二つの海外RCTについても言及する．

MOSAIC試験およびNSABP C-07試験ではFOLFOX4およびFLOX（急速静注の5-FU＋LVにオキサリプラチンを併用）と5FU/LVの投与スケジュールが異なるものの，オキサリプラチンの併用により再発抑制効果を認めたという試験成績である．問題となる末梢神経障害についても，投与終了1年で臨床的に問題にならないレベルに改善するということで，海外では術後補助療法の標準治療が5FU/LVから

FOLFOX4へ移行しているとのことである．FLOXは血液毒性が若干強く，まだ一般臨床での導入は少ないようである．このような状況で，国内臨床において術後補助療法にオキサリプラチンを導入するかどうかということが問題になっている．とくにまだ治療成績の良くないStage IIIbなどには積極的に使用したいとの意見もある．

しかしながら，現時点では術後補助療法としては国内保険承認が得られておらず適応外使用であること，FOLFOX療法は切除不能転移・再発大腸癌の標準治療でもあり，多くの医療機関で外来治療のキャパシティをすでに超えていることなどから現時点では実施できない．今後，オキサリプラチン併用療法の術後補助療法での意義を国内医療環境で再確認する必要があると考える．

II. 切除不能転移・再発大腸癌に対する化学療法

1. 目　的

この対象は，治癒の望めない患者であり，抗癌剤治療を行わない場合の生存期間は約8カ月である．今回の治療ガイドラインでは，予後に関する具体的な記述を行うことにより，抗癌剤治療による延命効果の可能性と，その限界を担当医自身に認識してもらう意図がある．治療経過を検討し，残された期間と使用可能薬剤および有害事象を考慮して総合的に治療継続の可否を判断することが必要である．

また，補助療法と同様に標準治療が確立され，一次治療，二次治療までは一定の治療方針が示されている．したがって，三次治療以降に関しては研究段階であり，一般臨床での推奨される抗癌剤レジメンはないことになる．患者の全身状態を客観的に評価し，継続治療の可能性に関して，患者本人，家族の意向も考慮したうえで，抗癌剤治療を選択するか，緩和ケアを選択するかを判断する必要がある．患者，家族の希望があるからといって，有効性が明らかでない治療を継続することは避ける必要がある．必ず抗癌剤治療に伴う有害事象が生活の質を低下させる可能性が大きいからである．

治療の目的は，腫瘍増大に関連する症状コントロールである．治癒ではないことを再度認識しておく必要がある．このためには，全身状態の良好なPS 0～2までの症例を対象とすることが勧められる．比較試験において抗癌剤治療により生存期間の延長が確認された対象はこのような対象であり，PS不良例ではその効果については不明であるからである．

抗癌剤治療の適応基準に関しては，PS良好例，臓器機能が保たれている，画像診断にて腫瘍部位が確認できるなどである．腹膜転移などは画像上判定できないこともあるが，他転移部位や腫瘍マーカー推移を参考にして総合的に適応を決定する．

2. 推奨レジメン

推奨されるレジメンとして5レジメンを掲載している．いずれの試験も国内外でのRCT試験を基礎としたレベル1のエビデンスを有する．臨床現場や対象患者のリスクを考慮して選択肢に幅をもたせている．

FOLFOX療法はN9741試験により，IFL (irinotecan/bolus 5FU/LV) 療法より優れることが確認されている．FOLFIRI療法はGercor試験により，FOLFOXとの投与順にかかわらず同様の生存期間を示すことから一次治療として推奨できる．全身状態が良好で，CVカテーテル・ポート造設が可能であれば，まず実施することを考慮すべき治療法である．IFL療法は末梢ルートから実施できる利点があるが，治療効果ではFOLFOXに劣る成績がある．したがって，利点と欠点のバランスを患者に説明し，理解が得られれば選択可能と考える．

オキサリプラチンやイリノテカンの適応とならない，高齢者や臓器機能低下例では5FUとアイソボリン併用療法が勧められる．末梢ルートは週1回投与のRPMI法，中心静脈ルートでは2日間持続点滴のde Gramont法および

sLV5FU2法，週1回投与のAIO法などがある．いずれも患者および医療者側の状況で選択してよい．

経口抗癌剤の選択では国内ではUFT/LV錠のみが5FU/LV療法との同等性が確認されたレジメンである．海外で承認されているが国内未承認のカペシタビンや国内承認のS-1に関しては今回の治療ガイドラインでは前者は適応症がないこと，後者はエビデンスがないことから推奨することができなかった．今後，臨床試験成績により選択肢に加えられることになるであろう．

3. 適応基準と有害事象

抗癌剤の適応基準は基本的には補助療法と同様である．しかしながら肝，肺，リンパ節，腹膜などに転移を有する症例を対象とするために，臓器機能に関しては若干ゆるい基準で実施することが多い．総ビリルビン2.0 mg/dl，AST/ALT 100 IU/lを一つの目安として判断していただければよいと考える．白血球数や好中球数は治療開始時にはそれぞれ4,000，2,000/mm^3を目安としてよいが，経過中には前コースでの推移を参考にして投与継続の判断を行う．血小板数はFOLFOX療法ではとくに注意が必要であり，75,000/mm^3以下になれば延期，休薬が必要である．治療開始前に注意すべき臨床症状は，便通異常の有無，食事摂取の情況，発熱などであるが，全身状態の指標であるPSを適正に判断する必要がある．治療経過中になんらかの有害事象が出現した場合には，1週間程度の治療延期で回復することが多いので，無理をしないことが肝心である．

5FUを含む治療レジメンでは食欲不振，倦怠感，下痢，皮膚障害，味覚障害などが徐々に増強することがある．また，軽度のうつ症状を訴える例がある．必要な場合には治療を延期，中断することも必要となる．

FOLFOX療法の末梢神経障害に関しては，蓄積性のしびれ，機能障害が問題となっている．6コース以降には発生頻度が増加し，治療継続ができない理由になる．臨床症状やその持続時間を問診し，ボタンをはめにくい，紙をめくれないなどの早期の機能障害を認めた場合には中止をする必要がある．また，皮疹や呼吸苦などが出現した場合には投与速度を遅くしたり，中止をする必要がある．全身性のアレルギー症状の先駆症状である可能性があり，次回投与は慎重に症状観察が必要である．

FOLFIRI療法の有害事象は下痢，食欲低下，倦怠感を中心とする消化器症状，白血球減少，好中球減少の血液毒性，脱毛，肝機能障害などである．血小板減少や末梢神経障害がなく，比較的長期に治療継続できる利点がある．

FOLFOXかFOLFIRIか，いずれを先に使用するかどうかに関しては，両者の違いは有害事象の種類の違いであり，患者・家族に説明して，治療法を選択することが勧められている．

4. 治療効果判定

治療効果の判定は，定期的に画像診断や腫瘍マーカーにより実施する．明らかな増大がなく，有害事象が回復しているようであれば同一治療を継続するのが原則である．CT検査の検査間隔は通常2～3カ月ごと，腫瘍マーカーは月1回程度で経過観察を行う．腫瘍マーカーとしてはCEAおよびCA19-9が使用されることが多いが，これ以外でも治療前高値のマーカーは継続的に検査してよい．

5. おもな治療レジメン

おもな治療レジメンを**図I-4-1，2**に示す．いずれも複雑な治療レジメンであり，できれば患者および家族に投与レジメンについて十分に説明し，簡単な解説文書などを渡して，共同で治療に臨むようにすると，カテーテル・ポートに関連するトラブルや有害事象の早期発見が可能となり，治療コンプライアンスが向上する．

6. その他

一般臨床で使用される肝動注に関しては，腫瘍縮小率が高く期待されるが，現時点では生存

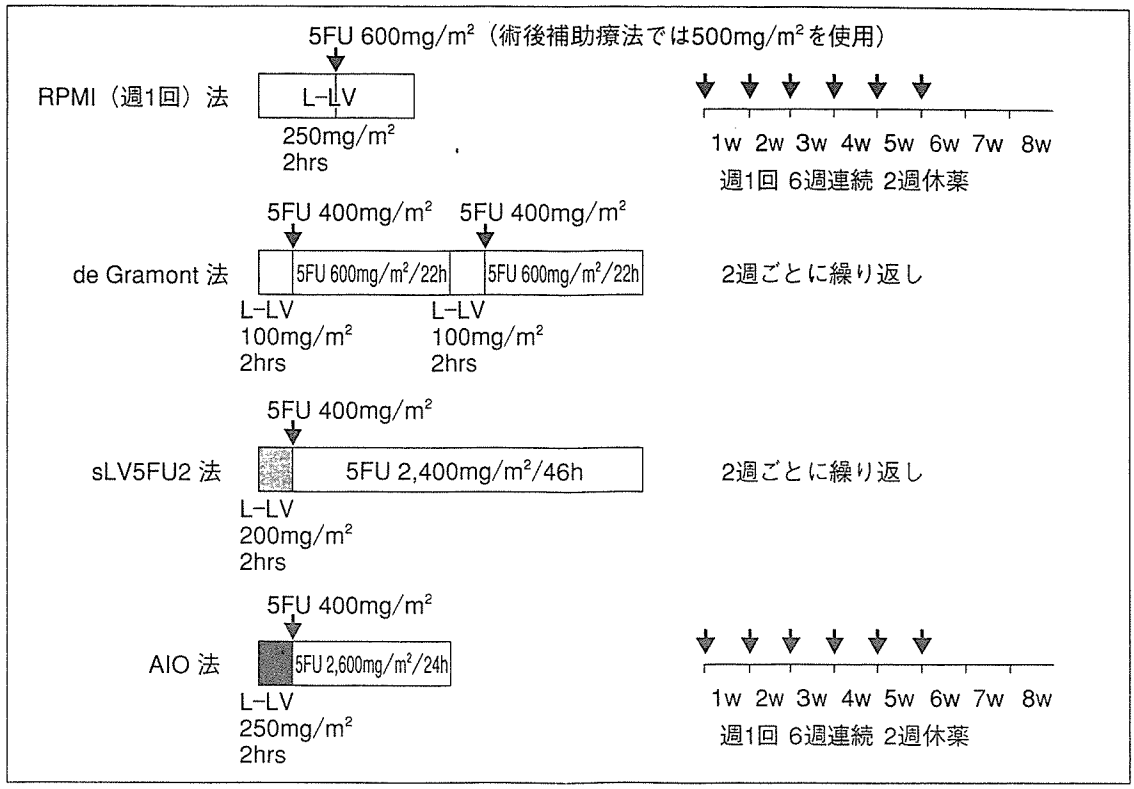

図 I-4-1　5FU/l-LV 療法

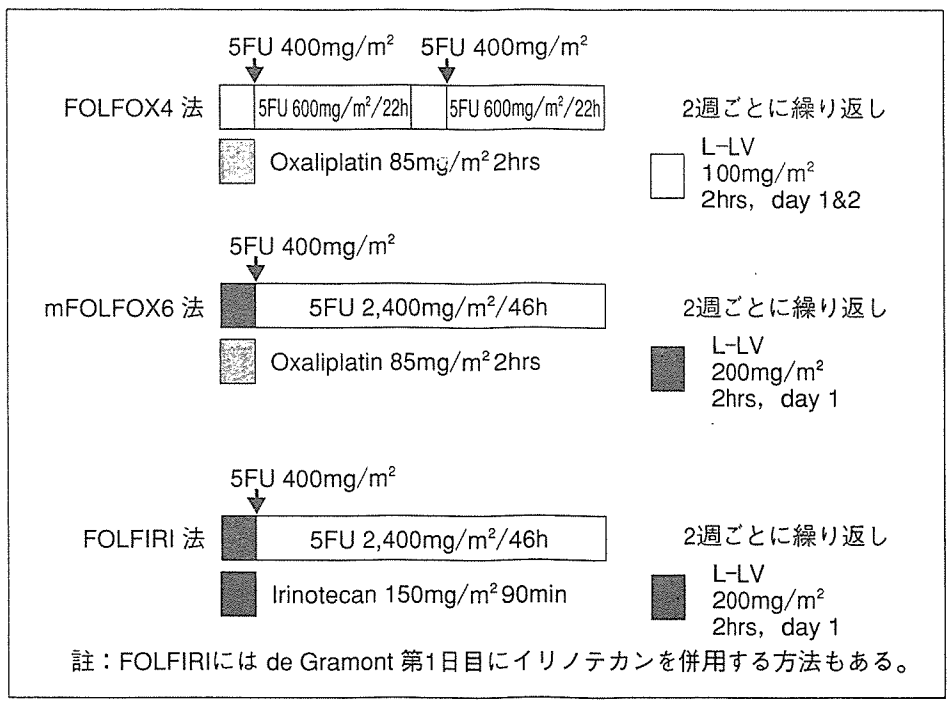

図 I-4-2　FOLFOX/FOLFIRI 療法

期間の延長を示すデータはなく，最近の全身抗癌剤治療成績を比較対象とした臨床意義を検討する必要がある．

おわりに

抗癌剤治療はここ数年急速な進歩を遂げている．しかしながら三次治療以降に関しては有効性は不明である．また全身状態の不良な患者での効果も不明である．臨床現場ではこのような状況での治療選択肢を求める声も多く聞くが，まずは治療効果が確認されている対象に対して標準治療をきちんと実施し，有害事象を最小限に抑える努力が必要と考えられる．

将来的には分子標的治療薬や抗体医薬品が登場することは間違いないが，これらの新規治療法の効果を最大限に引き出すためには，いま標準治療に精通し，多くの治療経験を積むことが重要である．がん治療の歴史が示すように，魔法の新薬で治癒が得られる可能性は少ない．遅々とした進みであるが，確実な治療成績向上は第一線の多くの臨床医が実感しているところである．今回の治療ガイドラインにより，熱心な若手臨床医が共通の理解と認識により臨床現場の問題点を把握し，治療成績のさらなる向上に繋げることができれば大きな喜びである．

文　献

重要文献に関しては，「大腸癌研究会 編：大腸癌治療ガイドライン医師用2005年版，金原出版，東京」に引用，紹介した．

1. FOLFOXの実際と副作用対策

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はじめに

2005年に，オキサリプラチンの使用が切除不能・転移性大腸癌に対して国内承認され，日本においても海外と同様に「標準治療」(NCCNガイドライン：http：//www.nccn.org/)としてFOLFOX療法(図1)が行われるようになった。しかし，オキサリプラチンも，FOLFOX療法を構成する5-FU＋ロイコボリン持続点滴療法も，いずれも海外での臨床試験の結果をもとに2005年になって国内承認された治療法であり，国内のほとんどの医療機関で使用経験が少ないのが現状であると考えられる。

本治療法は，中心静脈にポート造設を必要とし，薬剤投与が48時間に及ぶ治療法であり，そのうえ外来での治療をベースにしている。安全かつ有効に治療を行うためには，患者自身にも治療内容や副作用を十分に理解していただく必要がある。本稿では，当院での具体的な対応策を含めながら，FOLFOX療法の副作用対策について述べることとする。

副作用について

A. 末梢神経毒性

オキサリプラチンに特徴的な有害事象として，末梢神経毒性がある。これは可逆的なもので，手足末端や口唇周囲のしびれ，痛みなどの感覚異常として出現し，投与後すぐに出現する急性神経毒性と，投与を繰り返すことによる蓄積性の慢性神経毒性に大別される。

急性神経毒性は，手足末端や口唇周囲のしびれとして90％以上の症例で出現する。通常は感覚障害のみで，投与中もしくは投与後すぐに出現し，数時間から数日のうちに消失する。この「しびれ」は冷たいものや冷たい空気に触れることで誘発されることが特徴的である。また他に，1％弱の確率で起こる咽頭喉頭感覚異常がある。これ

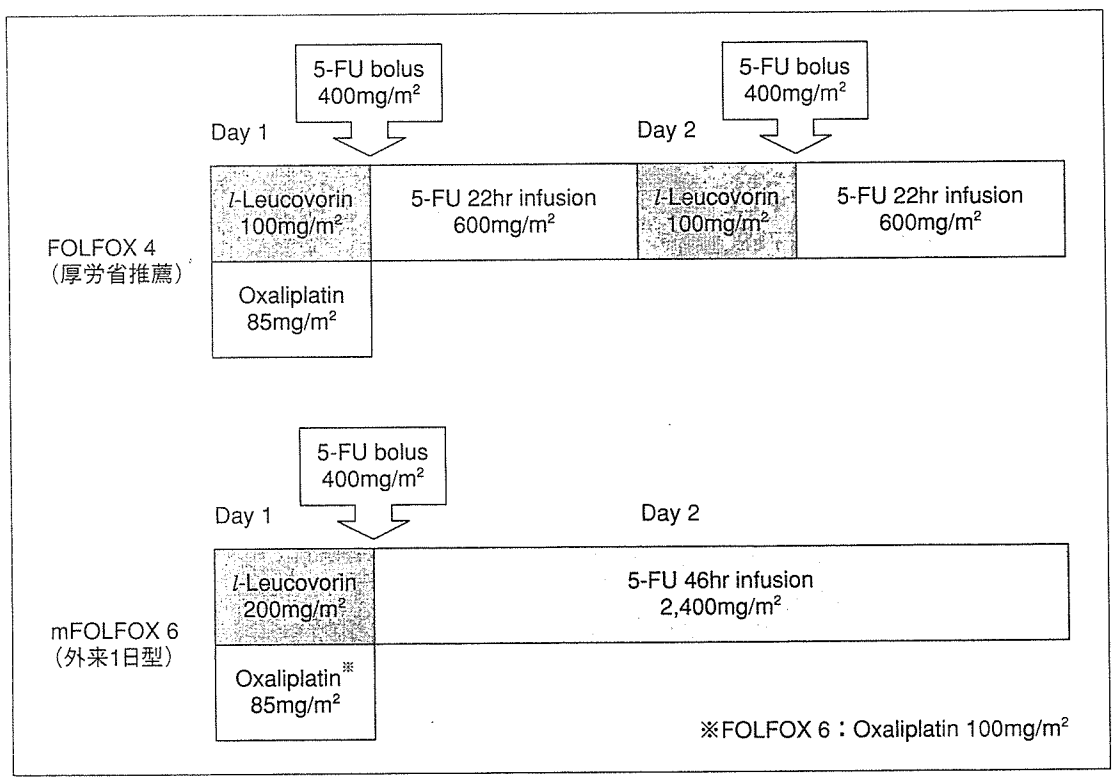

図1　FOLFOX治療スケジュール

は，主に投与中に呼吸困難感や嚥下困難感で出現するもので，実際に咽頭や喉頭が収縮・閉塞するわけではなく感覚異常のみであり，患者にあらかじめ十分にそのことを知らせておく必要がある。

慢性神経毒性は，オキサリプラチンを繰り返し投与するにつれて蓄積性に増強する神経症状である。急性神経毒性と同様に手足末端のしびれなどの感覚異常として出現し，総投与量が増加するにつれてしびれの出現期間が延び，程度も悪化する。重症例では投与サイクルの間(14日間)ずっとしびれが持続し，ボタンをかける動作ができないなど日常生活に支障をきたすほどになることもある〔総投与量1,170mg/m²になると全体の50%に出現[1]。添付文書の記載では，総投与量850mg/m²(10回投与)で10%，1,020mg/m²(12回投与)で20%に出現〕。その場合はオキサリプラチン投与を休止する。Grothey[1]の報告によると，日常生活に支障をきたし投与を中止してから神経毒性が改善するまで，中央値で13週間かかるとされている。慢性神経毒性は冷たいものにより誘発されることはなく持続的なもので，運動神経に障害が出ることもない。

オキサリプラチンの神経毒性に対する対処法・予防法については，現段階ではまだコンセンサスの得られている薬剤や方法はない。急性神経毒性については，まず冷たいものに触れるのを避けることが第一であり，咽頭喉頭感覚異常に関しては，オキサリプラチンの投与速度を遅くする(6時間かけて投与する)ことでほぼ防ぐことができる。慢性神経毒性については，オキサリプラチンをしばらく休薬することが必要である。現在有力視されている予防薬剤としては，Ca^{2+}/Mg^{2+}の点滴投与，carbamazepine，xaliprodenなどがあるが，いずれも信頼性のあるエビデンスはまだない。

B. 血液毒性

FOLFOXを構成する5-FU急速静注では，有害事象として好中球減少など骨髄抑制が出やすいことが知られている。そこにオキサリプラチンが加わることでやや血液毒性の頻度が増し，Grade 3以上の好中球減少は添付文書の記載では40～50%にみられるとされている。また血小板減少についてもGrade 3以上は4～5%でみられると記載されている。重度の骨髄抑制の場合は，次サイクルの投与延期や適切な減量を行う必要がある(詳細は次項参照)。

C. 消化器毒性

食欲不振・悪心は約60%で，嘔吐・下痢・便秘は約20%で，口内炎は20～30%でみられる。食欲不振，悪心，嘔吐については，前投薬としてリン酸デキサメタゾンナトリウム(デカドロン®)と塩酸グラニセトロン(カイトリル®)を点滴投与することである程度予防が可能である。また，筆者らはday 2とday 3にもデカドロン錠®(0.5mg錠)を8錠分2(1日4mg)で処方するようにしている。このように吐き気に対しては薬剤の予防的投与を行うことで，外来での治療をよりスムーズに行うことができると考えられる。

下痢に対しては，整腸薬(ビオフェルミン®など)や塩酸ロペラミド(ロペミン®)を使用して迅速に対応し，重症化，脱水を防ぐ必要がある。

口内炎に対しては，アズレンスルホン酸ナトリウム製剤(含嗽用ハチアズレ®)やステロイド含有軟膏(デキサルチン軟膏®など)などを使用し対応する。

筆者らは，外来での治療ということを考慮して，必ず常備薬として吐き気止め，下痢止め，整腸薬，抗菌薬，解熱薬を処方している。薬剤師との協力のもと患者教育を行い，状況に応じて常備薬を使用してもらう。そのさい患者には，主治医に連絡を忘れないようにさせることが大切で，状況によっては来院させて緊急採血などの検査を指示することもある。

D. 皮膚症状

5-FUの持続静注では，palmar-plantar erythrodysesthesia〔いわゆる手足症候群(hand-foot syndrome)〕が起こりやすく，ステロイド含有軟膏の外用で対応する。重症の場合はステロイド内服や5-FU(持続静注)減量を行う。

脱毛は約20%の頻度で出現する。また，5-FUの有害事象として皮膚の色素沈着がみられることもある。

E. アナフィラキシー

オキサリプラチンは，すでに複数回投与されている症例でもまれにアナフィラキシー様症状が出現することがあるので，観察を十分に行い，過敏症状が出現した場合には直ちに投与を中止し，抗ヒスタミン薬やステロイドを投与するなどの処置を行う必要がある[2]。

減量について

当院を含むグループにおいて，FOLFOX療法の臨床試験を行ったさいの反復投与基準(表1)と減量基準(表2)を示す。実際の臨床現場でもこれらの基準に従い，軽度の副作用であれば延期を行い，回復し

表1　FOLFOXにおける反復投与基準

白血球数　3,000/μl以上 血小板数　100,000/μl以上 水様性下痢を認めない 感染を疑わせる38℃以上の発熱がない 薬物有害反応と思われる非血液毒性（食欲低下と下痢を除く）がGrade 2以下	基準を満たすまで 1日単位で延期

表2　FOLFOXにおける減量基準

		5-FU	オキサリプラチン	
G4	好中球減少	400mg/m²	85 * mg/m²	100 † mg/m²
G3/4	血小板減少	＋600mg/m²×2 *	↓	↓
G3	発熱性好中球減少	＋2,400mg/m² †	65 * mg/m²	75 † mg/m²
G3	悪心　嘔吐　下痢	↓		
G3	口内炎	300mg/m² ＋500mg/m²×2 * ＋2,000mg/m² †		
G3	皮膚毒性	200mg/m² ＋1,500mg/m²		
G2/3	感覚異常/知覚異常 急性神経毒性		同　上 減量せず6時間投与	

神経毒性についてはDEBIOFARM-NTCを，それ以外にはCTC-AE ver3.0を使用
* FOLFOX4の場合，† FOLFOX6の場合

た時点で継続する[3]。中等度の副作用の場合は減量したうえで継続投与する。それでも許容できない重度の副作用の場合は治療を中止する。

中心静脈ポートの合併症について

FOLFOXを外来で安全・確実に行うために，皮下埋め込み型リザーバー（中心静脈ポート）が用いられる。当院では，逆流防止弁のついたカテーテルを使ったポートシステムを採用して，FOLFOX投与終了後の患者自身による自己抜針を容易にし，在宅化学療法をよりスムーズに行えるようにしている。

長期にわたり在宅化学療法を行う症例が増えるにつれ，カテーテルやポートに関連する合併症が，頻度は高くないがみられるようになる。①カテーテルピンチオフ，②フィブリンシース，③カテーテルに起因する血栓性静脈炎，④カテーテル損傷（捻れ，断裂など），⑤ポート造設部皮膚障害，⑥ポート感染などがある。ポート感染の場合は抗菌薬の全身投与およびカテーテルロックで対応できる場合があるが，それが無効の場合や①～⑤の場合はカテーテル抜去が必要となる。

おわりに

FOLFOXは外来で行うように工夫された治療法であり，患者が自宅で過ごす時間が長いぶん，十分な患者教育と有害事象への早期対応が重要となる。これらの治療の安全性を高めるには，医師，患者，コメディカルが共通の理解と認識をもつことが必要であると考えられる。

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Dietary Risk Factors for Colon and Rectal Cancers: A Comparative Case-Control Study

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Original Article

Dietary Risk Factors for Colon and Rectal Cancers: A Comparative Case-Control Study

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BACKGROUND: In Japan, the incidence rate of colon cancer has more rapidly increased than that of rectal cancer. The differential secular trends may be due to different dietary factors in the development of colon and rectal cancers.
METHODS: To compare dietary risk factors between colon and rectal cancers, we undertook a case-control study at Aichi Cancer Center Hospital, Japan. Subjects were 507 patients with newly diagnosed colon (n = 265) and rectal (n = 242) cancers, and 2,535 cancer-free outpatients (controls). Intakes of nutrients and food groups were assessed with a food frequency questionnaire, and multivariate-adjusted odds ratios (ORs) were estimated using unconditional logistic models.
RESULTS: We found a decreasing risk of colon cancer with increasing intakes of calcium and insoluble dietary fiber; the multivariate ORs across quartiles of intake were 1.00, 0.90, 0.80, and 0.67 (trend p = 0.040), and 1.00, 0.69, 0.64, and 0.65 (trend p = 0.027), respectively. For rectal cancer, a higher consumption of carotene and meat was associated with a reduced risk; the corresponding ORs were 1.00, 1.10, 0.71, and 0.70 for carotene (trend p = 0.028), and 1.00, 0.99, 0.68, and 0.72 for meat (trend p = 0.036). Carbohydrate intake was positively correlated with the risk of rectal cancer (ORs over quartiles: 1.00, 1.14, 1.42, and 1.54; trend p = 0.048). This association was stronger in women, while fat consumption was inversely correlated with the risk of female colon and rectal cancers.
CONCLUSIONS: Dietary risk factors appear to considerably differ between colon and rectal cancers.
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Key words: Diet, Colonic Neoplasms, Rectal Neoplasms, Case-Control Studies, Japan.

In Japan, the age-standardized incidence rate of colorectal cancer increased until around 1990 and has leveled off thereafter.[1] It is now at among the highest levels in the world; the incidence rate standardized with the World Population was estimated to be 49.9 (per 100,000 population) in men and 27.2 in women in 1999.[1]

The incidence of colon cancer has increased more rapidly than that of rectal cancer. Between 1975 and 1999, the colon-to-rectal ratio of incidence (standardized with the World Population) rose from 0.85 to 1.67 in men and from 1.17 to 2.13 in women.[1,2] The ratio greatly varies among countries,[3] being much higher in cancer registries in the United States and Canada (median = 2.1 in men and 2.6 in women) than those in Asian countries excluding Japan (1.2 in men and 1.4 in women). Registries in European countries have intermediate values (1.5 in men and 2.0 in women).

If dietary risk factors of colon cancer differ from those of rectal cancer, the different secular trends in incidence between the two sites and international variation in the colon-to-rectal ratio of incidence may partly be explained by changes and international varia-

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tion in dietary habits. In Asian countries, however, only a small number of studies[4-7] have examined differences in dietary risk factors between cancers of the colon and rectum. It is therefore not clear whether the predominant increase in incidence of colon cancer in Japan is ascribable to changes in diet. We need further data to know why the proportion of rectal cancer in all colorectal cancer cases is relatively high in Asian countries.

To further address these issues, we conducted the present case-control study comparing dietary risk factors between colon and rectal cancers in the Hospital-based Epidemiologic Research Program at Aichi Cancer Center (HERPACC).

METHODS

The Hospital-based Epidemiologic Research Program at Aichi Cancer Center

HERPACC was initiated in Aichi Cancer Center Hospital (ACCH), Nagoya, in 1988, with information on lifestyle factors collected from all first-visit outpatients, using a self-administered questionnaire checked by a trained interviewer. Each patient is asked about his or her lifestyle including dietary habits when healthy or before the current symptoms developed. The questionnaire data are loaded into the HERPACC database and routinely linked with the hospital cancer registry system to update the data on cancer incidence. Written informed consent for participation is obtained from each patient. The ethical board of Aichi Cancer Center reviewed and approved the protocol of this investigation. Further details of HERPACC have been described elsewhere.[6,8]

Cases and Controls

The present study is based on data collected between January 2001 and September 2004 because the present version of the food frequency questionnaire was adopted in January 2001. Among all first-visit outpatients during this period (n = 25,941), the questionnaire was given to 21,417 (82.6%). Of the remaining 4,524 patients (17.4%), 2,041 (7.9%) were excluded because of the absence of an interviewer and so were 1,222 (4.7%) due to a consultation visit by someone other than patients themselves. Others were left out because they were too young (< 18 years) or too ill to fill out the form or for other miscellaneous reasons. Of the 21,417 outpatients who were asked to complete the questionnaire, 20,814 (97.2%) provided adequate responses to the questionnaire.

Patients aged 20 to 79 years with cancers of the colon (n = 323) or rectum (n = 276) (International Statistical Classification of Diseases and Related Health Problems, 10th Revision [ICD-10]: C18 and C20), newly and histopathologically diagnosed, were deemed to be potential cases. We excluded 85 patients with a prior history of cancer and seven with an implausibly high or low estimated intake of total energy (<500 or 3,500+ kcal/day), leaving 507 cases eligible for the analysis (colon cancer: n = 265; rectal cancer: n = 242).

We randomly selected five controls for each case from the 14,931 cancer-free individuals, with matching for age (5-year strata), sex, and calendar year of the first visit. Those with a history of cancer (n = 1,188) and an extreme value of energy intake (n = 125) were excluded as in the case patients. Finally, 2,535 controls were included in this study.

Diet and Other Exposure Data

The HERPACC questionnaire applied included items on demographic characteristics, family and individual medical history, height and weight, exercise, smoking and drinking habits, and vitamin use, as well as consumption of selected foods and beverages.

The dietary component of the questionnaire comprised 47 food items.[9] We asked the subjects about the average intake frequency without specifying portion size, during the period of one year before onset of the present disease or before the interview. For staple foods such as rice, bread, and noodles, the usual number of bowls or slices consumed at one time, as well as the intake frequency, was inquired for breakfast, lunch, and supper, separately. The frequency of alcohol consumption was asked with the usual amount on one occasion. Nutrient intakes and food group consumption were estimated assuming the standard portion sizes.

Energy-adjusted intakes of nutrients and food groups were calculated by the residual method,[10] with natural logarithms used to improve the normality of their distribution except for the ratio of n-6 fatty acid intake to that of n-3 fatty acids. The food frequency questionnaire was validated by referring to 3-day weighed dietary records as a standard.[9] The de-attenuated correlation coefficients for energy-adjusted intakes of nutrients for the present analysis ranged from 0.12 to 0.86 in men (median = 0.43) and from 0.17 to 0.64 in women (0.38). The coefficients (not de-attenuated) for energy-adjusted consumption of food groups varied from 0.19 to 0.57 in men (median = 0.42) and from 0.19 to 0.61 in women (0.42).

Statistical Analysis

Body mass index (BMI) at baseline was calculated from reported height and weight: BMI = (weight in kg)/(height in m)^2.

To assess the strength of the associations between intakes of nutrients or food groups and risk of colon or rectal cancer, odds ratios (ORs) were computed. To directly compare dietary risk factors between colon and rectal cancers based on a common control group, we pooled controls matched to colon cancer cases and those matched to rectal cancer cases in the analysis. Cases and controls were categorized into four groups according to sex-specific quartile levels of energy-adjusted intakes of nutrients or food groups among controls. The ORs with 95% confidence intervals (CIs) for the second, third, and highest quartiles versus the lowest were estimated using unconditional logistic models[11] adjusted for the matching variables and potential confounding factors.[12-14]

The ORs were adjusted for sex, age (as a continuous variable), calendar year of the first visit to the hospital (2001, 2002, or 2003-2004), season of first visit (spring, summer, autumn, or winter), reason for the visit (self recommendation, recommenda-

tion by family or friends, referral by physicians, secondary screening, or others), family history of colorectal cancer in parents and/or siblings (yes or no), BMI (<20.0, 20.0-24.9, 25.0-29.9, or 30.0+ kg/m^2), exercise (none, <0.50, 0.50-0.99, or 1.00+ hours/day), alcohol drinking (nondrinkers, ex-drinkers, or current drinkers who daily consumed <1.0, 1.0-1.9, or 2.0+ Japanese drinks [one Japanese drink is equivalent to 23g of ethanol]), smoking habit (nonsmokers, ex-smokers, or current smokers), multivitamin use (at least once per week for one year or longer; yes or no), and total energy intake (as a continuous variable). Missing values for each covariate were treated as an additional category in the variable and were included in the logistic model. As a basis for the trend tests, we assigned scores of 0, 1, 2, and 3 to the first (or lowest), second, third, and fourth quartiles of nutrient intakes or food group consumption, respectively, and included the score in the model. All p values were two-sided, and all the analyses were performed using the Statistical Analysis System®, release 8.2.[15]

RESULTS

Table 1 shows the distribution of cases and controls by background characteristics; sex, age, and calendar year of the first visit were exactly matched between cases and controls. Values for mean age ± standard deviation were 61.7 ± 9.2 and 61.6 ± 9.3 years in cases and controls for colon cancer, respectively. The corresponding figures were 58.6 ± 10.7 and 58.5 ± 10.6 years for the rectal cancer subjects. As expected, the case group included a higher proportion of patients referred by physicians than the control group.

Cases of both colon and rectal cancers were more likely to have a family history of colorectal cancer than the controls. Other characteristics, such as season of first visit to the hospital, BMI, exercise, drinking and smoking habits, multivitamin use, and energy intake, were similarly distributed in cases and controls.

The greater the intake of calcium and insoluble dietary fiber, the lower the multivariate OR (OR2) for colon cancer (Table 2; trend p = 0.040 for calcium and 0.027 for insoluble dietary fiber). The risks for the highest quartile of intake of calcium and insoluble dietary fiber were 33% and 35% lower than those for the lowest quartile, respectively (OR2: 0.67 [95% CI: 0.46-1.00] for calcium and 0.65 [95% CI: 0.45-0.96] for insoluble dietary fiber). Inverse associations were also suggested between colon cancer risk and intakes of protein, fat, vitamin C, and total dietary fiber (trend p for OR2 < 0.10).

We found a decreased risk of rectal cancer associated with higher intakes of carotene and meat (Table 3; trend p for OR2 = 0.028 for carotene and 0.036 for meat). A negative correlation was also suggested between the risk of rectal cancer and intake of vitamin E (trend p for OR2 = 0.072). On the other hand, an increasing risk was found with increasing intake of carbohydrate (trend p for OR2 = 0.048).

In women, intakes of protein, fat, calcium, vitamin E, cholesterol, and total dietary fiber were inversely correlated with the risk of colon cancer (trend p < 0.10, Table 4), while no significant associations were noted in men. A reduced risk of rectal cancer associated with a higher consumption of carotene and meat was observed particularly in women (Table 5). Inverse associations were also found for fat, vitamin E, folate, monounsaturated and n-6 polyunsaturated fatty acids, and green-yellow vegetables in women (trend p < 0.10). In contrast, women who took diet high in carbohydrate were at more than twice the risk of developing rectal cancer. The ORs for the third and the highest quartiles were 2.14 (95% CI: 1.05-4.36) and 2.53 (95% CI: 1.22-5.24; trend p = 0.003), respectively. An increasing risk with an increasing ratio of dietary n-6 polyunsaturated fatty acids (PUFA) to n-3 PUFA was detected for male rectal cancer (trend p = 0.042).

DISCUSSION

In this case-control study, we found a decreased risk of colon cancer with increasing intakes of calcium and insoluble dietary fiber, while a higher consumption of carotene and meat was associated with a reduced risk of rectal cancer. Carbohydrate intake was linked to the risk of rectal cancer, particularly in women, while fat consumption was inversely correlated with the risk of colon and rectal cancers in women.

People take much less meat and more cereals in Asian countries than in the United States and Canada (http://faostat.fao.org/faostat/), which may account for the lower colon-to-rectal ratios in Asia. Further investigations, however, are needed because the differences in risk for the consumption of meat and carbohydrate between colon and rectal cancers have not been fully supported by previous investigations.

Calcium intake has been related to a decreased risk of colorectal cancer in prospective studies.[16-18] In addition, randomized controlled trials showed that calcium supplementation prevents recurrence of colorectal adenomas, precursors of cancers.[19] The present study provides further support for role of calcium in the prevention of colorectal cancer. Some investigations demonstrated a greater risk reduction for cancer of the colon than that of the rectum as in our case.[16,18]

An inverse association of dietary fiber and colon cancer risk was here detected specifically for insoluble dietary fiber. Many epidemiologic studies have not substantiated a protective association between dietary fiber and colorectal cancer,[20-22] although a recent large prospective study in Europe showed a decreased risk of colorectal cancer associated with dietary fiber intake.[23]

An earlier investigation reporting protective effects of dietary fiber against colorectal cancer did not find a substantial difference in risk between soluble and insoluble fibers.[24] Whereas adsorption of carcinogens to insoluble dietary fiber in the intestinal tract is one of the mechanisms by which dietary fiber is believed to protect against colorectal cancer,[25] the roles of different types of fiber should be further elucidated. Our finding that the association of dietary fiber was mainly with colon rather than rectal cancer is

Table 1. Background characteristics of cases and controls for colon and rectal cancers.

	Colon cancer		Rectal cancer	
	Cases (n = 265)	Controls (n = 1,325)	Cases (n = 242)	Controls (n = 1,210)
Sex				
Men	149 (56.2)	745 (56.2)	146 (60.3)	730 (60.3)
Women	116 (43.8)	580 (43.8)	96 (39.7)	480 (39.7)
Age (years)				
20-29	1 (0.4)	5 (0.4)	1 (0.4)	5 (0.4)
30-39	4 (1.5)	20 (1.5)	17 (7.0)	85 (7.0)
40-49	19 (7.2)	95 (7.2)	22 (9.1)	110 (9.1)
50-59	83 (31.3)	415 (31.3)	83 (34.3)	415 (34.3)
60-69	106 (40.0)	530 (40.0)	81 (33.5)	405 (33.5)
70-79	52 (19.6)	260 (19.6)	38 (15.7)	190 (15.7)
Calendar year of first visit				
2001	73 (27.5)	365 (27.5)	67 (27.7)	335 (27.7)
2002	83 (31.3)	415 (31.3)	69 (28.5)	345 (28.5)
2003-2004	109 (41.1)	545 (41.1)	106 (43.8)	530 (43.8)
Season of first visit to the hospital				
Spring	66 (24.9)	332 (25.1)	67 (27.7)	310 (25.6)
Summer	92 (34.7)	415 (31.3)	62 (25.6)	348 (28.8)
Autumn	51 (19.2)	341 (25.7)	62 (25.6)	314 (26.0)
Winter	56 (21.1)	237 (17.9)	51 (21.1)	238 (19.7)
Reason to visit the hospital				
Self recommendation	37 (14.0)	407 (30.7)	32 (13.2)	361 (29.8)
Recommendation by family or friends	49 (18.5)	289 (21.8)	47 (19.4)	245 (20.2)
Referral by physicians	136 (51.3)	366 (27.6)	126 (52.1)	301 (24.9)
Secondary screening	38 (14.3)	243 (18.3)	36 (14.9)	284 (23.5)
Others	5 (1.9)	20 (1.5)	1 (0.4)	19 (1.6)
Family history of colorectal cancer in parents and/or siblings				
Yes	38 (14.3)	100 (7.5)	24 (9.9)	77 (6.4)
No	227 (85.7)	1,225 (92.5)	218 (90.1)	1,133 (93.6)
Body mass index (kg/m^2)				
< 20.0	40 (15.2)	226 (17.3)	38 (15.8)	206 (17.1)
20.0-24.9	166 (62.9)	791 (60.4)	146 (60.8)	748 (62.2)
25.0-29.9	54 (20.5)	276 (21.1)	50 (20.8)	229 (19.0)
≥ 30.0	4 (1.5)	16 (1.2)	6 (2.5)	20 (1.7)
Exercise (hours/day)				
None	75 (29.1)	337 (26.0)	67 (29.1)	330 (27.8)
< 0.50	103 (39.9)	564 (43.5)	93 (40.4)	513 (43.3)
0.50-0.99	49 (19.0)	229 (17.7)	47 (20.4)	184 (15.5)
≥ 1.00	31 (12.0)	167 (12.9)	23 (10.0)	158 (13.3)
Alcohol drinking				
Nondrinkers	130 (49.4)	627 (47.8)	99 (41.8)	508 (42.6)
Ex-drinkers	25 (9.5)	103 (7.9)	16 (6.8)	82 (6.9)
Current drinkers (Japanese drinks/day)				
< 1.0	65 (24.7)	309 (23.6)	60 (25.3)	338 (28.4)
1.0-1.9	22 (8.4)	134 (10.2)	32 (13.5)	130 (10.9)
≥ 2.0	21 (8.0)	139 (10.6)	30 (12.7)	134 (11.2)
Smoking				
Nonsmokers	132 (49.8)	667 (50.4)	104 (43.0)	560 (46.4)
Ex-smokers	78 (29.4)	379 (28.6)	65 (26.9)	342 (28.3)
Current smokers	55 (20.8)	277 (20.9)	73 (30.2)	306 (25.3)
Multivitamin use (at least once per week for one year or longer)				
Yes	24 (9.1)	113 (8.5)	15 (6.2)	99 (8.2)
No	241 (90.9)	1,212 (91.5)	227 (93.8)	1,111 (91.8)
Energy intake (kcal/day, mean ± SD)	1,580 ± 351	1,616 ± 342	1,609 ± 370	1,634 ± 352

Percentages in parentheses

Table 2. Odds ratios (ORs) for colon cancer by quartile (Q1-Q4) of energy-adjusted intake of nutrients or food groups in men and women (265 cases and 2,535 controls).

Nutrients/food groups	OR1 (95% confidence interval)*					OR2 (95% confidence interval)†				
	Q1	Q2	Q3	Q4	Trend p	Q1	Q2	Q3	Q4	Trend p
Protein	1.00	0.82 (0.58 - 1.17)	0.76 (0.53 - 1.08)	0.84 (0.60 - 1.19)	0.28	1.00	0.74 (0.52 -1.07)	0.65 (0.45 - 0.95)	0.74 (0.51 - 1.07)	0.084
Fat	1.00	1.06 (0.76 - 1.49)	0.72 (0.50 - 1.05)	0.89 (0.63 - 1.28)	0.22	1.00	1.00 (0.71 - 1.42)	0.67 (0.45 - 0.98)	0.78 (0.54 - 1.13)	0.064
Carbohydrate	1.00	1.14 (0.79 - 1.66)	1.09 (0.75 - 1.59)	1.33 (0.93 - 1.91)	0.16	1.00	1.15 (0.77 - 1.70)	1.02 (0.67 - 1.53)	1.16 (0.76 - 1.79)	0.65
Calcium	1.00	1.03 (0.73 - 1.46)	0.90 (0.63 - 1.29)	0.78 (0.54 - 1.13)	0.14	1.00	0.90 (0.62 - 1.28)	0.80 (0.55 - 1.17)	0.67 (0.46 - 1.00)	0.040
Carotene	1.00	0.78 (0.54 - 1.13)	1.00 (0.70 - 1.42)	0.96 (0.67 - 1.37)	0.85	1.00	0.75 (0.51 - 1.10)	0.89 (0.61 - 1.29)	0.87 (0.59 - 1.28)	0.69
Retinol	1.00	0.87 (0.60 - 1.26)	0.93 (0.65 - 1.34)	1.12 (0.79 - 1.59)	0.44	1.00	0.86 (0.58 - 1.25)	1.00 (0.69 - 1.46)	1.06 (0.73 - 1.54)	0.57
Vitamin D	1.00	1.03 (0.72 - 1.47)	0.88 (0.61 - 1.28)	1.02 (0.71 - 1.45)	0.88	1.00	1.03 (0.71 - 1.49)	0.85 (0.58 - 1.24)	1.04 (0.72 - 1.51)	0.92
Vitamin E	1.00	0.81 (0.56 - 1.16)	1.03 (0.73 - 1.45)	0.79 (0.55 - 1.14)	0.44	1.00	0.75 (0.52 - 1.09)	0.95 (0.67 - 1.36)	0.73 (0.50 - 1.08)	0.28
Folate	1.00	0.73 (0.51 - 1.05)	0.89 (0.62 - 1.26)	0.88 (0.62 - 1.25)	0.70	1.00	0.65 (0.44 - 0.95)	0.82 (0.57 - 1.19)	0.75 (0.51 - 1.11)	0.32
Vitamin C	1.00	0.78 (0.54 - 1.12)	0.94 (0.66 - 1.33)	0.79 (0.55 - 1.14)	0.38	1.00	0.72 (0.49 - 1.04)	0.84 (0.58 - 1.21)	0.65 (0.44 - 0.96)	0.072
SFA‡	1.00	0.89 (0.62 - 1.28)	0.87 (0.60 - 1.24)	1.01 (0.71 - 1.43)	1.00	1.00	0.77 (0.53 - 1.12)	0.77 (0.53 - 1.12)	0.83 (0.57 - 1.20)	0.35
MUFA§	1.00	1.02 (0.71 - 1.46)	1.09 (0.77 - 1.56)	1.04 (0.72 - 1.51)	0.73	1.00	0.94 (0.65 - 1.36)	1.04 (0.71 - 1.52)	0.92 (0.62 - 1.36)	0.80
PUFA‖	1.00	0.92 (0.64 - 1.32)	1.03 (0.72 - 1.46)	1.01 (0.71 - 1.45)	0.80	1.00	0.79 (0.54 - 1.15)	1.00 (0.69 - 1.45)	0.90 (0.61 - 1.31)	0.88
Cholesterol	1.00	0.86 (0.60 - 1.23)	0.95 (0.67 - 1.36)	0.92 (0.64 - 1.30)	0.76	1.00	0.81 (.56 - 1.17)	0.88 (0.61 - 1.26)	0.77 (0.52 - 1.13)	0.25
Soluble dietary fiber	1.00	0.90 (0.64 - 1.28)	0.83 (0.58 - 1.18)	0.78 (0.55 - 1.13)	0.16	1.00	0.89 (0.62 - 1.28)	0.77 (0.53 - 1.12)	0.75 (0.52 - 1.10)	0.11
Insoluble dietary fiber	1.00	0.74 (0.52 - 1.05)	0.74 (0.52 - 1.05)	0.72 (0.51 - 1.03)	0.078	1.00	0.69 (0.48 - 1.00)	0.64 (0.44 - 0.93)	0.65 (0.45 - 0.96)	0.027
Total dietary fiber	1.00	0.84 (0.59 - 1.20)	0.79 (0.55 - 1.13)	0.76 (0.53 - 1.09)	0.13	1.00	0.78 (0.54 - 1.12)	0.71 (0.49 - 1.03)	0.72 (0.49 - 1.05)	0.074
n-3 PUFA	1.00	0.91 (0.63 - 1.30)	1.05 (0.74 - 1.49)	0.95 (0.66 - 1.36)	0.98	1.00	0.90 (0.62 - 1.30)	1.02 (0.71 - 1.47)	0.89 (0.61 - 1.30)	0.72
n-6 PUFA	1.00	0.88 (0.61 - 1.26)	1.10 (0.77 - 1.56)	1.02 (0.71 - 1.45)	0.65	1.00	0.75 (0.51 - 1.09)	1.01 (0.70 - 1.46)	0.84 (0.57 - 1.24)	0.77
n-6 PUFA/n-3 PUFA	1.00	0.93 (0.65 - 1.34)	1.22 (0.87 - 1.72)	0.90 (0.62 - 1.30)	0.97	1.00	0.95 (0.65 - 1.38)	1.24 (0.87 - 1.77)	0.84 (0.57 - 1.23)	0.71
Soy foods	1.00	1.37 (0.96 - 1.95)	0.97 (0.66 - 1.42)	1.07 (0.74 - 1.55)	0.76	1.00	1.41 (0.98 - 2.04)	0.99 (0.67 - 1.47)	1.02 (0.69 - 1.50)	0.59
Meat	1.00	1.06 (0.74 - 1.52)	1.17 (0.82 - 1.68)	1.06 (0.74 - 1.54)	0.62	1.00	1.11 (0.76 - 1.61)	1.19 (0.82 - 1.73)	0.95 (0.65 - 1.41)	0.93
Fish	1.00	1.20 (0.84 - 1.72)	1.03 (0.71 - 1.50)	1.11 (0.77 - 1.60)	0.78	1.00	1.18 (0.81 - 1.70)	1.00 (0.68 - 1.47)	1.10 (0.75 - 1.62)	0.83
Green-yellow vegetables	1.00	0.89 (0.63 - 1.27)	0.88 (0.62 - 1.25)	0.79 (0.55 - 1.14)	0.23	1.00	0.86 (0.59 - 1.23)	0.80 (0.55 - 1.16)	0.75 (0.51 - 1.10)	0.13
Other vegetables	1.00	1.17 (0.83 - 1.67)	0.83 (0.57 - 1.21)	1.09 (0.76 - 1.56)	0.90	1.00	1.11 (0.77 - 1.59)	0.78 (0.52 - 1.15)	0.96 (0.66 - 1.40)	0.45
Fruit	1.00	0.80 (0.56 - 1.15)	0.74 (0.51 - 1.06)	0.90 (0.64 - 1.28)	0.50	1.00	0.73 (0.50 - 1.06)	0.71 (0.48 - 1.04)	0.73 (0.50 - 1.06)	0.12

* : adjusted for sex, age, and year of first visit.

† : further adjusted for season of first visit to the hospital, reason for the visit, family history of colorectal cancer, body mass index, exercise, alcohol drinking, smoking, multivitamin use, and energy intake.

‡ : saturated fatty acids

§ : monounsaturated fatty acids

‖ : polyunsaturated fatty acids

Table 3. Odds ratios (ORs) for rectal cancer by quartile (Q1-Q4) of energy-adjusted intake of nutrients or food groups in men and women (242 cases and 2,535 controls).

Nutrients/food groups	OR1 (95% confidence interval)*					OR2 (95% confidence interval)†				
	Q1	Q2	Q3	Q4	Trend p	Q1	Q2	Q3	Q4	Trend p
Protein	1.00	0.81 (0.57 - 1.17)	0.92 (0.64 - 1.31)	0.70 (0.48 - 1.03)	0.13	1.00	0.83 (0.57 - 1.22)	0.91 (0.62 - 1.32)	0.71 (0.47 - 1.06)	0.16
Fat	1.00	0.86 (0.60 - 1.24)	0.85 (0.59 - 1.23)	0.73 (0.50 - 1.07)	0.12	1.00	0.86 (0.59 - 1.25)	0.90 (0.61 - 1.31)	0.73 (0.49 - 1.09)	0.17
Carbohydrate	1.00	1.03 (0.70 - 1.53)	1.27 (0.87 - 1.86)	1.37 (0.94 - 2.00)	0.060	1.00	1.14 (0.75 - 1.74)	1.42 (0.93 - 2.19)	1.54 (0.96 - 2.47)	0.048
Calcium	1.00	1.34 (0.92 - 1.94)	1.30 (0.89 - 1.89)	0.93 (0.62 - 1.40)	0.76	1.00	1.24 (0.85 - 1.82)	1.33 (0.89 - 1.97)	0.97 (0.63 - 1.50)	0.99
Carotene	1.00	1.07 (0.76 - 1.52)	0.75 (0.52 - 1.10)	0.74 (0.50 - 1.09)	0.044	1.00	1.10 (0.77 - 1.59)	0.71 (0.47 - 1.06)	0.70 (0.46 - 1.08)	0.028
Retinol	1.00	1.07 (0.74 - 1.55)	1.03 (0.71 - 1.50)	0.93 (0.63 - 1.37)	0.69	1.00	1.09 (0.74 - 1.60)	1.10 (0.75 - 1.62)	0.92 (0.61 - 1.39)	0.75
Vitamin D	1.00	0.81 (0.56 - 1.18)	0.88 (0.61 - 1.27)	0.95 (0.66 - 1.38)	0.88	1.00	0.77 (0.53 - 1.13)	0.81 (0.55 - 1.20)	0.97 (0.66 - 1.44)	0.91
Vitamin E	1.00	0.68 (0.47 - 0.99)	0.80 (0.56 - 1.13)	0.65 (0.45 - 0.94)	0.047	1.00	0.65 (0.44 - 0.95)	0.78 (0.54 - 1.13)	0.65 (0.43 - 0.97)	0.072
Folate	1.00	1.00 (0.70 - 1.42)	0.78 (0.53 - 1.14)	0.83 (0.57 - 1.21)	0.19	1.00	1.00 (0.69 - 1.45)	0.80 (0.53 - 1.19)	0.81 (0.53 - 1.23)	0.20
Vitamin C	1.00	0.91 (0.64 - 1.31)	0.78 (0.54 - 1.13)	0.84 (0.57 - 1.22)	0.24	1.00	0.94 (0.65 - 1.36)	0.82 (0.56 - 1.22)	0.84 (0.55 - 1.26)	0.31
SFA‡	1.00	1.25 (0.86 - 1.81)	1.21 (0.83 - 1.76)	0.89 (0.60 - 1.33)	0.58	1.00	1.19 (0.81 - 1.75)	1.25 (0.84 - 1.85)	0.86 (0.56 - 1.33)	0.57
MUFA§	1.00	0.76 (0.52 - 1.09)	0.66 (0.45 - 0.96)	0.82 (0.57 - 1.18)	0.22	1.00	0.73 (0.50 - 1.08)	0.64 (0.43 - 0.96)	0.76 (0.51 - 1.14)	0.15
PUFA‖	1.00	0.66 (0.45 - 0.96)	0.89 (0.62 - 1.27)	0.80 (0.56 - 1.16)	0.49	1.00	0.59 (0.40 - 0.88)	0.90 (0.62 - 1.30)	0.76 (0.51 - 1.12)	0.47
Cholesterol	1.00	1.04 (0.72 - 1.49)	0.79 (0.54 - 1.17)	0.97 (0.67 - 1.41)	0.57	1.00	1.06 (0.72 - 1.54)	0.79 (0.53 - 1.19)	0.89 (0.59 - 1.33)	0.33
Soluble dietary fiber	1.00	0.97 (0.68 - 1.39)	1.02 (0.71 - 1.46)	0.71 (0.48 - 1.06)	0.16	1.00	0.99 (0.68 - 1.43)	1.06 (0.73 - 1.54)	0.74 (0.49 - 1.12)	0.25
Insoluble dietary fiber	1.00	1.04 (0.73 - 1.49)	1.08 (0.75 - 1.55)	0.75 (0.50 - 1.12)	0.24	1.00	1.03 (0.70 - 1.49)	1.07 (0.73 - 1.56)	0.78 (0.51 - 1.20)	0.35
Total dietary fiber	1.00	0.91 (0.63 - 1.31)	1.01 (0.71 - 1.45)	0.72 (0.49 - 1.08)	0.21	1.00	0.88 (0.60 - 1.28)	1.01 (0.70 - 1.47)	0.76 (0.50 - 1.15)	0.35
n-3 PUFA	1.00	0.93 (0.65 - 1.34)	0.83 (0.57 - 1.20)	0.86 (0.59 - 1.24)	0.33	1.00	0.92 (0.63 - 1.34)	0.83 (0.56 - 1.23)	0.85 (0.57 - 1.27)	0.37
n-6 PUFA	1.00	0.99 (0.68 - 1.44)	0.87 (0.59 - 1.27)	1.01 (0.70 - 1.47)	0.90	1.00	0.93 (0.63 - 1.38)	0.85 (0.57 - 1.27)	0.97 (0.65 - 1.45)	0.78
n-6 PUFA/n-3 PUFA	1.00	0.87 (0.59 - 1.29)	1.03 (0.71 - 1.51)	1.23 (0.85 - 1.77)	0.18	1.00	0.88 (0.59 - 1.32)	1.03 (0.70 - 1.53)	1.23 (0.84 - 1.80)	0.21
Soy foods	1.00	1.11 (0.78 - 1.59)	0.81 (0.55 - 1.20)	1.03 (0.71 - 1.50)	0.73	1.00	1.19 (0.82 - 1.73)	0.85 (0.56 - 1.27)	1.03 (0.69 - 1.53)	0.70
Meat	1.00	0.93 (0.66 - 1.33)	0.65 (0.44 - 0.95)	0.76 (0.52 - 1.10)	0.050	1.00	0.99 (0.68 - 1.42)	0.68 (0.46 - 1.02)	0.72 (0.48 - 1.07)	0.036
Fish	1.00	0.77 (0.53 - 1.12)	0.81 (0.56 - 1.18)	1.00 (0.69 - 1.43)	0.99	1.00	0.75 (0.51 - 1.10)	0.75 (0.51 - 1.11)	1.03 (0.70 - 1.51)	0.98
Green-yellow vegetables	1.00	0.91 (0.64 - 1.30)	0.78 (0.54 - 1.14)	0.78 (0.54 - 1.14)	0.14	1.00	0.94 (0.65 - 1.35)	0.76 (0.52 - 1.13)	0.83 (0.55 - 1.24)	0.22
Other vegetables	1.00	1.19 (0.83 - 1.70)	0.90 (0.61 - 1.32)	0.84 (0.57 - 1.25)	0.21	1.00	1.13 (0.78 - 1.63)	0.92 (0.62 - 1.37)	0.78 (0.52 - 1.18)	0.16
Fruit	1.00	1.27 (0.88 - 1.84)	1.03 (0.69 - 1.52)	1.21 (0.82 - 1.78)	0.58	1.00	1.35 (0.92 - 1.97)	1.16 (0.77 - 1.76)	1.23 (0.81 - 1.87)	0.51

* : adjusted for sex, age, and year of first visit.

† : further adjusted for season of first visit to the hospital, reason for the visit, family history of colorectal cancer, body mass index, exercise, alcohol drinking, smoking, multivitamin use, and energy intake.

‡ : saturated fatty acids

§ : monounsaturated fatty acids

‖ : polyunsaturated fatty acids

Table 4. Odds ratios* (ORs) for colon cancer according to quartiles (Q1-Q4) of energy-adjusted intake of nutrients or food groups by sex.

	Men (149 cases and 1,475 controls)					Women (116 cases and 1,060 controls)				
Nutrients/food groups	Q1	Q2	Q3	Q4	Trend p	Q1	Q2	Q3	Q4	Trend p
Protein	1.00	0.79 (0.48 - 1.31)	0.79 (0.48 - 1.30)	0.78 (0.47 - 1.31)	0.38	1.00	0.71 (0.41 - 1.24)	0.48 (0.26 - 0.87)	0.67 (0.38 - 1.18)	0.077
Fat	1.00	1.05 (0.65 - 1.69)	0.70 (0.41 - 1.19)	0.94 (0.57 - 1.55)	0.49	1.00	0.96 (0.56 - 1.64)	0.60 (0.33 - 1.09)	0.59 (0.32 - 1.07)	0.035
Carbohydrate	1.00	1.21 (0.71 - 2.05)	0.89 (0.51 - 1.57)	0.81 (0.43 - 1.53)	0.33	1.00	0.93 (0.50 - 1.74)	1.04 (0.55 - 1.95)	1.51 (0.82 - 2.78)	0.15
Calcium	1.00	0.89 (0.54 - 1.47)	0.85 (0.51 - 1.41)	0.77 (0.46 - 1.30)	0.33	1.00	0.87 (0.51 - 1.51)	0.75 (0.42 - 1.33)	0.52 (0.28 - 0.97)	0.035
Carotene	1.00	0.71 (0.42 - 1.21)	0.95 (0.57 - 1.57)	0.86 (0.50 - 1.49)	0.88	1.00	0.81 (0.45 - 1.46)	0.81 (0.46 - 1.44)	0.92 (0.51 - 1.65)	0.78
Retinol	1.00	0.74 (0.44 - 1.24)	0.80 (0.48 - 1.33)	0.99 (0.60 - 1.63)	0.94	1.00	1.04 (0.57 - 1.88)	1.34 (0.74 - 2.40)	1.20 (0.67 - 2.17)	0.40
Vitamin D	1.00	0.98 (0.59 - 1.61)	1.02 (0.63 - 1.67)	0.97 (0.59 - 1.61)	0.96	1.00	1.09 (0.62 - 1.91)	0.63 (0.34 - 1.18)	1.19 (0.67 - 2.11)	0.96
Vitamin E	1.00	0.82 (0.49 - 1.37)	1.03 (0.63 - 1.68)	1.02 (0.61 - 1.71)	0.71	1.00	0.72 (0.41 - 1.24)	0.93 (0.55 - 1.59)	0.48 (0.25 - 0.90)	0.069
Folate	1.00	0.88 (0.53 - 1.45)	0.75 (0.45 - 1.27)	0.87 (0.51 - 1.48)	0.52	1.00	0.48 (0.26 - 0.89)	0.95 (0.55 - 1.63)	0.68 (0.38 - 1.23)	0.56
Vitamin C	1.00	0.74 (0.45 - 1.23)	0.74 (0.45 - 1.24)	0.72 (0.42 - 1.22)	0.26	1.00	0.74 (0.41 - 1.32)	1.03 (0.59 - 1.78)	0.61 (0.33 - 1.12)	0.25
SFA†	1.00	0.88 (0.53 - 1.46)	0.87 (0.52 - 1.46)	0.95 (0.57 - 1.60)	0.89	1.00	0.64 (0.36 - 1.14)	0.62 (0.35 - 1.10)	0.66 (0.38 - 1.17)	0.16
MUFA‡	1.00	0.87 (0.51 - 1.47)	1.27 (0.76 - 2.11)	1.21 (0.70 - 2.09)	0.27	1.00	1.07 (0.62 - 1.83)	0.87 (0.48 - 1.56)	0.67 (0.36 - 1.24)	0.16
PUFA§	1.00	1.14 (0.68 - 1.92)	1.22 (0.72 - 2.06)	1.32 (0.78 - 2.26)	0.29	1.00	0.55 (0.31 - 0.99)	0.88 (0.51 - 1.52)	0.58 (0.32 - 1.03)	0.18
Cholesterol	1.00	1.19 (0.71 - 2.01)	1.24 (0.74 - 2.09)	1.02 (0.58 - 1.80)	0.93	1.00	0.49 (0.28 - 0.87)	0.55 (0.31 - 0.95)	0.54 (0.31 - 0.95)	0.037
Soluble dietary fiber	1.00	0.95 (0.58 - 1.57)	0.91 (0.55 - 1.49)	0.77 (0.46 - 1.30)	0.32	1.00	0.85 (0.49 - 1.46)	0.61 (0.34 - 1.10)	0.77 (0.43 - 1.37)	0.22
Insoluble dietary fiber	1.00	0.62 (0.37 - 1.04)	0.72 (0.44 - 1.18)	0.67 (0.40 - 1.12)	0.20	1.00	0.84 (0.48 - 1.44)	0.58 (0.33 - 1.04)	0.69 (0.39 - 1.24)	0.11
Total dietary fiber	1.00	0.94 (0.57 - 1.56)	0.89 (0.53 - 1.47)	0.84 (0.50 - 1.43)	0.50	1.00	0.67 (0.38 - 1.17)	0.55 (0.31 - 0.97)	0.63 (0.35 - 1.13)	0.073
n-3 PUFA	1.00	1.03 (0.62 - 1.71)	1.14 (0.69 - 1.89)	0.97 (0.57 - 1.66)	0.98	1.00	0.72 (0.40 - 1.28)	0.88 (0.50 - 1.54)	0.81 (0.45 - 1.44)	0.60
n-6 PUFA	1.00	0.83 (0.48 - 1.43)	1.29 (0.78 - 2.13)	1.09 (0.63 - 1.87)	0.40	1.00	0.71 (0.41 - 1.24)	0.82 (0.46 - 1.46)	0.63 (0.35 - 1.12)	0.17
n-6 PUFA/n-3 PUFA	1.00	0.96 (0.58 - 1.59)	1.29 (0.80 - 2.07)	0.79 (0.48 - 1.31)	0.63	1.00	0.91 (0.51 - 1.64)	1.19 (0.68 - 2.07)	0.86 (0.47 - 1.57)	0.89
Soy foods	1.00	1.37 (0.83 - 2.26)	1.11 (0.66 - 1.88)	1.17 (0.69 - 1.96)	0.79	1.00	1.54 (0.88 - 2.69)	0.77 (0.42 - 1.43)	0.83 (0.44 - 1.54)	0.18
Meat	1.00	1.25 (0.75 - 2.09)	1.32 (0.79 - 2.20)	1.15 (0.68 - 1.95)	0.59	1.00	0.96 (0.54 - 1.69)	1.03 (0.58 - 1.83)	0.73 (0.40 - 1.34)	0.39
Fish	1.00	1.36 (0.82 - 2.26)	1.33 (0.79 - 2.21)	1.13 (0.66 - 1.92)	0.72	1.00	0.97 (0.55 - 1.70)	0.70 (0.38 - 1.29)	1.11 (0.63 - 1.95)	0.98
Green-yellow vegetables	1.00	0.97 (0.59 - 1.60)	0.96 (0.58 - 1.58)	0.88 (0.52 - 1.48)	0.62	1.00	0.90 (0.51 - 1.58)	0.71 (0.40 - 1.26)	0.69 (0.38 - 1.23)	0.15
Other vegetables	1.00	1.10 (0.68 - 1.80)	0.75 (0.44 - 1.28)	0.95 (0.58 - 1.58)	0.54	1.00	1.29 (0.74 - 2.27)	0.89 (0.48 - 1.62)	1.08 (0.60 - 1.94)	0.89
Fruit	1.00	0.57 (0.34 - 0.95)	0.67 (0.41 - 1.10)	0.67 (0.41 - 1.11)	0.19	1.00	1.00 (0.57 - 1.77)	0.75 (0.41 - 1.38)	0.90 (0.50 - 1.62)	0.54

* : adjusted for age, year of first visit to the hospital, season of first visit, reason for the visit, family history of colorectal cancer, body mass index, exercise, alcohol drinking, smoking, multivitamin use, and energy intake.

† : saturated fatty acids

‡ : monounsaturated fatty acids

§ : polyunsaturated fatty acids

95% confidence intervals in parentheses

Table 5. Odds ratios* (ORs) for rectal cancer according to quartiles (Q1-Q4) of energy-adjusted intake of nutrients or food groups by sex.

Nutrients/food groups	Men (146 cases and 1,475 controls)					Women (96 cases and 1,060 controls)				
	Q1	Q2	Q3	Q4	Trend p	Q1	Q2	Q3	Q4	Trend p
Protein	1.00	1.02 (0.61 - 1.69)	1.23 (0.75 - 2.01)	0.77 (0.43 - 1.37)	0.62	1.00	0.65 (0.35 - 1.21)	0.64 (0.35 - 1.20)	0.66 (0.36 - 1.24)	0.19
Fat	1.00	1.12 (0.67 - 1.88)	1.24 (0.74 - 2.09)	1.15 (0.67 - 1.96)	0.56	1.00	0.57 (0.31 - 1.02)	0.61 (0.33 - 1.12)	0.38 (0.19 - 0.75)	0.008
Carbohydrate	1.00	1.13 (0.67 - 1.92)	1.12 (0.63 - 2.00)	1.07 (0.54 - 2.10)	0.86	1.00	1.17 (0.55 - 2.52)	2.14 (1.05 - 4.36)	2.53 (1.22 - 5.24)	0.003
Calcium	1.00	1.44 (0.87 - 2.41)	1.40 (0.82 - 2.41)	1.26 (0.71 - 2.25)	0.51	1.00	1.11 (0.60 - 2.05)	1.27 (0.68 - 2.36)	0.73 (0.36 - 1.47)	0.53
Carotene	1.00	1.44 (0.87 - 2.36)	0.83 (0.47 - 1.45)	1.05 (0.58 - 1.91)	0.58	1.00	0.83 (0.46 - 1.48)	0.66 (0.36 - 1.23)	0.48 (0.24 - 0.95)	0.028
Retinol	1.00	1.12 (0.66 - 1.89)	1.39 (0.83 - 2.33)	1.18 (0.67 - 2.08)	0.40	1.00	1.09 (0.61 - 1.95)	0.82 (0.44 - 1.53)	0.76 (0.40 - 1.48)	0.31
Vitamin D	1.00	0.92 (0.56 - 1.51)	0.93 (0.56 - 1.53)	0.91 (0.54 - 1.54)	0.74	1.00	0.61 (0.32 - 1.16)	0.72 (0.38 - 1.37)	1.11 (0.60 - 2.03)	0.71
Vitamin E	1.00	0.87 (0.51 - 1.47)	1.18 (0.72 - 1.94)	1.00 (0.58 - 1.73)	0.69	1.00	0.48 (0.26 - 0.85)	0.47 (0.25 - 0.87)	0.42 (0.22 - 0.80)	0.006
Folate	1.00	1.17 (0.71 - 1.95)	1.06 (0.62 - 1.81)	1.14 (0.64 - 2.02)	0.77	1.00	0.87 (0.49 - 1.53)	0.60 (0.31 - 1.14)	0.59 (0.31 - 1.14)	0.063
Vitamin C	1.00	0.87 (0.53 - 1.41)	0.91 (0.55 - 1.52)	0.73 (0.42 - 1.27)	0.33	1.00	1.06 (0.58 - 1.94)	0.72 (0.37 - 1.41)	1.04 (0.55 - 1.97)	0.83
SFA†	1.00	1.14 (0.68 - 1.91)	1.32 (0.78 - 2.22)	1.02 (0.58 - 1.80)	0.83	1.00	1.39 (0.76 - 2.57)	1.21 (0.64 - 2.30)	0.72 (0.36 - 1.45)	0.32
MUFA‡	1.00	0.93 (0.55 - 1.57)	0.86 (0.50 - 1.48)	1.23 (0.71 - 2.14)	0.51	1.00	0.57 (0.31 - 1.04)	0.46 (0.24 - 0.88)	0.47 (0.24 - 0.89)	0.014
PUFA§	1.00	0.69 (0.40 - 1.19)	1.08 (0.65 - 1.79)	1.06 (0.63 - 1.78)	0.46	1.00	0.54 (0.29 - 1.01)	0.76 (0.43 - 1.36)	0.53 (0.27 - 1.01)	0.11
Cholesterol	1.00	1.15 (0.69 - 1.92)	1.05 (0.62 - 1.78)	1.11 (0.63 - 1.96)	0.82	1.00	0.98 (0.55 - 1.76)	0.54 (0.27 - 1.06)	0.73 (0.39 - 1.37)	0.15
Soluble dietary fiber	1.00	1.45 (0.88 - 2.38)	1.33 (0.80 - 2.23)	0.93 (0.53 - 1.65)	0.77	1.00	0.59 (0.32 - 1.09)	0.91 (0.51 - 1.63)	0.66 (0.34 - 1.26)	0.37
Insoluble dietary fiber	1.00	1.19 (0.72 - 1.98)	1.40 (0.85 - 2.33)	0.83 (0.46 - 1.50)	0.78	1.00	0.88 (0.49 - 1.58)	0.77 (0.41 - 1.42)	0.84 (0.44 - 1.60)	0.49
Total dietary fiber	1.00	1.04 (0.63 - 1.70)	1.17 (0.71 - 1.94)	0.83 (0.47 - 1.45)	0.68	1.00	0.69 (0.37 - 1.29)	0.92 (0.51 - 1.67)	0.78 (0.40 - 1.51)	0.64
n-3 PUFA	1.00	0.94 (0.56 - 1.57)	1.02 (0.61 - 1.69)	0.96 (0.56 - 1.65)	0.97	1.00	1.02 (0.57 - 1.82)	0.65 (0.34 - 1.25)	0.80 (0.42 - 1.53)	0.29
n-6 PUFA	1.00	1.07 (0.63 - 1.85)	1.10 (0.64 - 1.90)	1.57 (0.91 - 2.74)	0.11	1.00	0.86 (0.47 - 1.55)	0.73 (0.39 - 1.38)	0.58 (0.30 - 1.14)	0.098
n-6 PUFA/n-3 PUFA	1.00	0.73 (0.42 - 1.30)	1.28 (0.78 - 2.10)	1.45 (0.88 - 2.38)	0.042	1.00	1.16 (0.63 - 2.14)	0.70 (0.36 - 1.37)	1.03 (0.55 - 1.93)	0.71
Soy foods	1.00	1.32 (0.81 - 2.16)	0.88 (0.51 - 1.50)	1.12 (0.66 - 1.90)	0.93	1.00	1.00 (0.55 - 1.84)	0.77 (0.40 - 1.48)	0.96 (0.51 - 1.81)	0.71
Meat	1.00	0.97 (0.60 - 1.57)	0.56 (0.33 - 0.97)	0.85 (0.51 - 1.40)	0.24	1.00	1.05 (0.58 - 1.89)	1.01 (0.54 - 1.88)	0.52 (0.26 - 1.05)	0.093
Fish	1.00	0.92 (0.56 - 1.49)	0.79 (0.48 - 1.30)	0.89 (0.53 - 1.51)	0.53	1.00	0.55 (0.28 - 1.07)	0.77 (0.41 - 1.45)	1.29 (0.71 - 2.36)	0.33
Green-yellow vegetables	1.00	1.14 (0.70 - 1.86)	0.88 (0.52 - 1.49)	1.11 (0.65 - 1.90)	0.95	1.00	0.76 (0.42 - 1.38)	0.70 (0.38 - 1.28)	0.58 (0.30 - 1.12)	0.095
Other vegetables	1.00	1.47 (0.91 - 2.40)	0.96 (0.56 - 1.65)	0.92 (0.54 - 1.59)	0.41	1.00	0.81 (0.45 - 1.48)	0.92 (0.50 - 1.68)	0.72 (0.37 - 1.37)	0.40
Fruit	1.00	1.66 (1.01 - 2.72)	1.46 (0.86 - 2.49)	1.04 (0.58 - 1.86)	0.99	1.00	1.00 (0.53 - 1.88)	0.74 (0.37 - 1.49)	1.47 (0.79 - 2.73)	0.33

* : adjusted for age, year of first visit to the hospital, season of first visit, reason for the visit, family history of colorectal cancer, body mass index, exercise, alcohol drinking, smoking, multivitamin use, and energy intake.

† : saturated fatty acids

‡ : monounsaturated fatty acids

§ : polyunsaturated fatty acids

95% confidence intervals in parentheses

consistent with the finding of the European study mentioned above[23] and might be expected because the rectum is empty most of the time, reducing the putative protective effects of dietary fiber.[23]

The intake of carotene was negatively associated with the risk of rectal cancer, particularly in female subjects. Women who consumed much green-yellow vegetables tended to show a lower risk of rectal cancer. A risk-reducing effect of dietary carotene was suggested for rectal cancer in some earlier case-control studies.[4,26,27] The association, however, should be further examined in cohort studies because several large prospective studies have recently pointed to no preventive effects of fruit and vegetables, which are rich in carotene.[28-30]

Although red meat consumption has been linked to the risk of colorectal cancer,[31-33] we have failed to find any positive association of meat and in fact observed a relation to a somewhat decreased risk for rectal cancer. In Japan, red meat accounts for a smaller proportion of all meat consumption than in Western countries (http://faostat.fao.org/faostat/) and colorectal cancer risk may be reduced or unaltered by non-red meat,[32,34] so this might explain the lack of any deleterious effect of meat in our study. Our finding is consistent with the results of a case-control study in China, which reported an increased risk of rectal cancer associated with reduced consumption of meat.[5] Another case-control study conducted in Japan also reported that meat consumption was inversely correlated with the risk of rectal cancer.[6]

A high correlation between national per capita intake of fat and national rates of colon cancer has led to the hypothesis that consumption of fat increases risk of colon cancer. In general, however, neither case-control nor cohort studies have provided unequivocal support for this hypothesis.[35] In our study, intakes of fat, cholesterol, and monounsaturated fatty acids were inversely correlated with the risk of female colon and/or rectal cancer whereas a higher intake of carbohydrate was associated with rectal cancer risk, especially in women.

Some[36,37] but not all[38,39] case-control and cohort studies have suggested that higher intake of carbohydrate may increase colorectal cancer risk and this has been discussed in relation to insulin resistance. If this is the case, higher intake of fat and protein relative to carbohydrate may seemingly be linked to a decreased risk. As we suggested for colon cancer, Franceschi et al[40] found a decreased risk associated with a higher intake of protein.

Several significant associations between dietary variables and colon or rectal cancer risk appeared in women but not in men. This may partly be attributable to the difference in intake levels of nutrients or food groups between the sexes. For example, men took more carbohydrate (median of the estimated intake in controls: 242.6 g/day in men versus 207.2 g/day in women) but less green-yellow vegetables (median in controls: 49.5 g/day versus 69.2 g/day) from our present data (values are adjusted to the mean energy intake of 1,710 and 1,493 kcal/day for men and women, respectively). On the other hand, variation by sex may be due to random fluctuation because the numbers of cases by site of cancer and sex were relatively small.

Dietary risk factors could be directly compared between colon and rectal cancers in the present study because the procedures for identification of cases and data collection were exactly the same and the control group was common for the two sites of cancer.

Some methodological limitations, however, need consideration. First, because this was a hospital-based case-control study, the source population from which cases arise may differ from that for controls. To take this into consideration, we adjusted for the reason for the first visit to ACCH and the season. Second, as with other case-control studies, this study may suffer from recall bias. Although the questionnaires were completed before the diagnosis in ACCH, some case patients referred to the hospital might have known the diagnosis. It is unlikely, however, that the recall bias affected the findings differentially between colon and rectal cancers. Third, because we examined many nutrients and food groups in relation to the risk of colon and rectal cancers, multiple comparisons may be another issue. Some findings might have appeared by chance. The difference in dietary risk factors between colon and rectal cancers found in the present study, therefore, warrant confirmation in further investigations. The increase in incidence of colorectal cancer over time[1] may mean that most Japanese have changed their lifestyles, including their dietary consumption, so that detection of dietary risk or protective factors in case-control or cohort studies within the Japanese population faces particular problems. Finally, the limitations of the questionnaire may have prevented us from considering some potential confounding factors. For example, no information was available on non-steroidal anti-inflammatory drugs (NSAIDs), which may exert protective effects against colorectal cancer[41] and may confound associations between diet and the risk of cancer.

In conclusion, dietary preventive factors appear to considerably differ between colon and rectal cancers: calcium and insoluble dietary fiber may protect against colon cancer while carotene and meat may be more effective for rectal cancer. Carbohydrate intake was positively correlated with the risk of rectal cancer, especially in women.

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