include the following: eliminate mandates for direct physician note entry; provide alternatives, such as dictation, document scanning,9 and/or scribes10 for EMR note capture; make the EMR inbox smarter about when, and how, to present messages to PCPs; and train clinic support personnel to manage the same proportion of inbox messages they handled with paper systems and to think whether a message is important or just noise before pushing the so-convenient “Forward-to-PCP” button. If changes are not made to reduce or eliminate these time penalties on PCPs, there will be no PCPs left to penalize.

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Additional Information: Parties interested in obtaining the full survey instrument should contact the corresponding author.

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RESEARCH LETTERS
ONLINE FIRST

Young-Onset Colorectal Cancer: Is It Time to Pay Attention?

Is It Time to Pay Attention?

The 2010 Annual Report to the Nation on Cancer celebrated a steady decline in the incidence of colorectal cancer (CRC).1 This progress has been largely attributed to CRC screening, recommended for adults 50 years or older since 1996.2 In sharp contrast to overall trends, the incidence of CRC appears to be increasing among adults younger than 50 years,1,3 a group for whom average-risk screening is not routine. Particularly concerning is a trend toward advanced-stage CRCs,1,3 suggesting a potential role for increased clinical vigilance and more prompt evaluation of symptomatic patients. To raise clinical awareness and facilitate recognition, we undertook a cohort study to (1) examine incidence trends; (2) define the distinct clinicopathologic manifestations of young-onset CRC; and (3) identify risk factors for advanced-stage disease.

Methods. We used the National Cancer Database (NCDB), a hospital-based cancer registry sponsored by the American College of Surgeons and American Cancer Society that captures 70% of all incident cancers annually.4 We identified patients diagnosed as having invasive adenocarcinoma (behavior code 3 [malignant]; histology codes 8010, 8020-8022, 8140-8144, 8210-8211, 8260-8263, 8470-8473, 8480-8481, and 8490) of the colon and the rectum between January 1998 and December 2007, the most recent decade after the US Preventive Services Task Force (USPSTF) recommended CRC screening. Eligible patients (n=588 869) were stratified by tumor site (colon [site codes C180, 182-189, and 199] vs rectum [site code C209]) and by age at diagnosis (young onset [before age 50 years] vs later onset [at age 50 years or older]). Age-adjusted incidence rates (per 100,000 individuals) were calculated using the 2000 US standard population (SEER*Stat software, version 7.0.4; National Cancer Institute). The temporal trend in the annual percentage change (APC) was identified (Joinpoint Regression Program, version 3.5.1; National Cancer Institute). For a subgroup (n=34 781) of young-onset CRCs diagnosed between 2003 and 2007—the following years after the USPSTF strengthened its screening recommendation in 20025—independent predictors of advanced-stage disease (stages III and IV, nodal and distant metastatic disease) were identified by multiple logistic regression. This study was granted exemptation status by The University of Texas MD Anderson Cancer Center institutional review board.

Results. We identified 64,068 young-onset (10.9%) and 524 801 later-onset (89.1%) CRCs. Age-adjusted incidence declined for later-onset CRCs after 2001 (APC, –2.5%; 95% CI, –3.0% to –2.0%) but has consistently increased since 2001 for young-onset disease (APC, 2.1%; 95% CI, 1.1% to 3.1%). The increase was greater for...
young-onset rectal (APC, 3.9%; 95% CI, 3.1% to 4.7%) than colon (APC, 2.7%; 95% CI, 2.0% to 3.3%) cancers. The median age for young-onset CRCs was 44 years, with most (75.2%) occurring between ages 40 and 49 years. Compared with later-onset disease, young-onset CRCs were more prevalent among patients with nonwhite race/ethnicity (29.5% vs 17.6%; P < .001), who were not insured or insured by Medicaid (16.5% vs 4.7%; P < .001) and who lived in the southern and western parts of the United States (56.2% vs 50.3%; P < .001). Young-onset CRC more commonly arose from colon distal to the splenic flexure or the rectum (69.0% vs 57.7%; P < .001). Mucinous and signet-ring histologic subtype (12.6% vs 10.8%; P < .001) and poor or no differentiation (20.4% vs 18%; P < .001) were also more frequently exhibited. Advanced-stage disease was diagnosed significantly more commonly in young patients (Table). Independent risk factors for advanced-stage disease included younger age (age 30-39 years: hazard ratio [HR], 1.21; 95% CI, 1.1 to 1.4; age 18-29 years: HR, 1.4; 95% CI, 1.2 to 1.6; vs age 40-49 years); African American race (HR, 1.2; 95% CI, 1.1 to 1.3; vs white race) and lack of insurance or Medicaid insurance (uninsured: HR, 1.2; 95% CI, 1.1 to 1.3; Medicaid: HR, 1.6; 95% CI, 1.5 to 1.8; vs insured).

**Comment.** This cohort study of young-onset CRC, the largest to date, highlights an alarming rise in incidence since 2001. Most worrisome is the high proportion of stage III/IV disease (Figure), consistent with a prior smaller population-based report. In the absence of routine screening, contributing factors to these trends may include (1) a reluctance on the part of young adults to seek medical care; (2) the large percentage of young adults without insurance or ready access to care (18.3%-29.2% for adults aged 18-44 years vs 1.3%-13.6% for adults older than 45 years); and (3) an underappreciation of the increasing risk for young-onset CRC, leading clinicians to overlook or dismiss symptoms that are nonspecific but may be consistent with CRC (ie, rectal bleeding, abdominal pain or cramping, change in bowel pattern). Finally, the predilection of young-onset CRCs for the distal colon and rectum identify these as high-yield anatomic regions for endoscopic evaluation in symptomatic patients and as potentially cost-effective targets for screening programs in presymptomatic young adults.

This study could not establish the mechanisms underlying observed sociodemographic disparities, nor did it explore the molecular basis of young-onset CRC (familial adenomatous polyposis was excluded). Notwithstanding, these data argue for heightened awareness of these concerning trends in young-onset CRC. Symptomatic young patients should undergo timely sigmoidoscopy at a minimum, if not a full colonoscopy. Identifying high-risk cohorts for targeted screening should be a priority.

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**Online First**

**Supplemental Oxygen Therapy in Medical Emergencies: More Harm Than Benefit?**

In medical emergencies, such as acute coronary syndrome, cardiopulmonary resuscitation (CPR), stroke, and exacerbations of chronic obstructive pulmonary disease (COPD), supplemental oxygen is often routinely administered. Most physicians believe this intervention is potentially lifesaving, and many guidelines support the routine use of high-dose supplemental oxygen.

Over the decades, however, potential detrimental effects of supplemental oxygen appear to have been ignored. Many clinicians are unaware of the variety of preclinical studies that have been executed, showing that hyperoxia causes both coronary and systemic vasoconstriction, resulting in deterioration of several important (hemodynamic) parameters (Table). The prime candidate mechanism for these unintended effects is believed to be the formation of reactive oxygen species. In this Research Letter, we draw attention to the collective clinical evidence, which argues against the routine use of high-dose oxygen. Awaiting more thorough studies, we strongly recommend a policy of careful, titrated oxygen supplementation.

**Methods.** We conducted a search of the literature in MEDLINE and EMBASE to identify articles addressing the effect of oxygen therapy in acute coronary syndrome, cardiopulmonary resuscitation, stroke, and exacerbations of chronic obstructive pulmonary disease.

**Results.** Large (randomized) clinical studies addressing oxygen supplementation are scarce. In 1976, a double-blind randomized trial was performed in 200 patients with suspected acute myocardial infarction. In the supplemental oxygen group, 9 of 80 patients (11%) died, as opposed to 3 of 77 (3.9%) in patients breathing compressed air (relative risk [RR] of mortality, 2.9; 95% CI, 0.8-10.3). A recent Cochrane review combined this trial with a smaller similar one, which generated a composite RR of mortality of 3.03 (95% CI, 0.93-9.83). In acute decompensated heart failure, no clinical studies are available, despite the rather abundant evidence from preclinical studies, suggesting that such patients may experience the adverse effects caused by coronary and systemic vasoconstriction (Table).

In accordance with existing guidelines, supplemental oxygen is often administered during CPR. In the postresuscitation phase, evidence exists that 30% oxygen is more brain protective than pure oxygen. Recently, an observational study in 6326 patients showed that supplemental oxygen induced postresuscitation hypoxia was independently associated with increased mortality (odds ratio [OR], 1.8; 95% CI, 1.5-2.2). A subsequent analysis of the same cohort indicated that each 25-mm Hg increase in PaO₂ was associated with a sta-

| Table. Effects of Supplemental Oxygen in Different Clinical Conditions |
|-----------------------------|-------------------|-------------------|-------------------|
| **Clinical Condition**      | **Effect Parameter** | **Effect**        | **Reference**      |
| Exercise testing            | ECG alterations   | Prolonged         | JAMA. 1950;144:372-375 |
| Post myocardial infarction  | Heart rate        | Decreased         | Lancet. 1964;2(7364):825-832 |
|                            | Stroke volume     | Decreased         | Br Heart J. 1965;27:401-407 |
|                            | Cardiac output    | Decreased         | Br Med J. 1968;4(5627):360-364 |
|                            | Systemic vascular resistance | Increased | |
|                            | Mean arterial pressure | Increased | |
| Acute myocardial infarction | Vascular resistance of LAD | Increased | J Appl Physiol. 2007;102(5):2040-2045 |
|                            | Coronary blood flow | Decreased         | |
| Congestive heart failure    | Stroke volume     | Decreased         | J Am Coll Cardiol. 1996;27(2):353-357 |
|                            | Heart rate        | Decreased         | Am J Physiol Heart Circ Physiol. 2002;282(6):H2414-2421 |
|                            | Cardiac output    | Decreased         | Chest. 2001;120(2):467-473 |
|                            | Systemic vascular resistance | Increased | Heart. 2010;96(7):533-538 |
|                            | LV end diastolic pressure | Increased | |
|                            | Isovolumetric relaxation time | Increased | |
|                            | Mortality         | Increased         | BMJ. 2010;341:5462 |
| Stroke                      | Stroke severity score | Increased | Stroke. 2003;34(2):571-574 |
|                            | Mortality         | Increased         | Stroke. 1999;30(10):2033 – 2037 |
|                            | Mortality         | Increased         | JAMA. 2010;303(21):2165-2171 |
|                            |                   |                   | Circulation. 2011;123(23):2717-2722 |
|                            |                   |                   | Critical Care. 2011;15(2):R90 |

Abbreviations: COPD, chronic obstructive pulmonary disease; ECG, electrocardiogram; LAD, left anterior descending coronary artery; LV, left ventricular.

4 Trial was terminated (Clinical Trial of Normobaric Oxygen Therapy in Acute Ischemic Stroke, not published, clinicaltrials.gov Identifier: NCT00414726).