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Colorectal cancer screening

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Colorectal cancer (CRC) is the third most common malignant neoplasm worldwide and the second leading cause of cancer deaths in the United States. It is estimated that there will have been 150,000 new cases diagnosed in the United States in 2010 and more than 50,000 deaths as a result of this disease. Although there has been an increase in CRC screening rates from 30% in 1997 to 55% in 2008, it remains much lower than the 80% screening rates for breast cancer. Evidence suggests that CRC screening is simultaneously underused in patients who would derive benefit from screening, overused in patients with advanced age or comorbidities who would not derive benefit, and misused when abnormal results are not appropriately followed up or inadequate testing is performed. Compliance with CRC screening was primarily driven by primary care provider recommendations. Providers must be able to categorize patients as either average-risk or increased-risk based on personal and family history of CRC or adenomatous polyps. Reviewing the family history for CRC or polyps should be part of routine health maintenance. Screening for average-risk individuals should begin at age 50 and continue until age 75. Average-risk African-American men should begin CRC screening at age 45. Individuals at increased risk should begin screening at age 40 or 10 years before the earliest age of diagnosis in a family member. Colonoscopy has been recognized as the preferred method for CRC screening in the United States, and with regular screening more than 60% of deaths from CRC can be prevented.

Colorectal cancer (CRC) is the third most common malignant neoplasm worldwide and the second leading cause of cancer deaths in the United States, with only lung cancer being more prevalent.[1-3] It is estimated that there will have been 150,000 new cases diagnosed in the United States in 2010 and more than 50,000 deaths as a result of this disease.[4,5] The incidence of CRC has been declining since the 1990s owing to increased physician and patient awareness, better compliance with screening guidelines, and earlier and more effective treatment of precancerous colorectal lesions; however, screening rates remain low.[2]

The incidence is higher in men than in women (Fig. 1).[6] The age-adjusted mortality rates for men and women are 24.8 per 100,000 per year in men and 17.4 per 100,000 per year in women.[6] Approximately 6% of Americans are expected to develop CRC within their lifetime and about half of those will die from it. Age-specific incidence and mortality rates show that the vast majority of cases are diagnosed after age 50, with only approximately 7% of CRC occurring in those younger than age 50 years.[6]

Screening is an effective way to reduce CRC mortality, both by removing premalignant lesions and detecting early cancers. The US Preventative Task Force recommends screening beginning at age 50 years and continuing until age 75 years.[7]

Factors affecting screening

Evidence suggests that CRC screening is simultaneously underused in patients who would derive benefit from

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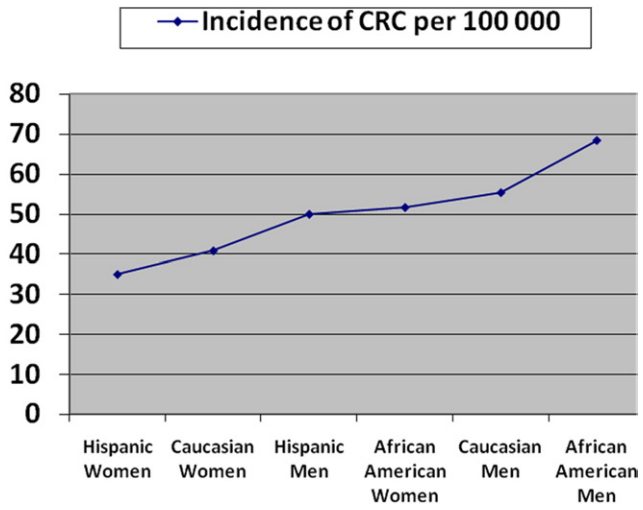

Figure 1 Incidence of colorectal cancer per 100,000 persons.

screening, overused in patients with advanced age or comorbidities who would not derive benefit, and misused when abnormal results are not appropriately followed-up or inadequate testing is performed.[2,8]

Although there has been an increase in CRC screening rates from 30% in 1997 to 55% in 2008, it remains much lower than the 80% screening rates for breast cancer.[2,5] Among Americans age 50 and older, 18% had a fecal occult blood testing (FOBT) during the preceding year and approximately 50% had a sigmoidoscopy or colonoscopy during the previous 10 years.[7] This suggests a need for continued improvement in depth and frequency of patient/provider discussions about CRC screening to improve screening rates.

Those with the lowest screening prevalence include persons aged 50 to 59 years, Hispanics, persons with lower income, those with less than a high school education, and those without health insurance.[3,9] Lack of a primary care provider or adequate health insurance and limited income contribute to the underuse of CRC screening. This may be compounded by the rising use of colonoscopy, the most expensive screening test, as the preferred method of screening.[10]

In 2001, Medicare approved payment for screening colonoscopy for those of average risk as defined by national guidelines as individuals without a personal or family history of CRC or adenomatous polyps.[10] Medicare does not pay for screening by computed tomography (virtual) colonoscopy (CTC).[11] Private insurance coverage is variable in the United States, resulting in patients with high deductible health plans being screened more often with FOBT testing than with colonoscopy.[12]

Emmons examined the impact of health insurance on racial/ethnic disparities in CRC screening. A low-income, racial/ethnic minority sample in which 97% had health insurance that covered CRC screening, identified a self-reported 67% screening rate with a 52% adjusted rate based on a validation substudy.[13] This rate was higher than among similar population-based samples that had lower levels of insurance coverage.[13] No screening rate differences based on race/ethnicity were identified. This study suggests that insurance coverage for CRC screening should be considered as part of a comprehensive approach to address CRC disparities.[13]

Multiple studies have shown that low rates of cancer screening are associated with socioeconomic status, ethnic origin, age, and gender. Psychological factors such as embarrassment, fear of cancer, and lack of knowledge may also affect cancer screening rates. More than 44 studies examining factors affecting compliance with CRC screening guidelines found that a positive attitude toward screening was the primary factor in compliance with screening.[14]

For many women, gynecologists are an important source of primary care. Thirty-seven to 93% of obstetricians/gynecologists consider themselves to be primary care providers.[15] In a study of gynecologic patients, it was found that having multiple providers recommend colorectal screening improved a patient's intention to undergo CRC screening. Compliance, however, was primarily driven by primary care provider recommendations.[15] Strategies should be in place to prompt gynecologists to discuss CRC screening in eligible patients as part of the annual maintenance examination, which may help to improve screening compliance in female patients.

A recent study published in the *British Journal of Cancer* found that men, older individuals, and those with South-Asian ethnic backgrounds were more likely to have a negative attitude toward CRC screening. Persons of Caribbean ethnic background and patients experiencing abdominal pain, bleeding, fatigue, or multiple symptoms were more likely to have a positive attitude toward screening.[14] Development of culturally relative screening strategies and increasing patient educational materials outlining the symptoms and signs of CRC may increase adherence in targeted screening populations.

Pathogenesis

More than 95% of CRCs are adenocarcinomas that arise from adenomatous polyps.[16] The progression from adenoma to carcinoma is slow and it is believed that the removal of adenomatous polyps is responsible for the decline in CRC in the United States.[17] Some CRCs arise from nonpolypoid adenomas that are flat or depressed and account for 22 to 36% of identified adenomas.[18] Flat and depressed lesions can be difficult to detect and may be more likely to contain dysplastic changes or cancer than polypoid ones of comparable size.[18]

The risk of developing CRC increases with adenoma size, number, and histology, with villous adenomas having a greater risk than tubular adenomas.[19] The finding of a single adenomatous polyp suggests a propensity to form polyps, and the patient should be evaluated for other lesions in the colon and rectum.

Risk factors for colorectal cancer

Patients are categorized as either "average risk" or "increased risk." Average-risk individuals are defined as those without a personal or family history of CRC or adenomatous polyps and account for the majority of the population. Most cases of CRC occur in average-risk individuals.[9] Increasing age, male sex, black race, and history of smoking are associated with an identified increase in incidence of CRC but are not used in the classification of average-risk versus increased-risk categories.[9]

Patients are considered to be at increased-risk under the following conditions: (1) A first-degree relative with colon cancer or advanced adenoma (≥1 cm, or high-grade dysplasia or villous elements) diagnosed at age <60 years; (2) two first-degree relatives diagnosed at any age; or (3) personal history of CRC, polyp, inflammatory bowel disease including ulcerative colitis or Crohn's Disease; Lynch syndrome/hereditary nonpolyposis colon cancer (HNPCC); or familial adenomatous polyposis (FAP)[20] (Table 1[1,17]).

Family history

In the United States, 5% of adults aged 20 to 79 years report a first- or second-degree relative with a history of CRC.[21] The incidence is believed to be because families share behaviors and environmental exposures along with their genes. When screening for genetic risks for CRC, the review of family history should include inquiry of blood relatives diagnosed with CRC or polyps (Fig. 2[22-24]). If positive, distinction of first-degree relatives (parent, sibling, or child) versus other relatives (grandparent, cousin, niece, or nephew) should be made for each family member identified along with the age at diagnosis.[22] Individuals with a sibling who has had CRC diagnosed before the age of 60 are at increased risk for CRC and may derive benefits from screening.[23,24]

Table 1 Risk factors for colorectal cancer

Personal history of colorectal polyps or colorectal cancer
Personal history of inflammatory bowel disease
Family history of colorectal cancer
Inherited syndromes including:
Familial adenomatous polyposis (FAP)
Lynch syndrome/Hereditary nonpolyposis colon cancer (HNPCC)
Turcot syndrome
Peutz-Jeghers syndrome
African American Race
Jews of Eastern European descent (Ashkenazi Jews)
Lifestyle-related factors including:
Diet high in red meats (beef, pork, lamb)
Diet high in processed meats (hot dogs and some luncheon meats)
Physical inactivity
Obesity
Smoking
Heavy alcohol use
Type 2 diabetes

Family history is commonly overlooked. In a survey of patients aged 35 to 55 years enrolled in a group practice, 39% of patients reported that they had not been asked about family history.[20] In patients with a strong family history of CRC, 46% of patients did not know they should be screened at an earlier age and 55% had not been appropriately screened.[20]

Reviewing the family history for CRC or polyps should be part of routine health maintenance and occur at least on a yearly basis because cancers may arise in family members as they age. A positive family history of CRC prompts screening to begin 10 years before the earliest age of diagnosis in a relative.[20] For example, during a routine history and physical examination, your 34-year-old male patient's family history reveals a brother diagnosed with CRC at 45 years of age. This would prompt CRC screening in your patient to begin at 35 years of age instead of 50 for average-risk patients.

Screening for a family history of CRC has been found to be cost-effective and has been estimated to save $58,228 per year of life gained.[25] The highest risk is seen in people with multiple first-degree relatives or relatives who have developed CRC before the age of 50 years and is greater for relatives of patients with colon, compared with rectal, cancer.[26] People with a family history of CRC are screened at an earlier age than people at average risk because cancer will occur earlier in their life, not uncommonly in the 30s or 40s.[26] If a patient has a family history of Lynch syndrome or FAP, aggressive screening consisting of an annual colonoscopy beginning at age 20 to 25, or 10 years before the earliest age of colon cancer diagnosis in the family (whichever comes first) and/or genetic testing should be pursued.[27-29]

Colorectal cancers occurring in distant relatives or a single first-degree relative after the age of 60 are associated with a small increased risk of developing CRC, which is not large enough to change clinical advice or screening practices from those recommended for the general population.[30] Patients who have a family member with an adenomatous colonic polyp may also be at increased risk for CRC but it is uncertain whether an earlier onset of screening is indicated in patients whose possible increased risk relates only to a family history of polyps.[30]

Colorectal cancer screening guidelines

CRC screening recommendations must be first approached by appropriate classification of patients as average-risk or increased-risk (Fig. 2).[22-24]

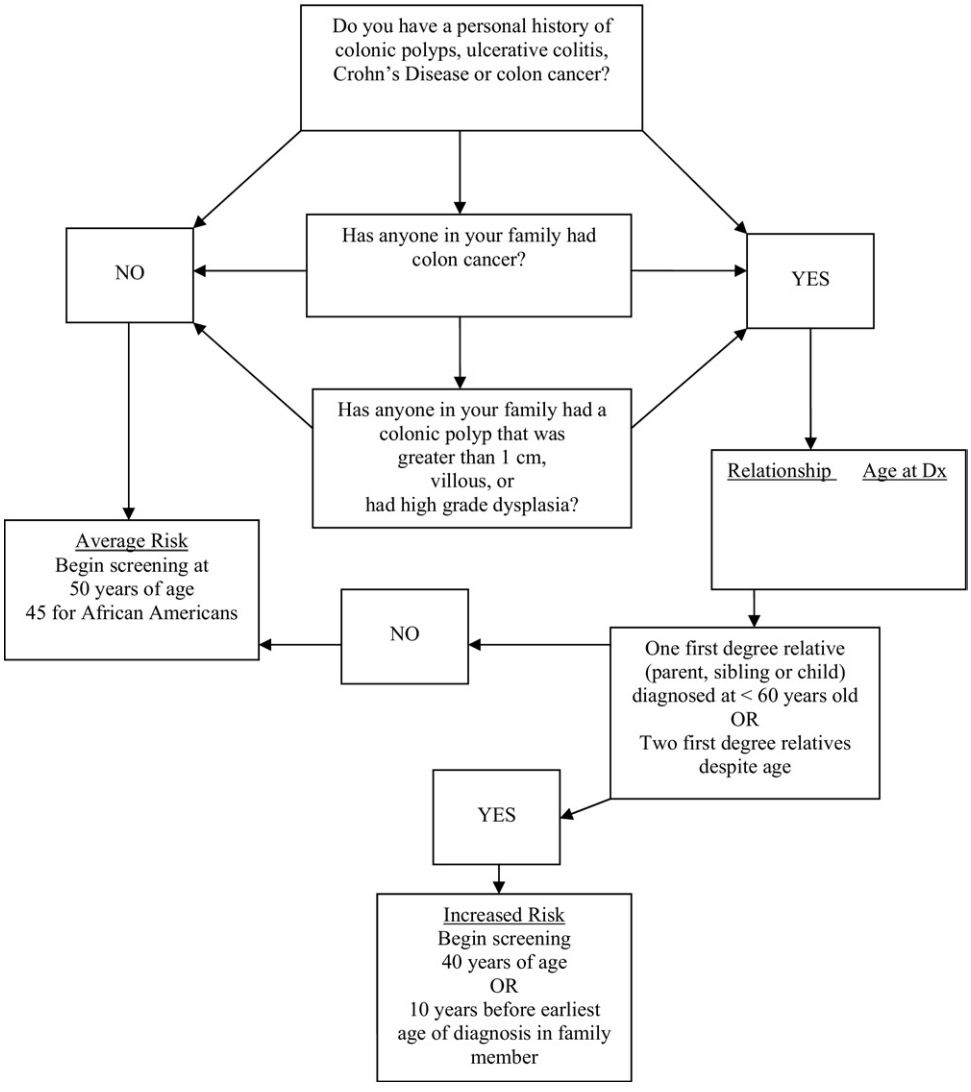

Figure 2 Colorectal cancer screening algorithm.

Screening for average-risk patients

For average-risk individuals, both men and women should begin screening for CRC at age 50. Frequency of testing is based on the method of screening used. Testing options are divided into two categories: tests that primarily find cancer and those that find polyps and cancer (Table 2).[31-33] The tests that are designed to find both early cancer and polyps are preferred if these tests are available and the patient is willing to have one of these more invasive tests.

Multiple guidelines for CRC screening have been published. The United States Preventive Services Task Force (USPSTF) recommends three screening options for adults ages 50 to 75 years, which have been found to be roughly equivalent in screening for CRC[31] (Table 3[31-33]). These guidelines did not weigh the value of identifying premalignant lesions (prevention) over the detection of cancer (screening). The National Comprehensive Cancer Network (NCCN) issued revised guidelines in January 2010 that recommend colonoscopy every ten years when available, as the preferred screening method beginning at age 50[32] (Table 3[31-33]). The NCCN did not come to consensus regarding CTC or fecal DNA as screening modalities. The American College of Gastroenterology (ACG) 2008 guidelines recommend colonoscopy as the preferred screening/prevention

Table 2 Colorectal cancer screening test options and frequency of evaluation

Tests that primarily find cancer	Tests that find polyps and cancer (preferred)
Fecal occult blood test (gFOBT)/yearly	Colonoscopy/every 10 years
Fecal immunochemical test (FIT)/yearly	Flexible sigmoidoscopy/every 5 years
Stool DNA test (sDNA)/interval uncertain	Double-contrast barium enema (DCBE)/every 5 years
	CT colonography (CTC)/every 5 years

Table 3 Colorectal cancer screening guideline comparison

United States Preventive Services Task Force Options 2008	National Comprehensive Cancer Network (NCCN), 2010	American College of Gastroenterology (ACG) 2008
Colonoscopy every 10 years	Colonoscopy every 10 years (preferred)	Colonoscopy (preferred)
Flexible sigmoidoscopy every 5 years, with sensitive FOBT every 3 years	Sigmoidoscopy every 5 years with or without annual stool testing	
Annual fecal occult blood test (FOBT) with a sensitive test	Annual stool testing with guaiac or immunochemical reagent	Fecal immunochemical test preferred for patients who decline colonoscopy
	Barium enema is only recommended when a colonoscopy cannot be performed	

test (Table 3[31-33]). The ACG recommends initiating screening at age 45, rather than 50, for African Americans.[33]

Screening for increased-risk patients

The ACG recommends the following guidelines for screening patients at increased risk for CRC because of a family history[33]:

- Screen with colonoscopy
- If a single first-degree relative was diagnosed at age 60 years or older with CRC or an advanced adenoma (≥1 cm, or high-grade dysplasia or villous elements), screening with colonoscopy is recommended every 10 years beginning at age 50
- If a single first-degree relative was diagnosed before 60 years with CRC or an advanced adenoma, or two or more first-degree relatives had CRC or advanced adenomas at any age, screening with colonoscopy is recommended at age 40 or 10 years before the youngest relative's diagnosis, and should be repeated every five years.

Screening in the elderly

The decision whether to recommend screening for a patient over 70 years of age should depend on the patient's health status, anticipated life expectancy, risk for CRC, and personal values.[34,35] The following factors should be considered in this decision:

- Patients with a life expectancy less than five years would not be expected to benefit from colorectal screening.
- The risks associated with the performance of a colonoscopy increase with age and comorbidities, including cardiopulmonary disease, diabetes mellitus, and history of stroke.[36] If the patient is expected to live long enough to benefit from screening, CTC should be considered.
- Sigmoidoscopy has reduced sensitivity in the elderly because advanced neoplasias tend to occur more proximally as patients age.

Most guidelines recommend that screening for CRC stop if the patient's life expectancy is less than 10 years.[16,31] The USPSTF guidelines recommend that patients over age 85 not be screened, and recommends against screening in adults 76 to 85 years, unless there are individual considerations that favor screening.[31] Overuse of screening in this population of advanced age and comorbidities and limited benefit remains a concern.

Screening modalities

There are advantages and disadvantages to each of the tests used in CRC screening (Table 4).[2,22,31] Screening with FOBT, flexible sigmoidoscopy, or colonoscopy reduces CRC mortality in adults age 50 to 75 years.[7,31] Follow-up of positive FOBT, sigmoidoscopy, or CTC requires colonoscopy. Misuse occurs when abnormal results are not appropriately followed up or inadequate testing is performed, such as FOBT performed only on a stool sample taken during digital rectal examination at an office visit. The multiple stool take-home test should be used. A single sample performed at the office is not adequate for testing.[2]

The benefit of less invasive screening tests is that they may reduce the number of colonoscopies required and their related risks. The benefits of detection decrease once a patient reaches 75 years of age. Competing causes of mortality make it less likely that the benefit of early detection will be realized with advancing age.[31]

Patient preferences have also been evaluated. One of the largest studies to evaluate procedure preferences in detail involved 614 increased-risk patients who underwent colonoscopy, CTC, and double-contrast barium enema (DCBE).[37] Patients preferred colonoscopy to the former two procedures and were least satisfied with DCBE.

Increasing colorectal screening rates

Current CRC screening rates range from 45 to 60% in the United States, which is lower than the 80% screening rates for breast cancer.[2] If everyone aged 50 years or older had regular screening tests, 60% or more of deaths from CRC could be avoided.[38] To continue to increase CRC screening, financial barriers will need to be eliminated and appropriate follow-up adhered to. Health reform is anticipated to reduce

Table 4 Advantages and disadvantages of colorectal cancer screening tests

Test	Advantages	Disadvantages
Fecal occult blood test (FOBT)	No bowel preparation is necessary Samples can be collected at home Low cost No risk of colon perforation/bleeding Minimal discomfort	Low detection rate for polyps False-positive results are possible. Dietary restrictions include avoiding: red meat, certain vegetables, vitamin C, iron supplements, and aspirin. (These restrictions and changes are not required for immunochemical FOBT.) Colonoscopy may be necessary if the test is positive
Sigmoidoscopy	Minimal discomfort Biopsy and removal of polyps during the test may be possible Less bowel preparation than for a colonoscopy	Only the rectum and the lower part of the colon can be viewed Serious complications* are estimated to be 3.4 per 10,000 procedures Colonoscopy may be necessary if the test is positive
Colonoscopy	The entire colon and the rectum can be visualized Diagnostic and therapeutic Highly accurate Biopsy and removal of polyps can be performed Covered by most insurance plans Cost-effective	Not all polyps (up to 27% are missed), nonpolypoid lesions, and cancers are detected Bowel preparation is necessary Sedation is required Perforation is estimated to occur in 3.8 per 10,000 procedures Serious complications* are estimated to occur in 25 per 10,000 procedures Absence from work Poor patient acceptance in some instances
Virtual colonoscopy	The entire colon and the rectum can be visualized Therapeutic only Highly accurate Risk of bleeding or tearing/perforation of the colon is very rare No sedation needed May detect clinically important extracolonic pathology Cost-effective in some analyses	Up to 50% of polyps <5 mm are missed Bowel preparation is necessary Detection of a polyp or nonpolypoid lesion 6-9 mm or larger requires optical colonoscopy to remove the polyp or lesion or perform a biopsy Extracolonic findings are found in 7% to 16% of cases requiring further testing, adding expense and morbidity Radiation exposure Limited insurance coverage (not covered by Medicare or Medicaid)
Double-contrast barium enema (DCBE)	The entire colon and rectum can be visualized Therapeutic only Complications are rare No sedation needed	Small polyps and cancers may be missed Bowel preparation is necessary Optical colonoscopy is required to remove polyps or perform a biopsy False positives are possible
Digital rectal examination (DRE)	Part of physical examination after age 50 No bowel prep required Test is quick and painless	Detection of abnormalities in the lower part of the rectum A colonoscopy may be necessary if the test is positive

*Serious complications include death, perforation, major bleeding, severe abdominal pain, cardiovascular events, or an event requiring hospitalization.

the financial barriers to CRC screening, but multiple factors influence screening.

Interventions that have proven effective at increasing CRC screening—including electronic medical records with patient reminder systems, one-on-one education, decision aids, referrals by providers and organization of office staff to support a program of patient education, monitoring, outreach, and follow-up—should be implemented along with systems to ensure appropriate compliance and follow-up of positive results of CRC screening.[5,39]

In a recent randomized, controlled trial conducted at Kaiser Permanente Northwest, it was found that automated telephone calls increased completion of FOBT over the traditional approach of mailing reminders.[40] Public education should be continued to help the public understand the benefits of colorectal screening.[3]

Risk factor modification

Patients should be encouraged to stop smoking and increase their intake of dietary fiber and increase their physical activity. Although there is some evidence that postmenopausal hormone therapy, aspirin, or nonsteroidal antiinflammatory drugs can decrease the risk for CRC, the risks of long-term use of these drugs outweigh the benefits, even for persons with a family history of CRC.[41]

Conclusion

CRC is the second leading cause of death among North Americans of both sexes.[1-3] Screening rates for CRC have increased over the past decade but remain below appropriate levels.[2,5] Improvement must be made through physician and patient education, patient reminders, and the use of electronic medical records. Providers should incorporate family history for CRC such as through a screening algorithm (Fig. 2) more frequently in patient encounters, and they should be able to correctly categorize patients as average-risk or increased-risk to provide screening options that include risks and required frequency of testing. Screening for average-risk individuals should begin at age 50 and continue until age 75. African-American men should begin CRC screening at age 45. Individuals at increased risk should begin screening at age 40 or 10 years before the earliest age of diagnosis in a family member. Colonoscopy has been recognized as the preferred method for CRC screening in the United States, and with regular screening, more than 60% of deaths from CRC can be prevented.

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