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Survival Comparison Between Sporadic, Familial Polyposis, and Nonpolyposis Colon Cancer

ABSTRACT & COMMENTARY

Source: Bertario L, et al. *Int J Cancer* 1999;80:183-187.

Colorectal cancer is projected to be diagnosed in 129,400 people in the United States this year and will be responsible for the deaths of about 56,600 people. It is estimated that about 10% of the cases of colorectal cancer occur in familial aggregations. The two hereditary forms of colorectal cancer that are best characterized are familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HNPCC), both autosomal dominant traits. A number of studies have suggested that the familial forms of colorectal cancer have a better natural history than sporadic colorectal cancer.[1-4] However, such studies may involve a selection bias.

In an effort to assess the natural history of FAP, HNPCC, and sporadic colon cancer, researchers at the National Cancer Institute of Milan examined 144 patients with HNPCC, 161 patients with FAP, and 2035 patients with sporadic colorectal cancer and compared their clinical characteristics and survival. Patients with hereditary cancers were significantly younger at diagnosis than those with sporadic cancers (FAP, 43 years; HNPCC, 49 years; sporadic, 60 years). Furthermore, 40% of those in the HNPCC group had right-sided tumors compared with 13% of the sporadic group and 14% of the FAP group. The stage distribution was not greatly different; Dukes A or B was n oted in 51% of the sporadic group, 48% of the FAP group, and 52% of the HNPCC group. The overall five-year survival was 57% for the HNPCC group, 54% for the FAP group, and 51% for the sporadic group. After adjustments for stage, age, location, and sex, there were no significant differences among the three groups.

COMMENTARY

HNPCC is related to a mutation in a DNA mismatch repair gene that leads to genetic instability in the colonic epithelium and an increased risk of colorectal cancer. FAP is a mutation in the adeno-

matous polyposis coli (APC) gene that leads to multiple adenomatous polyps, some of which undergo progression to invasive carcinoma. Both of these forms of hereditary cancer can be prevented with adequate efforts to screen families based upon the detection of an index case.

Suspicion of a familial pattern should be high in young patients and those with first degree relatives who also have colorectal cancer. In such a setting, screening asymptomatic family members can be life-saving.

It is important to note that similar benefits are noted in the general population not affected by genetic susceptibility through the screening of men and women age 50 years or older with fecal occult blood testing and colonoscopy every two years. ❖

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Which of the following statements is true about familial colon cancer?

a. Hereditary nonpolyposis colorectal cancer has a better natural history than sporadic colon cancer.
b. Hereditary nonpolyposis colorectal cancer has a better natural history than familial adenomatous polyposis.
c. Familial adenomatous polyposis has a better natural history than sporadic colon cancer.
d. Familial adenomatous polyposis has a better natural history than hereditary nonpolyposis colorectal cancer.
e. Sporadic colorectal cancer, familial adenomatous polyposis, and hereditary nonpolyposis colorectal cancer all have similar natural history.

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High-Dose Chemotherapy in Patients With Severe Autoimmune Disease

ABSTRACT & COMMENTARY

Synopsis: *High-dose cyclophosphamide (50 mg/kg for 4 consecutive days) without stem cell rescue was administered to eight patients with advanced autoimmune disease refractory to conventional approaches. Seven patients improved markedly, five achieved complete remission, and two achieved partial remission. Four of the patients remain in a sustained complete remission for 3-21 months of follow-up. The high-dose treatment was well-tolerated and there were no treatment-related deaths. The median times to a neutrophil count of 0.5 x 10^9 cells/L and platelet transfusion independence were 17 and 16 days, respectively. High-dose cyclophosphamide without stem cell rescue may be a useful clinical approach for selected patients with severe autoimmune disease.*

Source: Brodsky RA, et al. *Ann Intern Med* 1998; 129:1031-1035.

The management of severe autoimmune diseases remains a challenge. When standard approaches fail, clinicians are left with a variety of experimental approaches. Among these are low and high doses of agents more commonly used by oncologists, including antimetabolites and alkylating agents. In the current report, clinical investigators from Johns Hopkins and Hahnemann Universities treated eight patients with severe, refractory autoimmune disease with high-dose cyclophosphamide (50 mg/kg for 4 days), without stem cell rescue. All of the patients tolerated the therapy well without nonhematological life-threatening toxicity. Cytopenias occurred in all patients but there were no treatment-related deaths. Patients received G-CSF (5 mcg/kg) six days after the last dose of cyclophos-

phamide and daily until the white blood count reached 10^9 cells/L. The median time to resolution of neutropenia was 17 days and the median time that platelet transfusions were required was 16 days.

Five patients achieved complete remissions from their severe autoimmune disease and four of these remained in remission for 3-21 months at time of publication. Two patients achieved durable partial remissions, continuing to improve at 14 and 19 months of follow-up. Thus, Brodsky and colleagues suggest that high-dose cyclophosphamide (without stem cell rescue) might become a useful clinical approach for patients with refractory autoimmune diseases.

COMMENTARY

Treatment of refractory autoimmune disease remains problematic. In laboratory animals with experimental autoimmune disease, high-dose chemotherapy followed by syngeneic bone marrow transplantation has been shown to be highly effective.[1,2] However, high-dose therapy followed by autologous transplant in selected patients with advanced autoimmune disease has not been uniformly successful.[3,4] When high-dose therapy has failed, it has been speculated that relapses have occurred due to the failure of the high-dose therapy to eradicate the autoaggressive population of lymphocytes, the reinfusion of the autoaggressive lymphocytes with the autograft, or the reinitiation of the disease because of persistent challenge from the autoantigen.[3,4]

The last of these three hypotheses is difficult to address experimentally; however, therapy can be intensified and can be given without reinfusion of autologous hematopoietic cells. If such an approach were successful, one would be less concerned about antigen persistenct. Brodsky et al have shown that the great majority of patients with aplastic anemia achieve a sustained and gratifying response (complete remission) after high-dose cyclophosphamide treatment without stem cell reconstitution.[5] The success of this approach bodes well for the application of the technique to autoimmune disease because the pathogenesis of aplastic anemia in as many as 80% of adults with this disorder involves autoimmune mechanisms with marrow stem cells as targets.[6]

Brodsky et al point out that hematopoietic stem cells express high levels of aldehyde dehydrogenase, an enzyme responsible for cellular resistance to cyclophosphamide.[7] A theoretical rationale exists for the use of cyclophosphamide based upon a presumed favorable therapeutic index, with marrow stem cells resistant, but autoimmune lymphocytes sensitive to this drug.

In this preliminary report, it is difficult not to get excited about the findings. All eight patients had advanced and debilitating diseases (rheumatoid arthritis, lupus erythematosus, chronic inflammatory demyelinating polyneuropathy, severe hemolytic anemia, Evan's syndrome, and immune thrombocytopenia). All had been refractory to standard approaches, and all but one had a gratifying response to the high-dose chemotherapy. Clearly, this approach warrants additional investigation.

Certainly, any successful treatment of patients with these difficult and complex refractory autoimmune diseases will be met with great enthusiasm. However, some rheumatologists may not be fully apprised of the great risks associated with high-dose chemotherapy, with or without stem cell rescue, and others may be overly concerned about the potential toxicities. The decades of experience of the bone marrow transplanters who discovered and developed preventive approaches and treatments for toxicities from cyclophosphamide or similar drugs represent one of the triumphs of modern oncology and need not be repeated. In fact, rheumatologists and oncologists might best work together on these patients when further trials are conducted to confirm the impressive efficacy suggested in this preliminary report. ❖

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Which of the following statements about the use of high-dose cyclophosphamide (50 mg/kg for 4 consecutive days) for the treatment of patients with severe autoimmune disease is true?

a. Such an approach has been shown in a preliminary series to produce gratifying and sustained clinical responses.
b. Such an approach, when followed by stem cell rescue, has been shown to produce gratifying and sustained clinical responses.
c. Such an approach was found to be overly toxic for patients without malignant disease.
d. Such an approach was found to be well-tolerated but to have insufficient clinical response to warrant further investigation.
e. Such an approach cannot produce long-term disease control because of the persistence of the inciting autoantigen.

Loculated Pleural Effusions: Can Intrapleural Streptokinase Help?

Synopsis: *Streptokinase appears to improve the resolution of loculated pleural effusions when chest tube drainage fails to achieve symptomatic relief.*

Source: Davies CWH, et al. *Chest* 1999;115:729-733.

Malignant pleural effusion is a frequent complication of some common cancers. It is estimated that symptomatic pleural effusions affect more than 100,000 patients each year.[1] Drainage of the pleural fluid by thoracentesis or by chest tube is highly effective at relieving the dyspnea associated with pleural effusions. However, a substantial fraction of patients do not respond completely to the usual treatment measures because the pleural fluid collections are loculated and do not drain to the most dependent portions of the pleural cavity where therapeutic measures are directed. Pathologically, the usual structural basis for the loculations is the formation of fibrin strands that produce localized adhesions in the pleural cavity. These adhesions can be lysed by the blind passage of a rigid tube between the lung and pleural surface (a procedure that can be painful and can produce lung damage and pneumothoraces) or by thoracoscopic procedures that permit direct visualization of the fibrin sheets.

Loculated pleural effusions also occur in some infectious diseases. In the setting of infection, a randomized controlled trial demonstrated that intrapleural administration of streptokinase was able to improve pleural drainage.[2] However, streptokinase instillation has not been carefully studied in patients with cancer and at least one editorialist has expressed concerns that the use of the agent in patients with cancer might stimulate widespread fibrinolysis and hemorrhage.[3] No data support that fear, but the question has not been carefully studied.

Davies and colleagues treated 10 consecutive patients (aged 39-89 years) with loculated malignant pleural effusions with twice-daily intrapleural injections of streptokinase when a standard chest tube drainage had failed to drain the effusions. The dose of each injection was 250,000 International units. Based on improvements in the chest radiograph, amount of fluid drained, and symptom relief, all 10 patients responded to 500,000 to 1,500,000 International units of intrapleural streptokinase. Before administration of streptokinase, chest tube drainage averaged 843 +/- 690 mL; after streptokinase administration, 2368 +/- 1051 mL of fluid drained ($P < 0.001$). Treated patients survived from 1-15+ months after drainage; one patient died from sepsis unrelated to the procedure at one month. One patient had pain with the first instillation of streptokinase, but not with subsequent instillations. No allergic complications or hemorrhages were seen.

COMMENTARY

When chest tube drainage fails to achieve symptomatic relief in a patient with a pleural effusion and repeat chest radiograph demonstrates persistent fluid not being drained by the chest tube, it is reasonable to dissolve 250,000 International units of streptokinase in 30 mL of normal saline, instill it into the chest tube, clamp the chest tube for two hours, and then open the tube to drainage. When this maneuver is undertaken twice a day, remarkable improvements in chest tube drainage, chest radiograph appearance, and symptoms seem to be the usual outcome. The fear that stimulation of fibrinolysis in the pleural cavity might lead to systemic fibrinolysis and spontaneous hemorrhage was not confirmed in controlled studies of patients with infectious effusions, and did not appear to be any more likely in patients with cancer.

Although this paper reports a small retrospective analysis of a consecutive series of patients rather than a large prospective randomized trial, the results are impressive. Unless efforts to repeat the results in other centers turn up some unexpected toxicities or a poor success rate, controlled trials seem out of place. Streptokinase is an adjunctive therapy that appears to work well and it should be used to relieve symptoms from loculated pleural effusions. ❖

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A 67-year-old man with stage IV lung cancer presents with dyspnea and a large right pleural effusion. After two days of chest tube drainage, symptoms have not improved and repeat chest radiograph shows persistent loculated fluid in the upper lung fields. Which of the following approaches has recently been shown to be effective in this setting?

a. Using ultrasound guidance, insert a thoracentesis needle into the largest fluid-filled space.
b. Using a flexible bronchoscope, lyse adhesions under direct visualization.
c. Administer 250,000 International units of streptokinase into the chest tube twice daily.
d. Administer 150 mg tissue plasminogen activator into the chest tube twice daily.
e. Break down adhesions by replacing the chest tube with a rigid tube and blindly lyse the adhesions.

Assessing Prognosis by Magnetic Resonance Imaging in Patients With Myelodysplastic Syndromes

ABSTRACT & COMMENTARY

Synopsis: *Myelodysplastic syndromes (MDS) are a heterogeneous group of bone marrow disorders that have a full spectrum of clinical aggressiveness. A classification system has been developed that provides valuable prognostic information. Magnetic resonance imaging (MRI) of the femur in patients with MDS revealed five different patterns (fatty, faint, nodular, scattered, or uniform) and these correlated well with clinical outcomes, including the development of leukemia and survival. Scattered or uniform MRI patterns indicated advanced disease, with an increased number of myeloblasts and greater cytogenetic abnormalities.*

Source: Tokagi S, et al. *J Clin Oncol* 1999;17:277-383.

Myelodysplastic syndromes are a group of bone marrow disorders characterized by ineffective hematopoiesis. Although there is substantial heterogeneity, hematopathologists attempt to characterize the observed bone marrow morphology using the French-American-British (FAB) classification system.[1] Patients with refractory anemia (RA) or refractory anemia with ring sideroblasts (RARS) typically have a favorable prognosis, while those with refractory anemia and excess myeloblasts (RAEB) or RAEB in transformation (RAEB-T) have an unfavorable prognosis, often progressing to acute leukemia. A large number of factors other than FAB classification can be used to assess prognosis including age, sex, hemoglobin concentration, WBC, neutrophil count, platelet count, percentage of blasts in the blood or marrow, cytogenetic changes, and DNA ploidy.[2,3] In this report, an additional prognostic measure is considered.

Magnetic resonance imaging (MRI) of the femur (femoral marrow) was undertaken in 42 consecutive patients with newly diagnosed MDS and results were correlated with patterns of disease progression and survival. Five patterns of femoral marrow were described. These were: 1) "fatty," showing a low-signal intensity marrow that appeared dark on short T1 inversion recovery technique (STIR) but bright on T1-weighted spin echo (SE) images; 2) "faint," showing an abnormally faint signal intensity in the fatty-signal-density marrow; 3) "nodular," showing low signal marrow density with small nodules of a higher intensity on STIR images; 4) "scattered," showing multiple scattered areas of higher signal intensity in the low signal intensity marrow on STIR images; and, 5) "uniform," a uniform high-signal intensity marrow as compared with the low-signal intensity muscles on STIR images. Serial MRI scans revealed that the pattern changed from fatty, faint or nodular to scattered or uniform as the disease progressed.

In this series of 42 patients, leukemia developed in 13. In all 13, the MRI pattern was either scattered or uniform. In all, there were 13 patients (31%) with fatty, faint or nodular patterns and these patients all had either RA or RARS. None of these patients developed leukemia, and survival was excellent. In contrast, of the 29 (69%) who had femoral marrow with scattered or uniform MRI patterns, 11 had RAEB-T, six had RAEB, three had CMML, six had RA and three had RARS. Patients with scattered or uniform MRI patterns were more likely to have unfavorable cytogenetics (7 of 29 vs 0 of 13), leukemia (13 of 29 vs 0 of 13) and death (22 of 29 vs 2 of 13). The nonleukemic deaths in this group were primarily from hemorrhage or infection.

The overall survival of the 29 patients with scattered or uniform MRI patterns was significantly shorter than survival of the 13 patients with fatty, faint, or nodular MRI patterns (7-year survival 10.7% vs 73%, respectively, $P < 0.01$). Tokagi and colleagues have suggested that magnetic resonance images of the femoral marrow can provide valuable information for assessing the prognosis and determining the most appropriate management of patients with MDS.

COMMENTARY

MDS are a heterogeneous group of disorders which result in cytopenias and their well-characterized clinical consequences. Approximately one-third of patients with MDS progress to a disorder that resembles acute myelogenous leukemia. However, leukemia that has developed in patients with antecedent MDS is more difficult to treat and less frequently goes into complete remission when compared to de novo ANLL. The FAB classification system has provided useful prognostic information based upon bone marrow characteristics. Thus, the presence of dysplastic features, the involvement of more than one cell lineage, and the presence of increased numbers of myeloblasts characterize the more malignant variants of MDS (RAEB, RAEB-T).[1] Other features, such as the presence of karyotypic abnormalitites and patient age, also seem to be important.[3] The International Prognostic Scoring System[3] involves assessment of

the percent of marrow myeloblasts, the number of cytopenias, and a grading of the cytogenetic abnormalities: normal karyotype, Y chromosome deletion, del(5q) alone, and del (20q) alone are good, the presence of three or more abnormalities and any lesions involving chromosome 7 are bad, and any other abnormalities are intermediate in prognosis. Based upon these characteristics, four prognostic groups were determined. Thirty-one percent of patients fall into the low-risk category; median survival of this group is 5.7 years. Thirty-nine percent of patients fall into the first intermediate risk category; median survival is 3.5 years. Twenty-two percent of patients fall into the second intermediate risk category; median survival is 1.2 years. Eight percent of patients are in the high-risk category; median survival is 0.4 years.

Now there is another tool to assist in the assessment of risk for MDS patients. MRI scans of the femur may become routine testing for such patients. Patients whose femoral marrow demonstrated a scattered or uniform MRI pattern had a significantly more advanced disease ($P < 0.0001$) and a significantly higher percentage of blasts in the bone marrow ($P < 0.0013$) than patients whose femoral marrow had a faint, fatty, or nodular pattern. When the International Prognostic Scoring System[3] was applied to the same patients, those with the fatty, faint, or nodular pattern fell into either low or intermediate-1 risk, whereas those with a scattered or uniform pattern fell into either intermediate-2 or high risk, indicative of a much greater likelihood for developing leukemia.

It is interesting that the femur turns out to be the skeletal site of choice for this determination. Femoral marrow is typically fatty and has little hematopoietic tissue. Other sites, such as the spine, are rich in "red marrow" and more quickly become involved in leukemic processes.[4] It is suggested that changes in the femoral marrow occur more gradually and lead to MR images of greater variety. Studies that evaluated the vertebral marrow of MDS patients have shown no relationship of pattern to risk (number of blasts, FAB subtype, or severity of pancytopenia).[5,6] In this study of the femoral marrow, the MRI was successful in distinguishing these high-risk groups.

Skeptics might question the clinical value of the MRI, since the results did not really further define the risk groups when the more conventional parameters were available. For example, in this series, no additional information was provided beyond the demographic, marrow and cytogenetic findings that were already available. Yet, the MRI may indeed serve a useful role. Serial evaluations of patients with MDS might provide information to the clinician about disease stability or progression. If a shift in pattern to the scattered or uniform variant occurs, this may warrant therapeutic intervention, perhaps with investigational approaches. ❖

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The use of the MRI scan of the femur may be a useful clinical tool in the evaluation and treatment of myelodysplastic syndromes because:

a. the MRI images of the femur detect bone marrow microenvironmental changes that precede other markers of disease progression (such as cytogenetic changes or increasing blasts in the marrow).
b. the MRI images of the femur correlate with other prognostic indicators (such as cytogenetic changes or increasing blasts in the marrow) and thus might be a useful surrogate to these other tests in following the course of MDS.
c. the MRI images are predictive of response to chemotherapeutic agents.
d. the MRI images are predictive of response to trophic factors such as erythropoietin.
e. MRI images of the vertebral marrow are more informative than MRI images of femur marrow.

Worst: Or, Choosing the Wrong Recipe and Not Following One

By Thomas J. Smith, MD, FACP

In my referral practice, i see a lot of people for second opinions. As a consequence, I have the opportunity to review many records, and recently have been troubled by less than optimal care. In each of the cases below, the choice of drug treatment and/or subsequent modification seemed to be less than optimal practice.

In my role as chair of the American Society of Clinical Oncology (ASCO) Health Service Research Committee, I was regularly taken to task for advocating "cookbook medicine." From what I see, some of us do terrific jobs of keeping up and providing state-of-the- art compassionate care. I am not so certain about others.

In reviewing the quality of cancer care in the United States for the Institute of Medicine, colleague Bruce Hillner and I found some striking evidence for better outcomes associated with higher volume or specialized care for Hodgkin's disease, testicular cancer, breast cancer, and some others. This information will be available on the Institute of Medicine Website on April 6.

Please review the cases below, and tell me what you would do. (I have changed some of the details to make identity more difficult.)

- How would you communicate back to the primary oncologist?
- What would be a reasonable approach to improving that oncologist's practice?
- Do either of these cases breach the standard of care?

Case 1: A 25-year-old man is referred to you for treatment of recurrent Hodgkin's disease about a year after finishing his first treatment. At diagnosis in 1997, he received six cycles of COPP (cyclophosphamide, vincristine, prednisone, and procarbazine) then radiation. He has a recurrence in the lung/adjacent lymph nodes within the radiation field. Your concerns include:

1. You find, after conferring with the Hodgkin's disease expert, that the last publication on COPP was in 1975. It was judged to be no better than mechlorethamine, oncovin, procarbazine, and prednisone (MOPP) or CVPP, so never became mainstream practice. Was MOPP or its lesser cousin the-first choice of treatment for Stage IIA Hodgkin's disease in 1996?
2. When you calculate the dose of his prior treatment, you find that he only got about 50% of planned doses due to dose capping to whole vials, seemingly arbitrary dose modifications, etc. He never had febrile neutropenia. The dose modifications for COPP are not readily available to cross-check.
3. You also note, after talking to the family, that no mention was made before treatment of the possibility of sperm banking or sterility caused by the drugs.
4. The first oncologist was preparing to treat the lung nodule with "salvage" chemotherapy without a tissue diagnosis.
5. And give Bleomycin to a person who had received mantle radiation without checking pulmonary function tests.

Case 2: A 61-year-old woman is referred to you for recurrent breast cancer in the lung. She had a 7 cm, 5/8 node positive, Grade III, ER- and PR-negative cancer two years prior. She had a mastectomy, then six cycles of CMF. Your concerns include:

1. When you calculate her dose-intensity, you find that due to dose-capping to whole vials, and seemingly arbitrary dose modification, she received only 40-56% of the planned doses. Had the doctor used NSABP guidelines, she would have received 83% of each drug, and would have finished weeks earlier, here is cycle 3, day 1. (*See Table.*)
2. She was put on tamoxifen even though ER and PR negative. At recurrence, tamoxifen was stopped and megestrol acetate was started, for "weight loss."
3. She also has three first-degree relatives with breast cancer, some as young as age 33, and no one had documented consideration of genetic counseling or plans to ensure that she informed her relatives of increased risk of cancer.

Table

Case 2: Cycle 3, Day 1

	NSABP (mg)	Received (mg)	NSABP Total over 6 cycles	Received Total over 6 cycles
WBC	4700			
C	150/175 mix	100 x 14 days	83%	56%
M	62	35	83%	56%
F	936	375	83%	40%

How would you communicate with the primary oncologist?

In each case, the family had independently sought a second opinion, and the primary oncologist was not a

frequent referrer of patients to your practice. That makes it easy! Don't send anything back at all! No, that doesn't seem right.

I don't know what the etiquette is here, but if I were the first doctor, I would be angry if my patient saw someone else and I did not get a copy of the consultation. So, I would argue to send a full report.

What would be a reasonable approach to improving that oncologist's practice?

That is, if you agree that COPP is not the best treatment for a 25-year-old man who might reasonably want to preserve fertility and maximize chance of cure, and that dose-modification without good reason compromises CMF efficacy.

The options would be to:

1. Call the oncologist and discuss the case directly (maybe there was some unwritten, undiscussed reason for those choices and modifications).
2. Call your risk management team first to make sure you do not run afoul of any litigation risk.
3. Tell the patient and family that their survival may have been compromised by dose modification and suboptimal regimen choice.
4. Call the state board of medicine and issue an anonymous complaint.
5. Do nothing.

What would be the right approach? What would you do?

Does either of these cases breach the standard of care?

Sorry, but I don't want to discuss this. But, oncologists have nearly come to blows over a few people per 100 comparing MOPP/ABV to adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD). Should we not care if a regimen with less success is chosen, then modified?

Is cookbook medicine the answer?

I got tired of being skewered for suggesting standardization of what we do, but these appear to be a couple of clear cut cases for cookbook medicine. And following the recipe. Some would say it is a good case for weeding out some of the less-than-optimal practitioners. If someone does not do CMF by the book, how are they at palliative care?

Neither of the above cases are that difficult, at least in terms of describing some optimal therapy. Here is one simple way of maintaining optimal care for a practice:

1. Decide on one "best" treatment for each of the 20 most common oncology situations.
2. Update it each year by comparing it to the NCI's state-of-the-art treatment programs. They are not meant to be proscriptive or prescriptive, but offer the latest evidence. COPP is not listed.
3. Write down all the standard dose modifications for the 20 regimens chosen, from the original article or research protocol. No one can remember them all; if you improvise, you potentially compromise care.
4. Pick two charts per disease each year for "auditing" and see how the actual practice went. This two-chart audit is behind much of the Institute for Healthcare Improvement simple strategy for making care better.
5. Make your colleagues accountable for following the programs. (Where were the partners of the first Hodgkin disease oncologist when this was happening? She did not practice alone.) Education alone—"Well, we have the right antibiotics for febrile neutropenia 66% of the time. Here is what we did, without any names attached." This works well with no need for punishment.

I would predict that the whole "quality" movement will heat up this year. There is more and more evidence that some practice groups have better outcomes than others, often related simply to higher volume and experience. We should distill what makes for the best outcomes and practice in that way. To do anything less—to give a patient a 5% or 10% less chance of cure by choosing the familiar rather than the optimal—is simply not medically justifiable. ❖

Readers are Invited

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